**Publishable Summary**

# Summary Description of Project Context and Main Objectives

Prevention of malaria is best achieved by vector control which, today in Africa, relies almost entirely on the use of residual insecticides in the domestic environment. Wide scale implementation of tools such as indoor residual spraying (IRS) and long lasting insecticide impregnated bednets (LLINs) have led to impressive decreases in malaria transmission in some regions and these interventions are the cornerstone of malaria control programmes in most African countries. However these frontline interventions are dependent on a very limited number of available insecticides, whose efficacy is being continuously eroded by the evolution of insecticide resistance in the mosquito vectors. Furthermore, even without the threat of insecticide resistance, the current tools will not be adequate to achieve stable reductions in, or elimination of malaria transmission. Indeed the very success of LLINs and IRS in preventing transmission is highlighting additional challenges and opportunities, including the need to tackle mosquitoes that bite and rest outside the home. Significant advances are needed to secure the future of malaria prevention by vector control. The AvecNet consortium’s objectives were to:

* Ensure the **sustainability** **of current intervention strategies** by investing in the development and evaluation of new insecticides and approaches to overcome insecticide resistance,
* Design and evaluate **new tools and interventions** that target mosquitoes that evade current vector control practices
* Increase the knowledge base on the biology and behaviour of mosquitoes and plan for vector control in a changing environment
* Develop **research capacity** in malaria vector control in Europe and Africa and strengthen partnerships in Africa.

Overall the project aimed to add significant value to the international research effort in vector control by taking forward the state of the art and translating this into new or improved control tools to be trialled within the time frame of the project.

# Description of Work Performed and Main Results

## Ensure the sustainability of current interventions:

The new approaches developed by AvecNet partners to quantify the strength of insecticide resistance have now been adopted by the World Health Organisation and are being used to predict where ‘resistance breaking products’, such as dual active bednets, are likely to have maximum impact. Using the new experimental hut facilities created by AvecNet, we have evaluated four alternatives to current chemistries used for indoor residual spraying. By using a clear ‘stop-go’ decision framework we terminated testing of two chemistries, the other two moved forward to the next testing phase. One is currently under evaluation with the WHO Pesticide Evaluation Scheme, AvecNet generated data has been critical in this process. At the earlier spectrum of the product development pipeline AvecNet established and characterised insecticide resistant mosquito strains in the laboratories. Using these mosquitos, we screened all the new active ingredients being developed by our agrochemical partners. This information has been of critical importance in selecting new chemicals for further developments within and beyond the life of the AvecNet project.

## Design and evaluate new tools and interventions:

The first clinical trial of a new insecticide treated net, Olyset Duo® was completed in Burkina Faso. The results showed that this net works better than the standard nets, and the trial results will inform national and global malaria control policy. New approaches to deliver existing vector control products have been identified and published for example, we have tested a spatial repellent which is a promising means to provide long-lasting protection from outdoor biting mosquitoes. We have also identified more efficient means of applying larvicides and approaches to reducing insecticide use inside the home without compromising protection of householders. The evaluation of these products required improved methods for measuring mosquito movement and behaviour. Two major achievements of the AvecNet project are the development of a new host seeking trap that catches mosquitoes when they are looking for a person to bite (patent pending) and a tracking system which can record mosquito behaviour in flight in the dark. Both tools are being used to develop and evaluate vector control tools beyond the life of the AvecNet project.

The use of ‘Photo Voice’ (giving respondents disposable cameras to document an issue) has proved an insightful and practical way to gather local community views on vector control. Policy analysis and interviews with the full range of stakeholders involved in malaria vector control policy and implementation were also used to identify opportunities to accelerate the introduction of new tools for example by using local production of tools to reduce youth unemployment as well as improve health.

## Increase the knowledge base on the biology and behaviour of mosquitoes:

The infrared video system for mosquito tracking was evaluated in the insectaries in the first phase of the project and revealed, for the first time, critical parameters such as the length of time mosquitoes spend on insecticide treated nets and provided answers to long standing debates on the role of repellence versus toxicity in mode of action of bednets. This system is also functioning well in our field station in Northern Tanzania and as part of a new project, continues to provide invaluable data on the response of insecticide susceptible and resistant mosquitoes to insecticide treated surfaces. Studies on the physiology of mosquitoes have provided novel insights into the process by which insecticides penetrate the insect cuticle and are eventually metabolised. New funding has been obtained to further understand these processes and improve the formulation of insecticides for malaria control.

## Develop research capacity in malaria vector control

AvecNet providing mentoring in study design and statistical analysis of complex data sets. In addition, we led several workshops on Quality Assurance for field trials of new vector control tools and developed Standard Operating Protocols that have been adopted by the malaria scientific community. All six AvecNet PhD candidates have been awarded their PhDs and continue to work in malaria, and four of the postdocs from AvecNet African partners have been awarded prestigious fellowships.

## Dissemination activities

Dissemination activities have included contributions to WHO policy documents, 30 published manuscripts, four newsletters, information leaflets in French and English, contributions to the agrochemical industry trade publications and multiple presentations to the scientific community. AvecNet scientists continue to engage at a high level with major international and national level funding and policy making agencies. A major dissemination event was held in June 2016 to highlight the key outputs of the project and all presentations have been made publically available via the AvecNet project website.

# Expected Final Results and their Wider Impact

In the initial proposal we identified six areas in which we were committed to make a significant impact. Progress under each of these is briefly described below.

1. **New and improved vector control tools to reduce the malaria disease burden in Africa.** We have completed a clinical trial of a new combination bednet, Olyset Duo, from Sumitomo Chemical Ltd, in Burkina Faso. The trial showed that this new net was more effective than standard nets in areas of high resistance to insecticides. This evidence will contribute to the global policy debate on how best to control resistant mosquitoes. Our strong partnership with industry, and our investment in resources for laboratory and field evaluation of insecticides, has continued to accelerate the development of new insecticides for malaria control. For example, insectaries and experimental huts built with AvecNet support have enabled us to expand the number of field sites for evaluating new products. The value of data arising from these trials in making stop-go decisions, has been enhanced by detailed characterisation of the mosquito populations in each site. This means we have a much better idea of what works against resistant mosquitoes.
2. **New tools to aid planning and execution of malaria vector control strategies**. AvecNet has developed a number of tools to facilitate evidence based decision making on the most locally appropriate malaria vector control interventions to employ. These include application of Geographical Information Systems to improve targeting and cost effectiveness of activities to manage mosquito larval populations; development of a panel of recombinant enzymes for screening chemicals for insecticidal properties; application of an ethnographic tool, Photovoice, to explore householders response to mosquitoes; and development of a new trap, the mosquito electrocuting trap, to accurately record changes in host seeking behaviour of mosquitoes that would affect the efficacy of control tools. The tracking system, that enables mosquito behaviour to be tracked under natural settings, has generated a great deal of interest from industry partners, and data generated from this device by the AvecNet team has already resulted in a partnership with a major bednet manufacturer for a patented novel bednet design. This will be taken forward beyond the life of AvecNet, and would not have been possible without the funding provided to develop the tracking system.
3. **A better understanding of the biology and the population dynamics of mosquito vectors transmitting malaria in Africa**. New tools to monitor mosquito behaviour (including host seeking and resting traps) have been used to measure the key mosquito behaviours such as how they respond to insecticide treated nets when looking for a human to feed on, that impact on malaria transmission. This will directly inform the design of interventions to target mosquitoes exhibiting particular behaviours. The mosquito electrocuting trap is now being employed to study the behaviour of other mosquito vectors, including those responsible for transmission of dengue and Zika viruses. This is a huge step forward as it means that humans are not exposed to possibly infected bites while participating in disease research.
4. **Increase European contribution to on-going global efforts to control and eradicate malaria and strengthening research partnerships and research capacities in Africa**. AvecNet has directly supported six PhD candidates, all of whom are continuing to work in malaria control, and provided mentorship to many other early career African scientists, several of which have secured their own independent funding as a result of data they generated within AvecNet. We have also invested in the infrastructure of our African field sites by building and equipping insectaries and experimental huts. These field sites and the scientists that run them are essential to speed up development and testing of new vector control tools. Our focus on Quality Assurance is raising the standard of vector control trials within the local community with several sites preparing to apply for international accreditation.
5. **Contribution to Community societal objectives**. Half of the world's population is at risk of malaria and up to 500,000 die from this disease every year. In addition to the devastating impact on human health, malaria also imposes an enormous economic burden, estimated at 1.3 per cent of economic growth per year in sub Saharan Africa. The programme has a had direct societal impact through developing and testing a portfolio of vector control tools that are effective against insecticide resistant mosquitoes and acceptable to key stakeholders. Alongside this, AvecNet’s investment in human and physical scientific capacity has helped ensure a sustainable future for malaria prevention.
6. **Policy impact**. Translating effective new vector control tools into improved malaria control requires robust scientific and economic evidence. Early identification and active engagement of key stakeholders is required to feed evidence into the policy debate and positively influence relevant actors such as technical staff in donor agencies. In addition to contributing to this evidence portfolio, AvecNet has conducted studies on the national and global policy frameworks influencing uptake of vector control tools. Similarly, we have worked with global and national level policy making bodies to disseminate our findings and influence policy guidance and technical decisions. For example, AvecNet scientists provided data and advice to a WHO Evidence Review meeting on a new type of bednet. The outcome of the meeting was a guidance document for countries.