Activity 72572 Design Proposal (updated) – Operational pilot of *Wolbachia* technology to reduce the transmission of *Aedes aegypti* borne diseases in the Asia-Pacific region

29 November 2018

A. Executive Summary

In April, 2016, the World Mosquito Program (WMP) at Monash University, formerly known as the Eliminate Dengue Program, submitted a proposal to the Australian Government through InnovationXChange (iXc) within the Department of Foreign Affairs and Trade (DFAT) to undertake two implementations of the WMP *Wolbachia* method in key high-risk settings in the Asia-Pacific region. The first implementation was to involve a large-scale deployment in Indonesia (*Bali Implementation*), and the second to involve deployment in one-two Pacific country settings (*Pacific Implementation*). The proposal was successful and WMP began the project on 4 May 2016. There have been a number of developments since the project began:

- the scope of the Pacific Implementation was increased to three countries;
- following extensive engagement with Indonesian stakeholders it became clear that the Indonesian government was not going to support expansion of the existing WMP activity in Yogyakarta to Bali until the project in Yogyakarta was completed and evaluated. In response to the Indonesia development, and after discussion with DFAT, we decided to reserve funding for a future expansion in Indonesia once the government was ready to approve it. Existing funding was approved for activities in two-three new projects in neighbouring countries in the Asian region from a list that included Sri Lanka, Cambodia, Myanmar and the Philippines;
- inclusion of an independent monitoring and evaluation activity, and
- inclusion of a heath economic study.

At the request of iXc, this document updates our original proposal to capture the changes to the project since it began. This revised proposal covers project activities for the period 31 January 2018 to 31 December 2020, representing an extension to the end date of the grant from June 2019 to December 2020.

Under this revised proposal, WMP will undertake the following activities:

1. **Pacific** – continue existing implementations in three country settings, Fiji, Vanuatu and Kiribati, this is a change from our original proposal of one-two Pacific countries;
2. **South and Southeast Asia** – using a portion of the grant funds that were to be used for the Bali Implementation, undertake implementations in Sri Lanka and in another two countries out of three that have been selected for scoping – Cambodia, Myanmar and The Philippines.
3. **Indonesia** – scoping and design activities for a national roll-out strategy for Indonesia following the completion of the WMP randomised control trial (Applying Wolbachia to Eliminate Dengue, ClinicalTrials.gov: NCT03055585) that is currently underway in Yogyakarta and funded by the

Yayasan Tahija Foundation. Expansion of the current deployment activities in Indonesia subject to the approval and support of the Indonesian government.

At the conclusion of the activities under this revised proposal, it is expected that WMP will have *Wolbachia* implementations completed or underway in up to six countries across the Western Pacific and South and Southeast Asia (S&SEA).

4. **Independent Monitoring & Evaluation** – a competitive tender process will be run to select an independent expert to undertake an assessment of the effectiveness of the deployments in the three Pacific sites.

5. **Health Economic Study**- a health economic study will be undertaken using Fiji and Vanuatu as case studies. This study will provide a forecast measure of the cost effectiveness of the *Wolbachia* method for disease control under independent modelling-derived estimates of efficacy. This study will build on other cost-effectiveness studies already underway with funding from the Bill & Melinda Gates Foundation for Indonesia, Brazil and Colombia.

A1. Development and end-of-investment outcomes envisaged

Each implementation activity will consist of three phases covering scoping, preparation and deployment, and monitoring activities. The major outcomes will be to establish local support and obtain regulatory approval for the WMP *Wolbachia* method; establish high levels of *Wolbachia*-carrying mosquitoes in deployment areas using a delivery model that is cost-effective and site-specific and data sharing with government partners of mosquito-borne disease surveillance data to enable assessment of the impact of our intervention on dengue and other arboviruses. Achievement of these outcomes will ease the burden on public health care budgetary constraints and offer an affordable and self-sustaining solution to reducing the risk of disease caused by *Aedes aegypti* mosquitoes.

A2. Recommended delivery approach and key partnerships

The WMP collaborates closely with local partners to build their capacity to adapt and sustainably implement the *Wolbachia* method in each project area. Our Program forms partnerships with local entities including government health departments, academic institutions, NGOs, and community-based groups, which may support certain project activities. We undertake extensive community and stakeholder engagement in order to build awareness and support for the use of *Wolbachia* mosquitoes as a method of disease control. No *Wolbachia* mosquito deployment is undertaken in a project site before regulatory approval is obtained and broad public acceptance of the intervention has been established.

B. Analysis and Strategic Context

Dengue is an enormous economic and public health burden for affected countries, averaging an estimated $2.1 billion per year in the Americas (Shepard *et al*, 2011) and almost $1 billion per year in SE Asia (Shepard *et al*, 2013). At the household level, dengue is among the infectious diseases that can cause unexpected catastrophic medical costs for families living in low-income countries (Beatty *et al*, 2011). Indirect costs, such as those related to loss of education and productivity, add substantially to direct healthcare costs (Undurraga, 2015). In addition, other *Aedes aegypti* mosquito transmitted diseases such as chikungunya and Zika afflict the same regions as dengue. Although not usually lethal, chikungunya disease is crippling and can take a heavy toll on individuals, families, communities and even national economies. In 2016, outbreaks of Zika virus in South America saw the WHO declare Zika an international public health emergency due to the concern of it causing birth defects and the potential of the virus to spread swiftly. There is no specific treatment for these diseases and only one licensed vaccine against dengue, however safety concerns have meant that this vaccine is not being used programmatically in any dengue endemic country. Research on other vaccines, as well as therapeutic

drugs, is ongoing. It is important to note that even if a successful vaccine is developed, this will not preclude the need for improved vector control as modelling indicates that these two control methods would be highly complementary.

Existing public health efforts to control transmission of these diseases aim to reduce the population size of the *Aedes aegypti* mosquito by eliminating breeding sites or using insecticides to kill the adult mosquitoes. However, these efforts have failed to prevent the spread of *Aedes aegypti* (Kraemer *et al*, 2015). Costs of vector control programs can comprise a major portion of annual health program expenditures (e.g. Barreto *et al*, 2011; Undurraga, 2015). With a few exceptions, the implementation of vector control methods has not been sustainable and therefore has been largely ineffective at reducing the burden of arboviral diseases (Morrison *et al*, 2008).

New tools for prevention of these diseases are urgently needed. WHO (2015) has stated that innovations in vector control deserve more attention as they can play a key role in reducing disease transmission. In this context, the WHO has recommended that countries consider undertaking pilot implementations of the WMP *Wolbachia* method (WHO 2016).

B.1 The World Mosquito Program approach – The *Wolbachia* method

The WMP *Wolbachia* method is not a conventional infectious disease prevention intervention. Unlike continued programs for delivery of vaccines and other therapeutics requiring cold chains for supply, the WMP method represents a paradigm shift in how to control these diseases by utilising *Wolbachia*, a naturally occurring bacteria that is present in many insects, but not the *Aedes aegypti* mosquito. The WMP research has shown that the presence of *Wolbachia* bacteria in *Aedes aegypti* mosquitoes reduces their ability to transmit viruses including dengue, chikungunya, and Zika. Since this discovery, WMP has developed a way to introduce *Wolbachia* into wild mosquito populations in order to reduce the transmission of disease. This Australian-led research is the first of its kind in the world and could potentially benefit an estimated 2.5 billion people currently living in dengue transmission areas worldwide.

The approach works by seeding wild mosquito populations with *Wolbachia* through controlled deployment of relatively small numbers of *Wolbachia* infected mosquitoes (Figure 1). These mosquitoes then breed with local mosquitoes and the *Wolbachia* is passed on to the mosquitoes in the local area. Over several months, the frequency of *Wolbachia* in the local mosquito population increases, until such time as the majority of mosquitoes in the area carry *Wolbachia*.

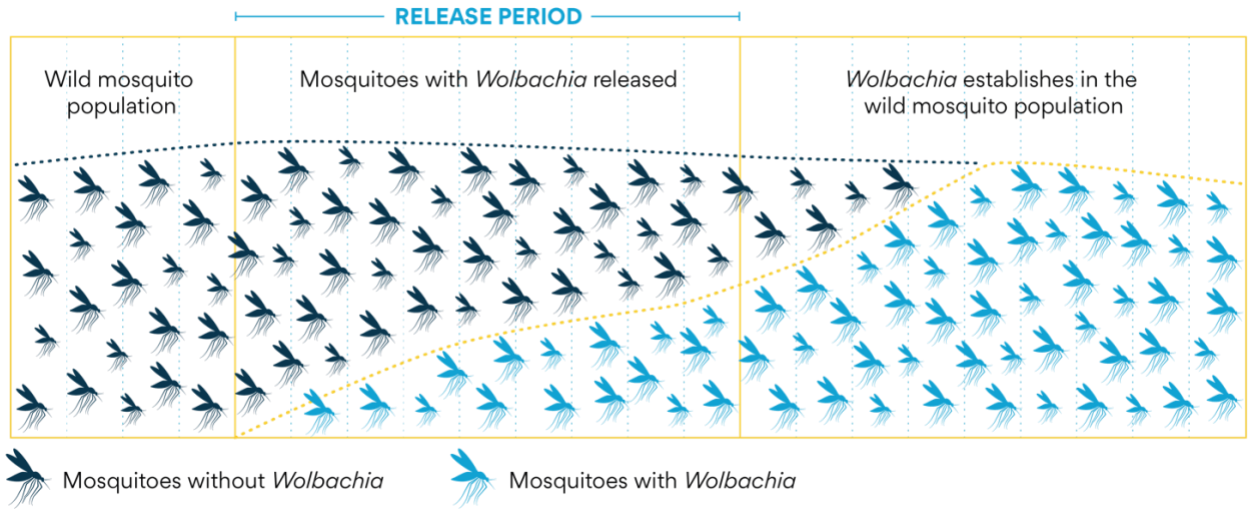


Figure 1: The *Wolbachia* biocontrol method. *Aedes aegypti* mosquitoes with *Wolbachia* (blue) are deployed into the wild mosquito population (black). Over a series of deployments, the percentage of

Wolbachia mosquitoes increases. Once a threshold frequency of *Wolbachia* mosquitoes is exceeded, *Wolbachia* will continue to spread after deployments have finished until the majority of mosquitoes carry *Wolbachia*. The *Wolbachia*-infected mosquito population has a significantly reduced ability to transmit dengue, Zika and chikungunya viruses.

Based on current WMP *Wolbachia* deployments in existing project sites, repeated release of *Wolbachia* mosquitoes over several months results in *Wolbachia* prevalence in the mosquito population typically climbing to more than 80% within six-nine months of the deployment starting, and then being maintained at levels generally above 90% thereafter. Compared with conventional insecticide-based or genetic population suppression control methods that may provide limited, short-term reductions in the mosquito population, once *Wolbachia* is established in the local mosquito population, it persists without the need for continual reapplication or additional insecticide-based control methods. In addition, the *Wolbachia* method does not require any long term particular behaviour change from community members in order to implement successfully and is compatible with existing vector control approaches currently being used worldwide.

In March 2016, WHO convened a Vector Control Advisory Group (VCAG) to review both new and existing vector control tools for use as part of the response to the Zika virus outbreak. The WHO reviewed the available evidence showing that *Wolbachia* reduces the ability of *Aedes aegypti* mosquitoes to transmit dengue, chikungunya and Zika viruses and field data showing long-term establishment of *Wolbachia* in mosquito populations under a range of environmental settings, and concluded that affected countries should consider undertaking pilot deployments of the method (WHO 2016). In April 2016, the Pan American Health Organization (PAHO), the regional office for the WHO in the Americas, announced that it would provide technical support for pilot deployment of new vector control tools, including *Wolbachia*, in member countries throughout the region (PAHO 2016).

B.2 Current World Mosquito Program project sites

The WMP project sites are currently operating in Australia, Vietnam, Indonesia, Brazil, Colombia, India, Kiribati, Fiji, Vanuatu, Sri Lanka, New Caledonia and Mexico (Figure 2). Across these countries, deployment of *Wolbachia* mosquitoes has been undertaken in over 40 sites, including city-wide deployments across the northern Australian city of Townsville; Medellin and Belo, Colombia; and Rio de Janeiro and Niteroi, Brazil. The WMP has gained regulatory approval to deploy *Wolbachia* mosquitoes at all locations, and through extensive community engagement and communication has established strong support and participation from local communities and stakeholders.

Our Program collaborates with key international partners to provide the scientific capability for development and deployment of the *Wolbachia* method for arboviral disease control. Field sites operate independently but sit under a common scientific program umbrella allowing technology and knowledge transfer across projects and the most rapid possible advancement of the initiative.

Figure 2: Current WMP project sites.

B.3 Dengue in the Asia-Pacific

Dengue represents a substantial health burden on the population in the Asia-Pacific, constituting one of the leading causes of hospitalization of children in SE&SEA and indirectly causing additional costs due to loss of carer productivity. Insecticide resistance in the mosquito population coupled with an inadequately resourced public health sector and limited laboratory diagnostic capacity has enabled dengue to become endemic in most countries in the region. Dengue is not only a significant public health problem in the Asia-Pacific region, but also represents a considerable financial cost, especially in those countries that are among the world's poorest. Affected countries in the region shoulder an estimated 70% of the global dengue burden. In addition to direct effects on human health and wellbeing, recent research estimates the cost of dengue in SE&SEA and the Pacific at over US$200 million annually (Shepard *et al* 2016). This calculation includes direct and indirect costs of medical treatment as well as deaths resulting from dengue, however does not take into account the economic impact of disease outbreaks on carer productivity and private sector industries such as tourism, from which many people in the region earn their livelihoods. Countries in the Asia-Pacific vary in their preparedness for outbreaks, and in their capacity to respond or allocate financial resources for the prevention and control of mosquito-borne disease.

In recent years there have been significant outbreaks of other arboviruses such as chikungunya and the Zika virus. Existing methods to control *Aedes aegypti* mosquitoes, the primary vector of dengue, Zika and chikungunya viruses, have generally failed to halt the seasonal or episodic outbreaks that occur throughout the Asia-Pacific region.

C. Investment description

C.1 Logic and Expected outcomes

Our revised proposal still aims to reduce the risk of local transmission of disease by *Aedes aegypti* mosquitoes through deployment of the *Wolbachia* method and also seeks to measure the cost effectiveness of the *Wolbachia* method. Our current projects show that successful deployment relies on achieving three primary outcomes described below, which can be achieved based on the logic model (Figure 3):

1. Establishment of support for the use of the *Wolbachia* control method, with approval from regulatory bodies, local authorities, and communities in deployment areas;
2. Establishment of high levels of *Wolbachia*-carrying mosquitoes in deployment areas; and
3. Surveillance of mosquito-borne disease in deployment areas in order to assess the effect of the intervention on local transmission of dengue and other arboviruses compared to the historical period and where possible, to neighbouring untreated communities.

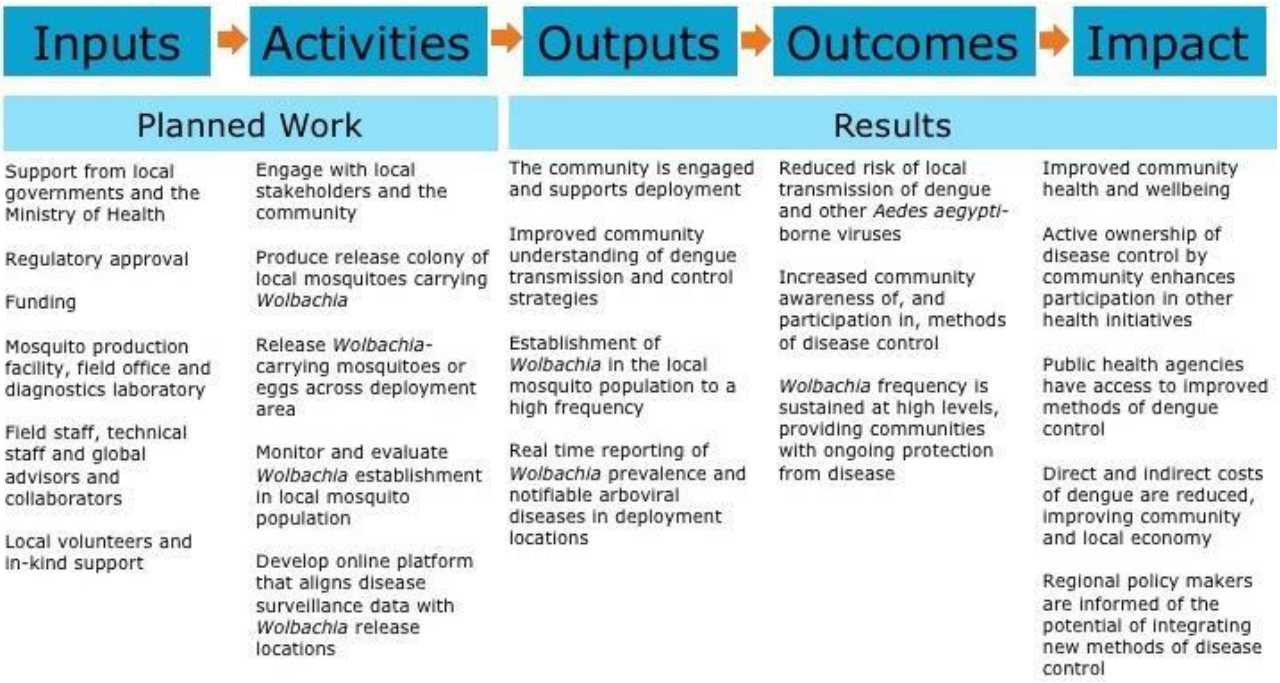


Figure 3: Logic model for use of *Wolbachia* technology to reduce the transmission of *Aedes aegypti*-borne diseases

C.2 Delivery Approach

As described in our original Activity Design Proposal (April 22, 2016), scoping of sites will focus on the following key criteria: entomological factors including the abundance and distribution of *Aedes aegypti* mosquitoes; burden of disease and ecology/epidemiology of transmission; population size and demographic considerations (e.g. population density); technical capabilities to undertake implementation activities; stakeholder engagement; governmental support; suitable regulatory framework for approval of activities, and community engagement and acceptance.

Based on site visits and assessments across these criteria, and in consultation with the Australian overseas missions, two countries will be selected from the Philippines, Cambodia and Myanmar for undertaking *Wolbachia* deployments. As with the Pacific, these implementations will utilise a phased approach, with initial site visits and scoping phase assessments in three sites in early 2018; followed by selection of one - two sites and commencement of preparation phase activities in the selected sites in early 2019. It is unlikely that full deployments of *Wolbachia* will be completed by the end of the overall project but the necessary foundations will be established for release projects to be commenced after completion of this project with alternative funding.

The WMP brings together experts from the fields of *Wolbachia* genetics, mosquito biology and ecology, dengue epidemiology and control, community engagement, as well as health education and promotion. The WMP collaborates closely with local partners to build their capacity to adapt and sustainably implement the method in each project area. To facilitate effective deployment, our Program seeks out

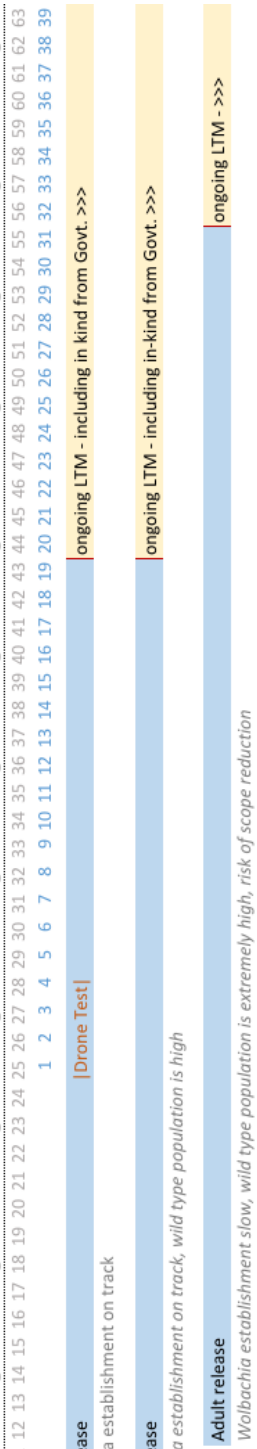
opportunities to form partnerships with local entities (including government health departments, academic institutions, NGOs, and community-based groups), which may be able to support certain project activities. In addition, WMP conducts scoping of local private sector industries to ascertain if goods and services needed for deployment of the *Wolbachia* method might be procured locally. Scoping opportunities for partnership is a key consideration throughout the entire process of deployment and implementation. Where possible, WMP employs local suppliers for equipment and materials needed by the in-country project teams to avoid shipping costs and to provide additional support to the communities we deploy in. Local private or Non-Governmental Organisations may also be contracted to act as local procurement agents to expedite the process for resourcing the project and also allow for flexibility as resourcing needs change.

Our Program undertakes extensive community and stakeholder engagement in order to build awareness and support for the use of *Wolbachia* mosquitoes as a method of disease control. No *Wolbachia* mosquito deployment is undertaken in a project site before regulatory approval and broad public acceptance of the intervention has been established. WMP has developed a flexible model of public acceptance which provides a framework for community engagement within large scale deployments. This model can be adapted to each project site to help enable the implementation of effective communications and engagement strategies in each setting.

D. Implementation Arrangements

D.1 Pacific Implementation

Our original proposal described *Wolbachia* deployments to be undertaken in 1-2 Pacific countries selected from Fiji, Vanuatu and Kiribati. Under this revised proposal, we will be conducting deployments in three countries, with current indicative timelines shown in Figure 4.



Key Impacts:

Mosquito production issues
Temperature controlled shipments
Higher travel costs - experts travelling to site for long periods
Additional trays and cages for production
Additional staff for production
Suva site office and team accommodation

Project time extension - additional cost of project management and overheads
Intense monitoring for 1-3 months per site plus diagnostics
External M&E and Health Economics impact assessment

Figure 4: Timelines for the WMP projects in Kiribati, Fiji and Vanuatu. The Suva, Fiji timeline also describes the timing for the activities funded by NZAID through MFAT.

The description of the laboratory and field activities to be undertaken at each phase remain as described under our original proposal. We are currently experiencing time delays in the Pacific implementation due to challenges involving –a) the mass production of mosquitoes, at the Monash University laboratories, specific for each of the three Pacific countries, b) unreliable air-shipping of temperature-controlled mosquito eggs to all three countries, but Kiribati in particular and c) workforce training of local project staff to achieve high-levels of competence in field operations. Combined, these time delays have led to cost overruns, which are more fully described in the budget section below.

The main changes from our original proposal in relation to Vanuatu, Kiribati and Fiji include;

1. The end date for mosquito releases and establishment of *Wolbachia* in Suva and Port Villa has been extended to March 31st 2019 based on current operational indicators (Figure 5). We have high confidence in these end-dates.
2. The end date for Kiribati mosquito releases has been extended to June 31st. However even with this time extension it is possible that the scope of deployment will need to be scaled back from the original ambition of ~6 km^2 of South Tarawa to ~3-4 km^2 of the most densely populated living in the communities of Betio and Bairiki. This reduced scope reflects unreliable supply lines to this location (egg shipments fail to be loaded on board the twice weekly flights), technical challenges in mass production of Kiribati mosquitoes plus the very high abundance of wild-type mosquito populations which requires longer and more intense mosquito releases per km^2.
3. We anticipate ongoing long-term monitoring of *Wolbachia* establishment will include an in-kind contribution by national/local Governments who have expressed a willingness to collect field mosquitoes and part of their routine activities and ship them to WMP laboratories for *Wolbachia* testing. This activity is captured in the timeline (Figure 4).
4. For information purposes, we note the trial of mosquito releases using unmanned aerial vehicles commenced on 21st November 2018 and will run for 1 month in the Lakasi area of Nasinu (this is a USAID-funded activity)
5. For information purposes, we note that NZAID has provided support to WMP to perform *Wolbachia* deployments in Nadi and Lautoka in the Western Division of Fiji in 2019.

A detailed report of the progress of activities for the Pacific implementation will be provided in our upcoming report (Milestone 5).

D.2 South and South-East Asia Implementation

As previously reported to DFAT, following the Asia Country Workshop that our Program held in Melbourne in June 2017, which was attended by government health officials and researchers, a number of countries expressed interest in running pilot projects. Attending countries included Myanmar, the Philippines, Cambodia, Sri Lanka and Thailand. The S&SEA Implementations will include the phases, noting that an agreement has already been reached with the Sri Lankan Government for a pilot project and so no scoping phase is required for Sri Lanka.

Phase 1: Project Scoping in three countries – Cambodia, Myanmar and The Philippines (15 months) will cover the following activities:

- Desktop based review of these three countries. Assessment criteria to include disease burden and risk (dengue, chikungunya, and Zika), population demographics, mosquito ecology/distribution, social and political environments, local leadership, expertise and infrastructure, geographic location including access and logistics, regulatory approval pathways.

- Site visits to each country involving meetings with key in-country stakeholders to share information on the *Wolbachia* technology, identify potential collaborating agencies/institutions, and also assess local capabilities and infrastructure to undertake project activities.
- signing of partnering agreements for each country between Monash University and the relevant Ministry of Health;
- initiate baseline studies of local mosquito population and abundance;
- identifying and mapping of release sites;
- Based on the above, selection of one-two countries that will be the sites for pilot implementations (i.e. Phase 2), in consultation with DFAT. It is unlikely that full deployments of *Wolbachia* will be completed by the end of the overall project but the necessary foundations will be established for release projects to be commenced after completion of this project with alternative funding.

Phase 2: Preparation activities in Sri Lanka and in one-two sites selected from Cambodia, Myanmar and The Philippines (12 months in each site)

This phase involves the following key activities:

- For Sri Lanka only, signing of a partnering agreement between Monash University and the relevant Ministry of Health and selection of the *Wolbachia* release sites in Colombo;
- continue baseline studies of local mosquito population and abundance;
- For Sri Lanka only, identifying and mapping of release sites;
- establishment of the local project team include hiring of staff and training in the *Wolbachia* method;
- identification of existing medical surveillance systems;
- stakeholder mapping, development of community engagement approach and communications materials;
- development of local *Wolbachia* mosquito lines in preparation for releases;
- development of infrastructure to undertake project activities, for example insectary, laboratory and office facilities, and
- obtaining of regulatory approval for mosquito releases.

Phase 3: Deployment and monitoring activities (18 months and in Sri Lanka only)

- mass rearing of the *Wolbachia* release mosquitoes;
- mosquito releases;
- community engagement activities will continue during this phase;
- monitoring of the *Wolbachia* establishment in the release areas through mosquito capture and diagnostic testing to ensure continued presence of *Wolbachia* in the mosquito population;
- impact of the intervention will be monitored through existing health surveillance systems.

D.2.1 Sri Lanka Implementation

We are currently in Phase 2 for this implementation. Figure 5 shows the current timeline.

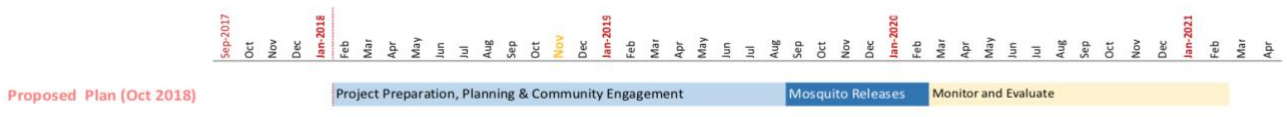


Figure 5: Indicative timelines for the WMP project in Sri Lanka.

A detailed report of the progress of activities will be provided in our upcoming report (Milestone 5).

D.2.2 South East Asia Implementation

We are currently in Phase 1 for this implementation, with indicative timelines for all Phases as shown in Figure 5A. A detailed report of the progress of activities will be provided in our upcoming report (Milestone 5).

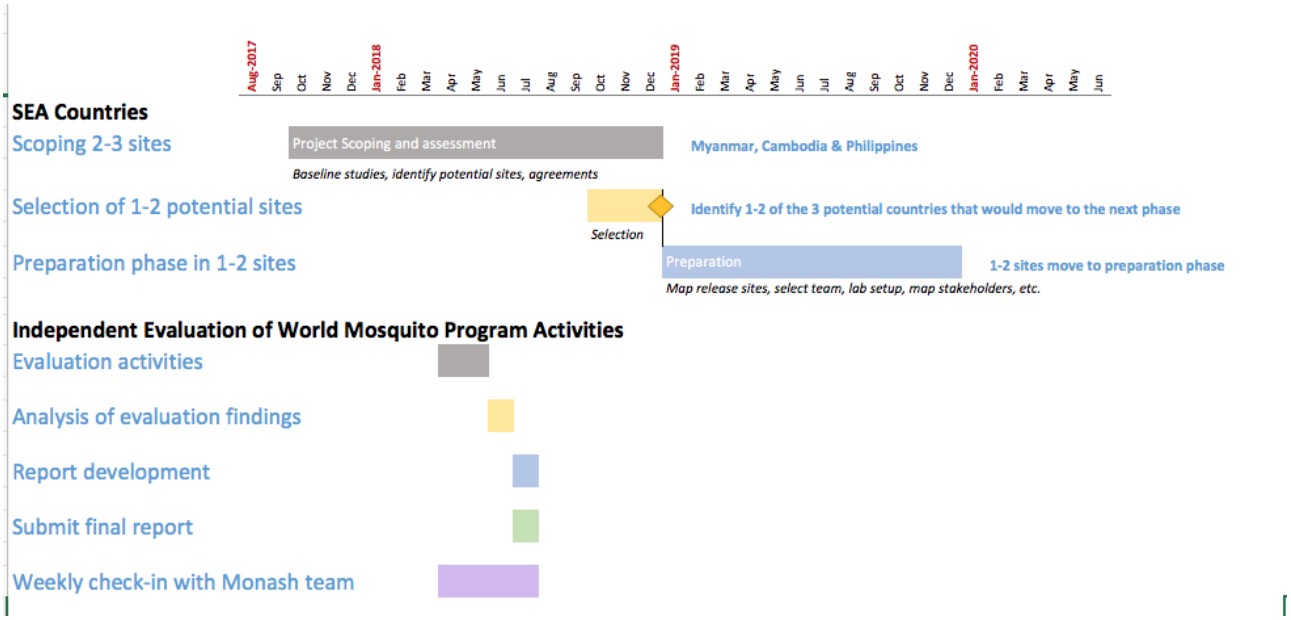


Figure 5A: Indicative timelines for the WMP projects in South-East Asia.

D.3 Indonesia

Currently WMP, in partnership with Universitas Gadjah Mada (UGM), is involved in delivering an RCT on the efficacy of the *Wolbachia* method in Yogyakarta, Indonesia, which is expected to provide results at the end of 2020. The RCT is being funded through separate funding from the Indonesian based Tahija Foundation. As part of that project some of the required work is subcontracted to the Eijkman institute including supply of dengue virus laboratory strains for vector competence studies and some dengue diagnostics QA studies as part of the Randomised Controlled Trial. The Indonesian government has indicated that it does not wish to expand the WMP program in Indonesia until this clinical trial is completed and the results analysed. In the interim, we plan to undertake a series of activities that will be preparatory for future scale up in Indonesia on the assumption that the RCT and other supportive evidence of public health impact is positive.

These activities will be undertaken between now and the end of the Yogykarta RCT in 2020 and will include:

1. Undertake a desktop targeting exercise within Indonesia to better understand which geographic locations will deliver the greatest health return for Indonesia and would be potentially cost-saving for the government.

2. Development of a technical plan which would represent a priority ranking of key locations and method of deployment, quality assurance and partnering to enable expansion.

3. Development an advocacy and communications plan based on global progress of WMP to effectively communicate to the Indonesian government in collaboration with UGM.

4. Better understand the characteristics of arboviral disease in Indonesia through virological studies as part of an existing collaboration with the Eijkman Institute in Jakarta. The Dengue Research Unit at the Eijkman Institute is GCLP certified and recognised as a national reference laboratory.

The Eijkman Institute currently provides reference laboratory diagnostic support to the Yogyakarta RCT. We intend to expand on this existing relationship to molecularly characterise the dengue viruses that circulate in Yogyakarta and at other sentinel sites in Indonesia. Such data will provide important baseline information on the virus population and inform evidence-based, mathematical modelling forecasts of public health impact.

The Tahija Foundation is currently discussing the possibility of undertaking future deployments with UGM in two separate cities in Indonesia as well as completing the current activity in Yogyakarta. The scoping activities we have described in points 1-4 above will not overlap with the Tahija Foundation activities but they may become a subset of a broader strategy we are wanting to develop with DFAT funding, seeking to achieve a coordinated national strategy for an Indonesian rollout, which can be used to guide future deployments. Existing staff from UGM who will be key implementers of future expansion in Indonesia will be trained by WMP in the latest technology we have developed in other deployment countries so that when the Yogyakarta trial finishes they will have the required capacity to undertake the expansion activities with WMP technical guidance. Our strategy will likely involve new partners beyond UGM and the Tahija Foundation and will have both the national government of Indonesia as well as provincial governments in key deployment locations as key audiences to build support for national expansion.

A separate proposal for Indonesian expansion will be submitted once the RCT successfully completes and the Indonesian government indicates willingness to proceed to next steps.

D.4 Funding Management and Governance Arrangements

D.4.1 Funding relationships

The WMP has received over AUD$130 million of sponsored investment since its establishment in 2005. Major funding partners have included the Foundation for the National Institutes of Health (FNIH), since 2005, as part of the Bill & Melinda Gates Foundation's 'Grand Challenges in Global Health' initiative; The Wellcome Trust; USAID; the Yayasan Tahija Foundation; the Gillespie Family Foundation; the Australian and Queensland Governments and the Brazilian Government (Appendix 2).

D.4.2 Governance and Organisational Framework

Our Program works closely with our funding partners to ensure appropriate management and governance arrangements are in place for project activities. This is achieved through the following elements.

1. While Monash University remains the grantee organisation for this project, as it has been since 2011, over the past year, we have commenced our transition to a new organisational structure (Figure 6). Professor Scott O'Neill continues as the Program Director of WMP and lead of this project supported by the senior leadership and functional teams operating out of the Oceania and Asia Regional Hubs. The Asia Regional Hub, based in Ho Chi Minh City, Vietnam, has been established using funds from other benefactors and became fully operational in May of 2018. Senior WMP leadership staff are positioned in each of the Hubs, along with representation from functional teams. The Americas Regional Hub is to be located in Panama and is planned to be operational in in the first half of 2019. A regional presence enhances understanding of local contexts and the identification of key local stakeholders and partners. It also moves operations closer to the countries we work in and decreases travel costs and staff fatigue.
2. The implementations at the country level are led by the WMP Implementation teams working with local project staff. For the Pacific projects, WMP staff are based in Fiji, with regular travel to Vanuatu and Kiribati. The implementation team for the Asia projects is based in Ho Chi Minh office in Vietnam. Support for the projects is also provided from the functional teams based in the Oceania Hub.

3. Each WMP project requires a written agreement to be in place between WMP, through Monash University, and the country partner. These agreements describe the key obligations and expectations of each party, including reporting requirements, use of intellectual property and communications protocol. In addition, the budgets and workplans which are developed for each project, are incorporated and updated as necessary throughout the project term and provided to DFAT.

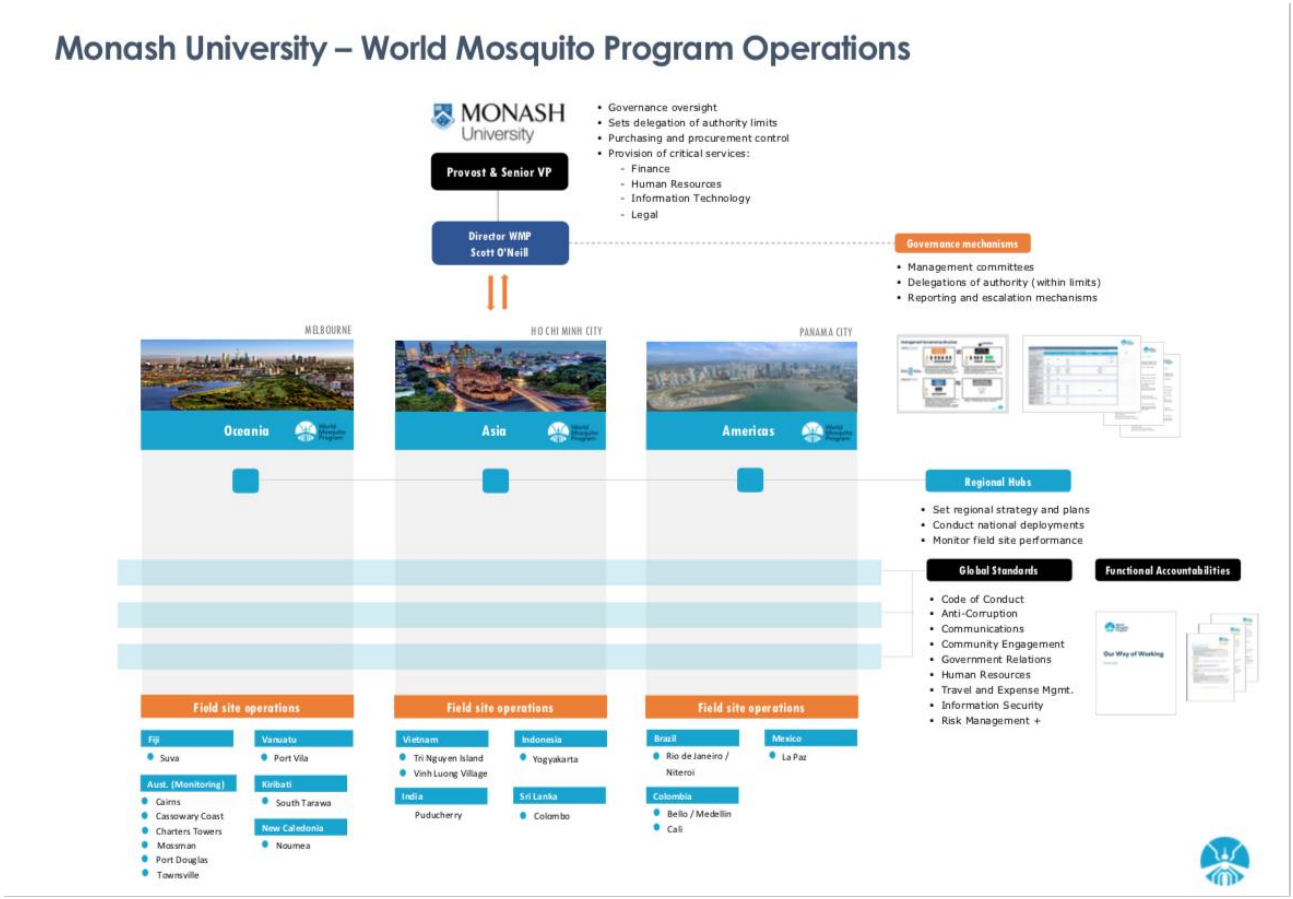


Figure 6. WMP organisational framework.

D.4.3 Indicative Budget

The financial requirements for this proposal have been revised and are estimated at approximately $17.97m (plus $551k estimated interest earned over 4.7 years – this period reflects the extended grant end date from June 2019 to December 2020 (Figure 7). A more detailed indicative budget is shown in Appendix 3. Our Program believes that to develop a true partnership with the countries we deploy within, not only should they have input through an advisory committee in a governance capacity but also be involved through suggesting and, where possible, providing a means of local fund raising. Any increase of funding through these means would result in an increase in the size of the deployment and or enable maintenance of monitoring activities beyond the 4.7-year period of this project to demonstrate the true impact of the *Wolbachia* method and assist in the uptake of this technology by policy makers. The indicative budget provided estimates what is required for the project having been benchmarked against costs observed at our existing project sites and updated with recent experience. A more detailed budget will be developed at the end of the scoping phase (Phase 1) for the S&SEA projects when more information of the scope and the availability of any local funds is known. Should the funding required for the described project not be attained, costs will be saved through a decrease in the size of the implementation areas.

Activity	Cost AUD
Pacific Implementation (including M&E)	10,344,000
Sri Lanka Deployment (including M&E)	2,457,000
1-2 of Cambodia, Myanmar and Philippines Deployments (including scoping)	1,169,000
Indonesia (scoping work)	530,000
Indonesia	3, 470,000
Total	**17,970,000***

Figure 7: High level proposed costs for the project.
*The total maximum payable under this Grant Agreement is $17,970,000. Total estimated interest earned by the end of the project is $551,000. The interest earned will be used for activities in the Pacific sites (Fiji).

For the reasons described in section D.1, the budgeted cost of the Pacific Implementations has increased from $7.968m to $10.344m largely as a consequence of extended project times affecting both local costs, WMP support costs and also by the requirement for temperature controlled egg transport to the sites, the establishment/operation of the Suva Hub office and adding external M&E and Health Economic Analysis. As a consequence, the available funds for scoping new sites (Cambodia, Myanmar, Philippines) have reduced from $3.777m to $1.169m.

The WMP will deliver value for money by ensuring that funds are used in accordance with Monash University procurement policies and processes. A key aim of WMP is to ensure scaling delivers value for money through innovation and optimisation to deliver a reduced cost of deployment per person. Deployment options for staffing, equipment and consumables will be carefully reviewed to ensure value for money but without a reduction in the quality of the intervention. Our Program is operated on a not-for-profit basis with significant in-kind contributions made by other partner organisations. As such, no profit is required or desired and our challenge will be to develop methods for large scale *Wolbachia* releases at reduced cost.

D.4.4 Management of funds

With total revenue for the year ended 31 December 2017 of $2,431.7 million, Monash University employs best practice financial standards to support the University's financial requirements in all of its teaching, research and business activities. The University's Annual Financial Statements are audited by the Victorian Auditor-General, ensuring the utmost scrutiny of its financial recording and reporting. At the program level, financial records are maintained using the SAP accounting system with extensive control, oversight and management by the University's Central Finance Division. Funds received from separate sources are maintained in discrete cost centres to ensure all transactions are recorded against the relevant fund source. The WMP has a dedicated finance officer who is responsible for preparing regular financial reports, also reviewed by central University financial staff, independent of WMP, to

maintain regular oversight and transparency of received funds. These reports are issued to our funders at regular reporting periods.

D.5 Exit Strategy from Implementation Sites

Our overarching aim is to empower country partners to take ownership of the technology and adopt into their own national disease control programs. Capacity building and knowledge transfer to local staff and institutions is therefore a critical feature of our projects. In many cases, our local operational teams include staff on secondment from national or municipal public health agencies. This effectively embeds a deep understanding of the WMP method within public health institutions and Ministries of Health during the 2-year timeframe of most WMP projects. Nonetheless, there is inevitably a range of country-level capacities needed to become independent implementers and evaluators of the WMP method after the first pilot project has completed. Small Pacific Island countries such as Kiribati and Vanuatu have limited capacity to become wholly independent adopters and would require additional external assistance and funding to do so. In other settings, such as Fiji and Sri Lanka, there is sufficient local capacity and resources to adopt the method into their own disease control programs with a small ongoing advisory role for WMP to assist and help interpret long term monitoring. The WMP does not have a fixed and predetermined strategy for all countries. Instead, the country-strategy is shaped by:

1. The WMPs global strategic plan and priorities,
2. The WMP's core operation's funding success,
3. The country-level willingness to invest (cash or in kind) into long term monitoring and evaluation, and
4. Policy, community and political momentum to adopt the WMP method into their own disease control program. Inevitably, these ingredients are dynamic and linked to the success of the first country pilot project.

Below we give examples of the WMP's country-level engagement under three different scenarios.

Scenario 1: No additional project funding to WMP after demonstration project completes and government is unable or unwilling to locally support

Under this scenario our expectation is that the deployments made under the existing project will maintain themselves without the need for any "maintenance" releases. Without funding from other sources or from the country itself and if WMP does not have core operational funding to dedicate to particular sites then:

1. No long-term monitoring of deployments will take place.
2. No expansion of deployments to other geographical regions will be possible.
3. Monitoring through existing arboviral disease surveillance systems will take place as it currently does. Our expectation is that outbreak intensity should be reduced in areas that received *Wolbachia* during this project.
4. If large outbreaks did occur WMP would seek funding to explore the reason for breakdown in the intervention and any mitigation steps to be taken. WMP is routinely in dialogue with public health stakeholders in the countries where it works and consequently WMP would be made aware of local outbreaks in the normal course of business during and after deployments. Other methods of outbreak detection are also relevant, e.g. country reporting under International Health Regulations. WMP would use or seek external funding for research into intervention breakdown through the normal channels of competitive research grants, philanthropy and where possible in-kind contributions from national governments.

Scenario 2: No further funding support to WMP after the demonstration project but support is available from country

In this scenario, we anticipate significant ongoing in-kind contributions will be required from national/municipal governments in the areas of communications and stakeholder management plus entomological and arboviral disease surveillance to enable long term monitoring and evaluation of Project outcomes. As an adjunct to local in-kind contributions the WMP could provide one or more of the following services in the absence of new funding if our core funding allowed:

1. Expert advice and digital information services to support a program of long-term mosquito trapping (performed in kind by national/local government partners) and subsequently the prevalence of *Wolbachia*-infected mosquitoes.
2. As required, remote laboratory diagnostics for *Wolbachia.* These diagnostics would be done by WMP in its laboratories. This could involve shipments of mosquitoes to the laboratories at Monash University or elsewhere in the WMP laboratory network (e.g. New Caledonia) for *Wolbachia* testing. Laboratory testing would be funded from WMP's core funds. Alternatively, WMP could provide its external quality assurance panels to support the quality of *Wolbachia* diagnostics being performed in country where they have the capacity and expertise to do so.
3. Expert advice scaling the program to other parts of the country.
4. Measurement of medium and long term Public Health benefits by coupling existing arboviral disease surveillance systems to Wolbachia prevalence surveys – these would be communicated on a yearly basis to key national and international stakeholders. Arboviral disease surveillance is a routine activity of national governments and the data is provided to WMP through collaboration. The WMP Global epidemiology dashboard aggregates Wolbachia surveillance results with arboviral disease incidence in a spatially aligned manner and is the natural vehicle to share this information. This would utilise the results from activity 2 above together with the health data available in country. The WMP costs would be covered from our core programmatic funding.
5. Advocacy and communications to regional and international stakeholders.

Scenario 3: Long term funding support to WMP targeted to countries where demonstration projects have taken place.

With continuous funding support to WMP from Government (e.g. DFAT), or philanthropy, we can perform or co-ordinate with country partners a portfolio of activities. In this scenario, WMP would require specific funding against a particular country to enable it to provide one or more of the following services:

1. Expert advice and digital information services to support a program of long-term mosquito trapping (performed by WMP and/or by national/local government partners) and subsequently the prevalence of *Wolbachia*-infected mosquitoes.
2. Expert advice to support a program of expanded releases to other parts of the country or design and assistance with a national deployment program.
3. Technical support, equipment and consumables for a local *Wolbachia* diagnostic testing platform within an in-country institution – this would be supported by a WMP-administered External Quality Assurance Program.
4. As required, remote laboratory diagnostics for *Wolbachia (as described in Scenario 2).*
5. Medium and long term Public Health impact measured by arboviral disease surveillance systems and Wolbachia prevalence surveys - these will be communicated on a yearly basis to key national and international stakeholders. Where there is direct funding then *Wolbachia* surveillance could be performed by WMP. Arboviral disease surveillance is a routine activity of national governments and the data is provided to WMP through collaboration. The WMP Global epidemiology dashboard aggregates Wolbachia surveillance results with arboviral disease incidence in a spatially aligned manner and is the natural vehicle to share this information.

6. Empirically-derived evidence of cost effectiveness. WMP would engage under subcontract independent parties to perform this work, most likely academics with international credibility and discipline expertise.
7. Carefully calibrated and targeted stakeholder and community engagement to explain the medium and long-term outcomes of the Project. This is a standard business activity of the WMP Global Comms team and would be delivered in country using our standard methods of partnering.
8. Assessment of the medium and long-term clinical and environmental safety profile of *Wolbachia* deployments.
9. Support for policy development and funding applications that could expand the national footprint and benefits of the technology.
10. Access to new technologies, including 2nd generation *Wolbachia* diagnostic tests, digital tools and deployment methods.

E. Communications Plan

E1. Communications approaches

The following outlines the two communications approaches for iXc funded projects.

E.1.1 Multi-country approach

The WMP's Program Director will contact iXc's Director, Scaling Innovative Culture and Program Manager directly for any multi-country, or general contract enquiries or issues. The following specialists from WMP will be copied on this communication as required: iXc will coordinate with Posts for relevant responses. Where required, meetings may also be organised to discuss in further detail.

E.1.2 Country-specific approach

Communications and engagement campaigns are specifically developed by experienced practitioners for each project site. Before distribution of communications materials into the public domain, input and approval is sought from a range of internal and external specialists. The materials are approved internally by specialists from the local and global WMP teams, using a set of approval criteria. This collaborative approach helps to build relationships and local capacity, while ensuring materials are culturally appropriate, technically accurate and accessible for the target audience, align with global WMP brand guidelines, adhere to the brand requirements of individual partners and funders, and support the specific goals of the project.

If external consultation is required, consultants may include but are not limited to, technical specialists from the Ministry of Health, health promotion and vector control promotion officials, the Ministry of Education, local representatives from funders such as the DFAT, local community leaders or partner organisations, multilaterals and NGOs.

The WMP will follow the 'DFAT InnovationXchange Grantee Communications Toolkit' (**Toolkit**) to ensure the correct use of the Australian Aid and InnovationXchange logos, as well as written and verbal acknowledgements. Acknowledging the value of DFAT's local understanding and in-country relationships, WMP will also continue to involve local Posts through consultation on high-level communications materials and participation in events.

High-level communications materials
The WMP's Communications and Engagement Advisers or Program Development Managers will contact individual country posts for input and/or notification about high-level communications materials.

Following the key communications materials and principles outlined in the Toolkit, WMP understands high-level communications materials to include:

- Television commercials and videos
- Media releases
- Human-interest stories and case studies about the project*
- Schools programs
- Radio advertisements - script only

The WMP proposes that local turnaround times are developed collaboratively by local WMP project staff and local Posts to ensure the process is agile, allows for any necessary amendments and subsequent approvals, without creating delays that impede the delivery of the project. While every effort will be made to provide ample time for feedback, there may be circumstances where these timeframes are not possible. Once finalised, high-level communications materials will be shared with iXc by the WMP's Program Director, or a delegated representative.

The WMP encourages feedback from local Posts and while not requiring approval before distributing communications materials, agrees to apply where possible. When time permits, the local project team may meet with the local Post (and other stakeholders) to discuss and share ideas. Meeting minutes will be circulated to WMP Global, who will distribute to iXc.

Human-interest stories and case studies may be produced by the WMP Communications and Marketing team. In this instance, the WMP Director, Marketing and Communications may contact the posts and/or iXc directly for input, copying in the iXc Director, Scaling Innovative Culture and relevant staff. Similarly, for specific requests for human-interest stories and case studies, iXc will contact the WMP Director, Marketing and Communications, copying in WMP's Director and relevant iXc staff.

Events

The WMP's Communications and Marketing Advisers or Program Development Managers will contact individual country posts to inform them about major public events, media tours or press conferences, and visits from high-level stakeholders (see country breakdown for specific details). The WMP's Program Director, or delegated representative, will contact iXc to notify them about the event.

The WMP will provide 21 days' notice of upcoming events, noting that some flexibility is required to accommodate the shifting and uncontrollable schedules of partners, especially where these partners are governments. Where detailed information is not available, the WMP will provide a list of tentative dates of events and/or visits, with details to be confirmed closer to the date.

E.2 Communications contacts by country

The WMP Communications and Marketing team will consult with key contacts in countries where we operate according to preferred contact lists shared with us by iXc.

F. Cross-cutting issues

F.1 Sustainability

Our *Wolbachia* method of arboviral disease control offers an innovative, disruptive technology that provides the potential for a sustainable, long-term intervention for communities affected by *Aedes aegypti*-borne diseases. Once there are high levels of *Wolbachia* mosquitoes in the local mosquito population, these levels should be sustained indefinitely and the risk of infection with dengue, chikungunya and Zika viruses is expected to decrease in target communities. The vast majority of residents are not asked to change their behaviour before, during or after releases. For a relatively small number of residents and for short time period, we ask them to participate by hosting a mosquito trap or a specifically provided container that grows Wolbachia-carrying mosquitoes. The WMP's Wolbachia

method has an advantage over other traditional disease control methods (e.g. household/community clean-ups) that require sustained behaviour change to achieve impact. Similarly, no change in existing insecticide control activities is required before, during or after implementation. Our exit strategy, described above, ensures a smooth transition between WMP and country involvement.

Our Program also works closely with collaborating partner institutions to enhance their capacity to implement and monitor the intervention over the long-term. Capacity-building activities include regular training for project staff and local partners, implementation of standard operating procedures (SOPs) and best practice frameworks, as well as briefings and meetings to educate communities and key stakeholders about the method.

The WMP maintains a publicly available website (www.worldmosquitoprogram.org) which provides up-to-date information about the *Wolbachia* method, copies of research publications and current activities in each of our project sites. In addition, we have developed an online support platform (Catalyst) accessible to our project sites, which provides access to information and the opportunity to share learnings from each different deployment environment. Catalyst utilises a number of strategies to engage and educate project staff and is available in multiple languages. Ongoing access to the Catalyst platform is a key mechanism by which projects can refresh their learning and stay up-to-date with the latest global developments.

F.2 Gender equality and disability inclusiveness

The *Wolbachia* method is designed to deliver improved health outcomes for all members of a community including women, men, girls and boys. In this respect, it is a truly egalitarian public health response, providing equal protection from disease without reference to a person's gender, age, wealth, or any other characteristic. The effect of the intervention is experienced equally by all people residing within the target areas, without requiring any ongoing changes to behaviour.

Women are actively involved in our field sites and are represented at all levels of the organisational structure. In every field site, women play an important role in our Program's engagement with target communities by helping to educate and build public support for the use of *Wolbachia*. Community meetings and activities recruit both women and men to participate, ensuring that a broad section of the community is able to ask questions or address potential concerns about the *Wolbachia* method.

As part of Monash University, our Program adheres to all Monash policies relating to equity and diversity. This includes the Monash Equal Opportunity Policy (which provides the framework for gender equality and disability inclusiveness), and the Wellbeing and Support Policy (which promotes the use of positive workplace arrangements for staff members with disability). Monash University is well-known for its commitment to advancing women in the STEMM (science, technology, engineering, mathematics, medicine) fields, and the World Mosquito Program supports and promotes the participation of women in its laboratory research and field implementation. Monash University is committed to creating a safe inclusive and respectful environment for all members of its community believing everyone deserves an equal opportunity to succeed in their career. We're leading the way in promoting workplace inclusion regardless of race, gender or beliefs and foster a safe and respectful community and support individuals of all genders to succeed.

F.3 Monitoring, evaluation & learning

The WMP is committed to independent assessments of the impact of *Wolbachia* deployments. Our overall strategy is to accumulate a portfolio of country-level monitoring and evaluation (M&E) assessments from a range of external agencies. As an example of our commitment to measuring long term outcomes, in Australia we are subcontracting the CSIRO to prepare an independent evaluation of the outcomes of *Wolbachia* deployments in north Queensland, eight years after the first deployments

occurred. This evaluation will consider economic, health, environmental and entomological outcomes and will commence in late 2018. It is intended to complement and update the original risk assessment performed by CSIRO in 2009, prior to first releases of *Wolbachia* in Australia. Elsewhere, monitoring and evaluation of our projects in Brazil and Colombia will be performed in late 2018 by a group of independent experts led by Dr Raman Velayudhan, Coordinator of the Vector and Ecology Management unit at WHO, Geneva. This activity is co-ordinated with the Pan-American Health Organisation and the respective Ministries of Health in Brazil and Colombia. In the Western Pacific, independent monitoring and evaluation (M&E) will be performed by subcontracted independent experts selected through a competitive tender process. The detailed tender document, describing the terms of reference, reporting requirements and timing for the M&E is attached as Appendix 1. The M&E will commence in the first quarter of 2019 and be completed by April/May 2019. DFAT and WMP will be joint recipients of the M&E output. In S&SEA project sites, while they are still in their infancy and too young to develop an M&E plan, a similar regional tendering process will be performed to identify eligible program evaluation and subject matter experts. The scope of work for these activities will be informed by best-practice M&E considerations plus stakeholder priorities (e.g. local and national Government, WHO). The WMP will share M&E reports with key national and international stakeholders, solicit feedback and use the process to improve the Program and individual country projects. In due course and with permission from our partner organisations, the WMP will make the outcomes of monitoring and evaluation activities public documents.

The proposed deployments will join a global network of field sites, each of which contributes to refining the method and building the evidence base for *Wolbachia* as an effective and sustainable method of disease control. The *Wolbachia* method is an evidence-based public health initiative, and ongoing monitoring, evaluation and learning is a key aspect of each field release.

F.3.1 Measuring success

Success for both WMP and the communities that have accepted the method will be the sustained (multi-year or multi-decade) elimination of *Ae. aegypti*-borne arboviral diseases as a public health concern. In the short-term period of the program (end-2020), we'd expect to see no evidence of local transmission of the commonest arboviral disease, dengue, in locations where *Wolbachia* has established itself to high levels in the local *Ae. aegypti* population. Measurement of the public health impact in Western Pacific countries will be performed on an annual basis in accordance with a prior defined analysis plan (Appendix 2). The analysis plan describes the methods of analysis and the frequency of reporting.

At a technical level, a monitoring and evaluation framework (Appendix 4) forms the basis for measuring progress towards the desired technical outcomes. Information and data resulting from our monitoring and evaluation framework will be provided to DFAT every 6 months in the biannual and annual reports. A summary of the approach to monitoring and evaluating each of the primary outcomes is provided below.

1. Establishment of support for the use of the Wolbachia method, with approval from regulatory bodies, local authorities, and communities in release areas

An evaluation framework will be used to determine the impact of various communications and community engagement activities undertaken as part of the public acceptance model. This model includes aspects of social research to determine pre-existing community knowledge and awareness of the project, and allows ongoing monitoring of public sentiment and acceptance of *Wolbachia* deployment. The establishment and regular meetings of a community reference group will provide opportunity for input and feedback from a range of groups within the community. A stakeholder management system will allow for close monitoring of stakeholder engagements in line with each project's stakeholder engagement strategies.

2. *Establishment of high levels of Wolbachia-carrying mosquitoes in deployment areas*

This outcome depends on capacity and infrastructure to produce sufficient *Wolbachia* mosquitoes with the traits necessary to successfully spread into the local mosquito population. Measures will include the number of mosquitoes produced, analysis of the genetic suitability of mosquito lines produced (genetic similarity of the *Wolbachia* mosquito line to local mosquito population achieved through back-crossing), the frequency of *Wolbachia* within mosquito lines, and the level of insecticide resistance in mosquito lines (compared to the local mosquito population). The frequency of *Wolbachia*-carrying mosquitoes in deployment areas will be monitored throughout the deployment period and in the post-deployment period to ensure that *Wolbachia* is able to sustain itself in the deployment areas.

3. *Monitoring mosquito-borne disease in release areas in order to assess the effect of the intervention on local transmission of dengue and other viruses*

We expect that broad-scale establishment of *Wolbachia* in mosquito populations in the intervention areas will result in a significant reduction in dengue transmission within these areas. Arboviral disease incidence in these areas will be monitored through the existing notifiable disease surveillance system and our digital tools will enable reporting of disease burden in relation to spatial and temporal patterns of Wolbachia prevalence.

F.3.2 Health economic analysis

The analysis of the forecast health economic impact of the *Wolbachia* method in Fiji and Vanuatu (and Kiribati if possible) is an activity that sits outside of the scope of the independent M&E. The reason for this is that the expertise to perform this activity at an internationally credible level is not readily available within M&E service providers and consequently will be outsourced to an internationally recognised academic expert in dengue health economics, Prof. Don Shepard, Brandeis University, USA. The health economic study will involve two activities:

1. Estimation of the cost of *Aedes aegypti*-borne viral illnesses in Fiji and Vanuatu (and where possible Kiribati) using local disease incidence data with costings extrapolated from other dengue-affected countries with similar socioeconomic environments and per capita income. This activity will estimate the cost of dengue (median, range) in epidemic and non-epidemic periods. Costs will be separated into components, which could potentially encourage different stakeholders to help prevent their respective losses. These include overall direct medical costs (i.e. costs to the health system overall). The project will also generate estimates important to the economy overall — direct non-medical costs (primarily for transportation), and indirect costs (primarily from lost time and productivity).
2. Description of the costs of *Wolbachia* deployment and evaluation of the economic impact of *Wolbachia* in Fiji and Vanuatu (with extrapolation to Kiribati). This activity will apply cost functions to estimate the costs of *Wolbachia Aedes aegypti* mosquito propagation, establishment and maintenance. It will examine the costs of various functions and modalities, including paid workers and volunteers and where applicable, public education, regulatory approval, egg generation, release of eggs and/or adult mosquitoes, entomological and epidemiological surveillance. Finally, this activity will then forecast the cost-benefit and cost-effectiveness ratios in the planned *Wolbachia* deployment locations. Where possible the cost of existing of disease control programs will be estimated from public health sources and compared against the *Wolbachia* method, albeit there is no evidence that existing control methods are able to deliver substantive reductions in disease burden.

The main deliverable of this study will be a concise and accessible report that describes the assumptions and outputs of the cost-effectiveness analysis. The report is anticipated in the 3rd quarter of 2019.

F.4. Risk management

Part of the success of our Program to date can be attributed to its comprehensive assessment of risk prior to any deployment and risk management being an integrated part of the organisation's governance framework. After an initial, comprehensive risk assessment conducted by the CSIRO in 2010, the Program has developed a dynamic end to end approach to risk that is considered in planning processes at the strategic and operational levels and factored into each stage of design, delivery and deployment, underpinned by risk management principles and guidelines. This aims to ensure uncertainty regarding organisational objectives being achieved is significantly reduced and avoided as much as possible.

The Program risks (Appendix 5) are reviewed and modified regularly to reflect changes in design and delivery for new and existing sites. It is also part of our Program's commitment to risk management continuous improvement. This is done in conjunction with team leads at each field site, with each risk being assigned to a risk owner. The Risk Register is supported by mitigation and response tools including a Crisis Communications Plan.

Each field site also develops a site-specific risk register reflecting a flexible approach that accommodates challenging environments, changes that may occur over time and unique, local operating conditions. These processes incorporate input from donors and other key stakeholders. As part of the proposed implementation, both the Indonesia and Pacific Implementations will develop and maintain a risk register, which captures key decision points and the risks associated with these.

A key part of the WMP risk mitigation strategy is to engage closely with communities and stakeholders, using an informed and targeted approach to community engagement and media coverage to ensure broad understanding and acceptance of the *Wolbachia* method prior to any planned deployment. This targeted approach has been highlighted in research (Murray, Jansen & De Barros 2016) as a key recommendation for reducing uncertainty and minimising risk.

F.4.1 Safety, health and environmental risk assessments

Three publicly available and comprehensive risk analyses of the *Wolbachia* method have been conducted, all concluding negligible risks to human health or the environment. No adverse environmental or health impacts have been observed as a result of releases already undertaken across five countries.

1. Risk analysis on the Australian release of *Aedes aegypti* (L.) (Diptera: Culicidae) containing *Wolbachia* (http://www.eliminatedengue.com/library/publication/document//riskanalysisfinalreportcsiro.pdf)

2. Risk assessment of the pilot release of *Aedes aegypt*i mosquitoes containing *Wolbachia* (Vietnam) (http://www.eliminatedengue.com/library/publication/document//july_2011_ra_report_eng.pdf)

3. Risk Assessment on the release of *Wolbachia*-infected *Aedes aegypti* (Indonesia) (http://www.eliminatedengue.com/yogyakarta/download/view/publication/379)

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