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Innovative Vector Control Consortium

Working together to save lives

Annual Report 2009

IVCC
COMBATING INSECT BORNE DISEASE

The IVCC is a Product Development Partnership (PDP) established as a not for profit company and registered charity. We are committed to the development of new insecticides for public health vector control and of information systems and tools to enable new and existing pesticides to be used more effectively.

Vector control has been a cornerstone of every effective campaign against malaria and dengue. These interventions are under threat from the emergence and spread of insecticide resistance and limitations in the ways that insecticides are used.

As more elimination campaigns are funded, so the need to improve the effectiveness and affordability of vector control increases.

Our mission is to improve health by enabling partnerships for the accelerated development and delivery of new products and tools that increase the effectiveness and efficiency of the control of insects which transmit disease.

Contents:

Chief Executive Officer's Report

The IVCC was established almost five years ago to stimulate the development of new public health pesticides, better formulations of insecticides and new diagnostics and information systems to revolutionise monitoring and evaluation of vector borne disease control programmes.

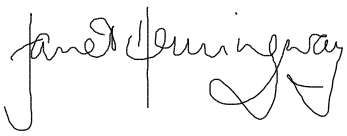
The initiative was timely given the massive increase in malaria, dengue and other vector borne disease control activities during the last four years, all of which are primarily based on increasing control of the insect vector. The increase in indoor residual spraying and insecticide impregnated bednet distribution in Africa has already resulted in an increase in pyrethroid resistance in the two major insect vectors, bringing added urgency to the search for new active ingredients (AIs) that can replace the pyrethroids before they fail catastrophically.

I am delighted to report that the first of the IVCC-sponsored new formulation products will shortly be released onto the market, providing alternatives to pyrethroids for IRS with a similar residual life. The new AI pipeline is also healthy with initial programmes with several industrial partner companies bringing promising new leads to light that are under active investigation.

On the diagnostics side, the first batch of products are nearing the end of their development phase. The decision support system for malaria is undergoing in-country validation and we expect the first large-scale operational implementation to begin in 2011. The dengue decision support system will build on this platform, with a multi-disease decision support system that can be simply tailored to the end users' needs. The multi-disease approach has evolved out of development work on the original decision support system and we expect it to be ready for release later this year.

Methodologies for more accurate diagnosis of resistance have been published and are being simplified for operational implementation. The first diagnostic kit for insecticide quantification is now undergoing field validation. Our efforts over the next year will focus on the implementation of these diagnostics and expanding the vector range they cover from the African into the Middle Eastern and Asian vector species.

Our major donors continue to be very supportive of our programme, although further funding will still need to be raised if we are to achieve our ambitious targets over the next decade. Our healthy pipeline of much needed products, and growing track record of success, should make it easier to get the backing of the global donor community. We look forward to working with them over the coming months and to achieving real reductions in disease transmission through the application of the products and systems we are supporting.



Professor Janet Hemingway,
Chief Executive Officer, IVCC

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Chief Executive Officer, IVCC

DID YOU KNOW?

One in every five childhood deaths in Africa is due to the effects of malaria.

Chief Operating Officer's Report

Tom McLean answers questions about the growth and development of the IVCC over the last year.

Tom McLean,
Chief Operating Officer, IVCC

What have been the major achievements for IVCC in 2009?

2009 has been the year in which the projects initiated in the previous two years really started to deliver impressive results. Long lasting indoor residual spray formulation products from our industrial partners hit their target performance criteria and moved into the commercialisation phase, information systems for vector control monitoring and evaluation were field validated, and the active ingredient data mining and screening projects started to throw up large numbers of hits.

What have been the key lessons learned in the last year?

I think the central lesson for IVCC has been the need to step in to some projects and assert businesslike quality assurance and delivery standards. At the start of 2009, with the help of our partners, we introduced Terraframe, a commercial software house, to create parts of the Malaria Decision Support System when it became clear that our institutional partners were just not set up to deliver to the required timescales. That has been a great success and the project is now back on track and has delivered the software to a far higher standard than could have been possible before.

In the same way, we are finding that data variability from trials is causing problems in interpreting some trials and indicating a need to upgrade statistical experimental design and quality assurance standards in the trials sites that we use.

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How are IVCC's interactions with the wider world of vector control evolving?

In 2009 we recognised the need to communicate far more widely with the wider vector control community and especially the malaria community. We need to be working closely with the normative bodies who create global policy on such issues as resistance monitoring and management, with the regulatory authorities who are the gatekeepers for these products, and with the country disease control managers who will eventually use the products we create. The realisation of this need led us to meet these audiences in a wide variety of fora in 2009 and culminated in a major presence at the MIM conference where we demonstrated our decision support system products to some 500 people.

As we go forward from this start in communication IVCC will adopt a convening role in the arena of resistance monitoring and management and a supportive role in the evolution of regulatory process.

What are the key issues for IVCC in 2010?

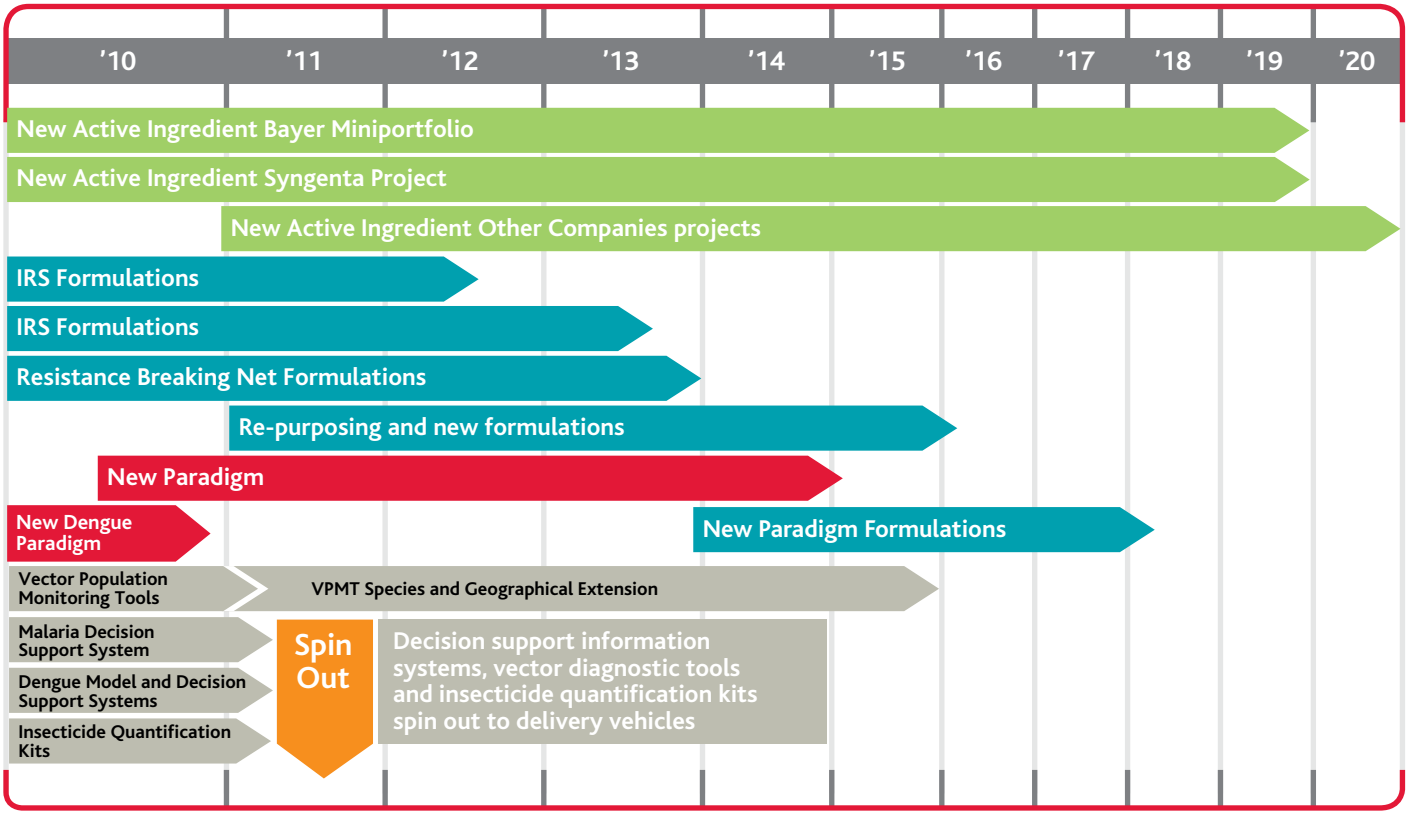
The primary issue for IVCC now is future funding. Our overall strategy calls for a funding stream of $150m over the next 5 years and we will have to fight hard to find that. We need to show delivery of results and great value for money.

DID YOU KNOW?

Approximately half of the world's population – 3.3 billion people – is at risk of malaria, particularly those living in lower-income countries.

What do we need to do?

The IVCC Roadmap 2010 to 2020



IVCC Core Objectives for 2010-2015

1. Advance and expand the portfolio of AIs Discovery and Development programmes so as to provide three new AIs by 2020.
2. Complete the development of the existing Formulation and Re-purposing portfolio to deliver products that will enable rational and effective resistance management programmes and reduce by ~25% the cost of application of IRS programmes.
3. Establish a process and capability for the rapid assessment of the effectiveness of New Paradigms in Vector Control so as to increase the number of available interventions and define target product profiles for AI and formulations required so as to enable rapid development, widespread adoption of and effective use of those that are verified.
4. Complete the development of a set of malaria and dengue control decision support systems, analytical tools and strategies, and establish an effective process for these products to be widely and sustainably implemented so as to enable effective disease control and resistance management programmes.
5. Contribute to, and influence the global debate on innovative vector control and engage the processes of regulation, policy and advocacy to ensure swift and widespread adoption of best practice.
6. Develop an organisation that is capable of delivering the ongoing Mission Statement of the IVCC, with an evidence-based roadmap of future needs and a strategy for their resolution.

The IVCC Roadmap

New Active Ingredients (AIs)

IVCC's long term objectives call for the creation of three new AIs that are unaffected by current resistance mechanisms by 2020. Two substantial data mining rescreening programmes are under way to build the candidate base from which these AIs will be developed. In addition molecular design projects will provide targeted candidates for development. A third screening programme is at proof of concept stage and several other proposals are in preparation. It is well known that new AI discovery has a very high attrition rate and that success in this field requires the creation of a large and diverse pool of candidates.

Formulations and Re-purposing

The formulation and re-purposing development projects initiated in 2007 are planned to deliver, in 2012-2013, long lasting IRS products and insecticide combinations which will mitigate the effects of pyrethroid resistance. Our portfolio of Proof of Concept studies will give rise to a smaller number of re-purposing projects to be initiated in 2011, and yielding products in 2016 that will bring alternative agricultural insecticides to bear on the vector control market.

New User Paradigm and Target Product Profile (TPP) for Vector Control

We have identified that a key barrier to innovation in vector control is the lack of an established user driven intervention paradigm. We have started the process of consultation with a broad range of stakeholders to develop a coherent, efficient process for the establishment of such a paradigm and plan to begin work to develop the products, protocols and distribution routes for such a product. Concepts for innovative product approaches to address this paradigm have already been proposed by our industry partners.

Verification of a new paradigm will feed back into the design of the new AI TPP and spark a new round of formulations designed to achieve that paradigm.

Information Systems and Tools

The IVCC projects in Information Systems and Tools will come to fruition in late 2010, and emerge as a series of first generation products. IVCC is currently planning the establishment of suitable vehicles to take these products forward and help the disease control programmes to implement them broadly and sustainably within the disease endemic countries.

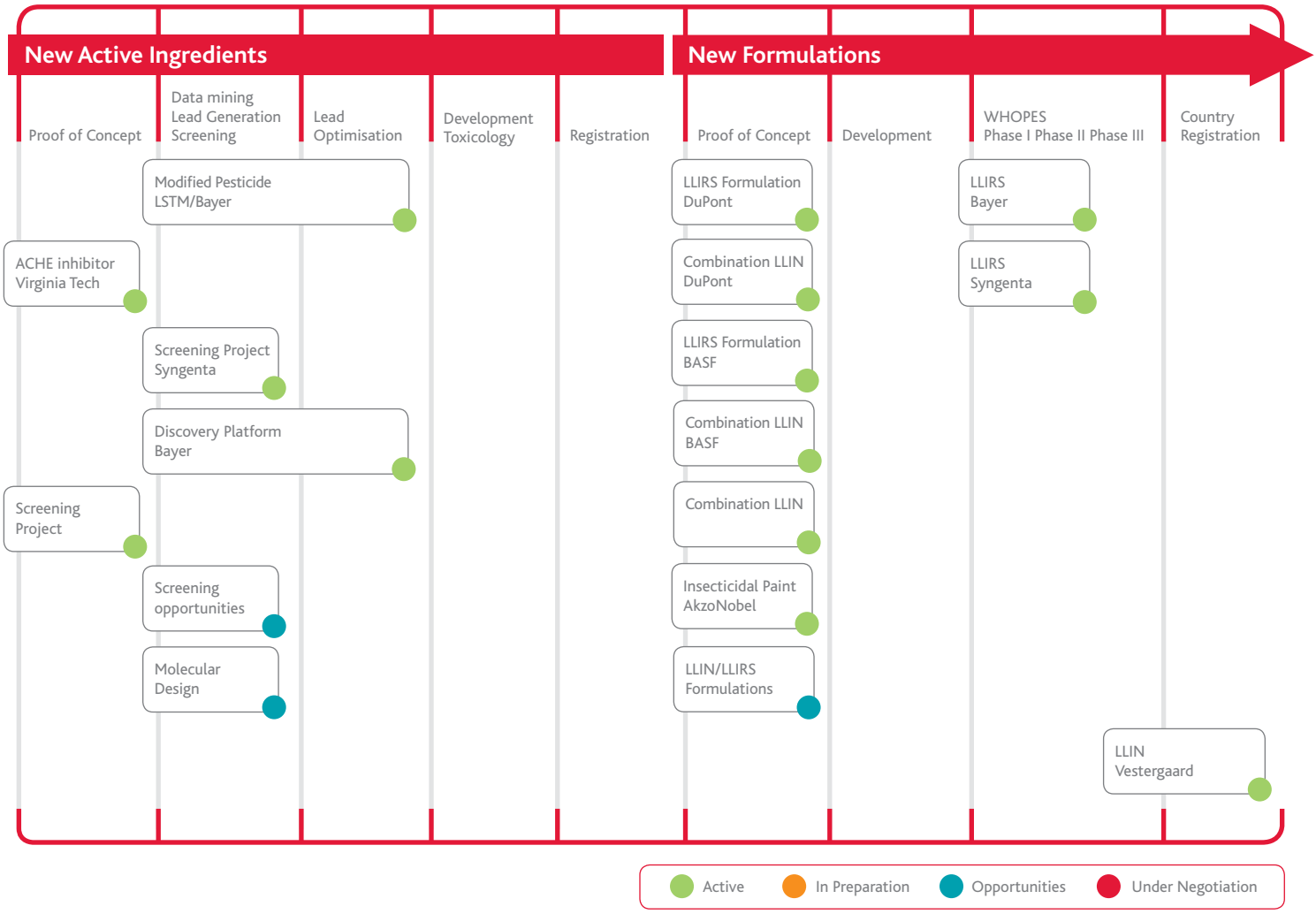
DID YOU KNOW?

Two-fifths of the world's population are now at risk from dengue.

PHP project updates

The IVCC has an actively managed portfolio of PHP projects in various stages of preparation. The PHP portfolio is divided into projects looking for new Active Ingredients for insecticides and those looking to optimise insecticide formulations using new technologies or by re-purposing existing agricultural insecticides.

Our current portfolio



DID YOU KNOW?

In Africa, a child dies from malaria every 45 seconds.

Active Ingredient Projects

LSTM/Bayer Modified Pesticide new AI

This project is focused on the synthesis and development of at least one novel insecticide based on a known insecticide backbone with the potential to control malaria vectors and crop pests, including those with an acquired cytochrome P450 dependent (monooxygenase based) resistance mechanism. The new product will involve novel chemistry and approaches that are fully patentable. Utilising the insecticide backbone as a starting template will increase the probability of producing a molecule with appropriate development characteristics and will also help to ensure that the new insecticide could be produced using existing plant capacity, thereby reducing the cost of development and production significantly.

In the first phase of the project the initial lead compounds have been synthesised and activity has been demonstrated against resistant strains for a number of these compounds. The compounds that have demonstrated activity are now being optimised and taken through further secondary screening programmes as well as continued screening against resistant and susceptible mosquito strains to select candidates for further development.

The aim of the project is to produce an optimised list of potential development candidates by the end of 2010 which can be considered for the next phase of the new active ingredient development process.

Project Leader: Steve Ward, Liverpool School of Tropical Medicine (LSTM)
Partners: Bayer, LSTM, University of Liverpool
Contact: robert.sloss@liv.ac.uk

Bayer Public Health Insecticides Discovery Platform

This project is focused on the discovery of at least one novel contact insecticide, with a novel mode of action, and the potential to control malaria vectors. The new developed insecticide will not be affected by known resistance mechanisms in order to help mosquito control programmes manage resistance issues. The project is making use of Bayer's historic chemical library to generate potential leads in order to develop totally new active ingredients for vector control insecticide products.

The project involves researching the chemical library for potential vector control insecticides using any data that has already been collected to identify compounds that may have activity. Once the compounds are selected they will be screened for activity against mosquitoes and their mode of action determined. The most interesting compounds from the initial screening programmes will be used to direct analogue synthesis to optimise the activity of a class of chemistry against adult mosquitoes whilst minimising the potential toxicity.

This project is due to run for 3 years and began in September 2009. Several interesting classes of chemistry have already been identified. This project is the first phase in the development of a new active ingredient for vector control that will take approximately 10 years to deliver a product to the market.

Project Leader: Volker Gutsmann, Bayer
Partners: Bayer, Medical Research Council SA, LSTM, London School of Hygiene and Tropical Medicine (LSHTM)
Contact: robert.sloss@liv.ac.uk

Syngenta Vector Control New Active Ingredient Screening Project

This project is aimed at identifying one or more lead areas of novel chemistry that are free of cross-resistance to existing chemistries used for adult mosquito control and are suitable for optimisation and potential development into products for the control of adult mosquitoes via appropriate delivery systems.

The project involves reviewing the available biological data from Syngenta's historic chemical collection and from existing insecticide research projects to select compounds and classes of chemistry that may have potential as vector control insecticides. These compounds are then screened against adult mosquitoes to produce a portfolio of compound and chemical class hits to be reviewed as potential areas of chemistry to optimise in a later project.

Syngenta have completed their search of their historic chemical collection and identified compounds for testing. They have developed an adult mosquito screening method, and have begun to screen these compounds. The hit rate is encouraging and promising numbers of novel mosquito-active areas of chemistry have been discovered.

This project is due to run for two years and began in August 2009. This project is the first phase in the development of a new active ingredient for vector control that will take approximately 10 years to deliver a product to the market.

Project Leader: Andy Bywater, Syngenta
Partners: Syngenta, LSHTM
Contact: robert.sloss@liv.ac.uk

PHP project updates

Active Ingredient Projects

Formulation and Re-

Proof of Concept projects

A third company has completed a successful proof of concept screening project in which they reviewed their chemical library and screened up to 1,000 compounds from several different chemical classes against adult mosquitoes. The hit rate has been promising and we plan to agree on a full project with the company in 2010.

Virginia Tech have started a proof of concept study to demonstrate contact toxicity of novel bivalent carbamates against susceptible and carbamate resistant strains of mosquitoes. If this proof of concept study proves successful a full project will be proposed to develop novel bivalent carbamates for vector control and assuming success would result in a new product based on a new active ingredient being available approximately 10 years after the start of a full project.

Projects in Development

Three other agrochemical companies have expressed initial interest in screening their chemical libraries for new vector control active ingredients. The IVCC has also had contact with a contract screening organisation which also owns a chemical library. This offers the IVCC the possibility of screening further chemical libraries unattached to the major crop protection companies, but still containing chemistry with potential for insecticide activity.

Bayer Long Lasting Deltamethrin IRS Formulation

The aim of this project is to develop a long lasting residual formulation for Indoor Residual Spraying (IRS) programmes to improve malaria vector control in disease endemic countries. The formulation will use proprietary technology to dissolve an active ingredient into a polymer. The concept is based on the idea that a polymer can be used as a barrier between an AI and an aggressive surface, to increase the probability of producing a long lasting residual formulation.

The new formulation will reduce the cost and logistical problems associated with IRS spraying in endemic countries. Long lasting formulations would allow a reduction in the number of application rounds per year, significantly decreasing the application cost. The reduction in cost achieved would reduce IRS treatments to similar operational costs as current insecticide treated material types of control. Deltamethrin was used as the AI to develop the first new formulation.

Bayer have now completed the development of a deltamethrin formulation based on patented technology to deliver a long lasting residual effect. In laboratory trials it has shown 12 months residual effect on concrete and wood surfaces and nine months on mud surfaces. The experimental hut trial work is continuing, the latest data confirms residual activity up to 36 weeks on all surfaces.

Bayer have taken the decision to commercialise the formulation and will take it through the WHOPES process and develop a regulatory package for the formulation.

DID YOU KNOW?

There were 247 million cases of malaria in 2008, causing nearly one million deaths, mostly among African children.

purposing Projects

Syngenta Long Lasting non Pyrethroid IRS Formulation

Indoor Residual Spraying (IRS) is a key intervention for malaria prevention. There are significant challenges to the continued use of DDT and pyrethroids due to regulatory pressure and insecticide resistance, and therefore long lasting products with different modes of action are required. Current WHO recommended carbamate and organophosphate formulations typically have a very short residual effect of three months which can lead to increased product and logistical costs compared to longer lasting products. Therefore, a non pyrethroid product that can deliver at least six months control of mosquitoes will help deliver cost-effective IRS and an opportunity to help manage pyrethroid resistance as part of an integrated program with nets and pyrethroid-based IRS.

The aim of this project was to develop a long lasting non pyrethroid IRS formulation using advanced microencapsulation technology to provide at least of six months residual control of malaria mosquitoes on all typical wall surfaces. Syngenta has now developed a new microencapsulated formulation of the WHO recommended insecticide, pirimiphos-methyl, which has demonstrated at least eight months residual activity in laboratory and field trials.

Experimental hut trials conducted at three different sites in Tanzania, Benin and Côte D'Ivoire have confirmed that at least eight months residual efficacy has been achieved on wood and concrete surfaces and six months or more on mud, which is a significant improvement on current products. Syngenta have decided to commercialise this formulation and the product has been submitted to WHOPES for evaluation. The product will be available for malaria control program use from 2011, depending on country registrations.

Vestergaard resistance breaking LLIN

Vestergaard have developed a pyrethroid based long lasting net aimed at maintaining its efficacy in areas where pyrethroid resistance is high. The IVCC has designed a community based trial aimed at showing whether this product has a significant impact in areas where pyrethroid resistance is prevalent. The sites have been selected for this trial and the work has started.

Proof of Concept projects

The IVCC has tested two DuPont agricultural insecticides for their potential to be used as IRS and ITN insecticides. These insecticides have different modes of action to those currently used in vector control. Both of these insecticides have shown some potential as vector control IRS and ITN insecticides and we are currently discussing a possible full project with DuPont.

The IVCC has completed another proof of concept study looking at alternatives to pyrethroids for ITNs. This project has produced some interesting and positive initial results and we are discussing a potential full project with the industrial partner.

The IVCC has started a proof of concept study with BASF looking at the potential for one of their currently approved agricultural insecticides to be used in vector control as an IRS and LLIN. This insecticide's mode of action is different to those currently used in vector control. If this project proves positive for both or either intervention, a full development project will follow.

A proof of concept project has recently been agreed with AkzoNobel to test whether modern surface coatings technology can be used to deliver very long lasting IRS formulations (2-5 years residual activity). If this project proves successful a full development project will follow.

Interventions Consortium Information Systems & Tools (IS&T) portfolio

To effectively control insect vectors of disease, policy makers and programme managers must have the information that allows them to choose the right control strategy for each situation. To achieve this, the IVCC is developing a range of systems and tools to support decision making in vector control programmes.

It is now widely accepted that vector control can be highly effective in reducing the burden of diseases like malaria and dengue. In fact in some cases, vector control is the only intervention proven to reduce disease levels. Effective planning, quality assurance (QA) and monitoring and evaluation are vital to ensuring that vector control measures achieve their full potential impact; and in large-scale intervention campaigns carried out in inhospitable environments, this can be a major challenge.

To help ensure that policy makers and programme managers have the information they need to plan and implement effective control strategies, the IVCC is developing a range of systems and tools to support planning, information management, decision making and QA.

At the core of our development programme are Decision Support Systems for malaria and dengue. Operated through a user-friendly computer based interface, the DSSs will hold a range of relevant data, which can be presented in easy to interpret graphical and map-based outputs. This will help policy makers and programme managers ensure that resources are used most effectively. We are also developing modelling software to help programme managers forecast the spread and growth of the insect vectors that spread dengue and the likely rates of disease development.

To work effectively these systems need good quality, timely information. Part of our development work therefore has been to develop systems for the collection of field data and the integration of data already available. Accurate data on insecticide resistance and its underlying causes is one example of the information that control managers need to maintain the effectiveness of their campaigns. The IVCC's Vector Population Monitoring Tool project is developing kits that can be used in disease endemic regions for monitoring resistance and to determine its underlying molecular basis. These kits will also allow programme managers to quickly identify the vector species present and the diseases they are carrying.

To maintain high QA standards in IRS campaigns and in insecticide treated bednets and materials, the IVCC is supporting the development of a further range of test kits. The Insecticide Quantification Kit project will provide a quick, simple and affordable means of measuring insecticide concentration, allowing programme managers to ensure that treated surfaces, bednets and other treated materials continue to provide the protection needed.

Vector Population Monitoring Tool (VPMT):

VPMT

Vector control programme managers need up to date information on mosquito populations to ensure that the interventions they plan are as effective as possible. Data on mosquito species, infection status and resistance to insecticides are vital elements in planning successful interventions. However, the current means of gathering this information is costly and inaccurate. Monitoring for each of these traits is currently performed using individual tests, some of which require sophisticated equipment and expensive consumables. Furthermore, these tests are not reliable for the detection of insecticide resistance at low levels.

The IVCC is funding the development of a simple molecular biology kit which will enable scientists in disease endemic countries to reliably identify the mosquito species, infection status (malaria positive or negative) and the presence of insecticide resistance genes by detecting a gene or sequence of DNA.

One example is resistance to pyrethroid insecticides. Gene mutation has resulted in the development of mosquito populations which are less vulnerable to insecticides. Bednets treated with pyrethroid insecticides are the primary method of malaria prevention in many countries so resistance to pyrethroids is of great concern for malaria control programmes.

The first indication of resistance development is usually the failure of control programmes. The new kit is designed to screen the DNA of individual mosquitoes to determine whether they carry the resistance mutation, allowing programme managers to detect resistance earlier and crucially before control failure has occurred. This will give these health professionals more time to respond by changing insecticides or altering control strategies.

Following successful field trialling in Africa, VPMT protocols are now being used routinely in labs in South Africa to support the MDSS. A number of protocols have been published and are now available. Work will continue until the end of the current funding round in 2010 to identify novel markers of metabolic resistance in both *Anopheles gambiae* and *Aedes aegypti* from a range of field collected strains. Candidate resistance genes are still being identified, and tests and protocols being developed. The next funding round will commence in 2010, and will see the expansion of the VPMT into new regions and new malaria vectors.

Project Leader: Martin Donnelly, LSTM
Partners: Colorado State University (CSU), Rothamsted Research, Agricultural University of Athens (AUA)
Contact: m.j.donnelly@liv.ac.uk

Insecticide Quantification Kit (IQK):

IQK

Bednets and Indoor Residual Spraying (IRS) are major control measures in the fight against malaria and other diseases carried by insects.

Apart from carrying out logistically complex and unreliable bioassays in the field, the only way to check that protection is being provided by a spray or treatment intervention is to measure the actual amount of insecticide residue remaining.

Such information is also important for local manufacturers of bednets who are now moving into the production of more technically complex Long Lasting Insecticide Nets (LLINs). Currently, the level of insecticide has to be measured using gas chromatography or high performance liquid chromatography. These methods are expensive and technically demanding, requiring skilled staff and sophisticated laboratory and insectary facilities.

This project is producing simple, cost-effective and user-friendly kits for monitoring insecticide residues on insecticide-treated materials. We now have a pipeline of simple kits for a range of relevant insecticides (including pyrethroids and DDT), some of which are in the final stage of development and are currently being field trialled in Africa. Work is also continuing to broaden the usability of the test kits both in terms of application and products detected.

Project Leader: John Vontas
Contact: vontas@imbb.forth.gr
Partners: LSTM, LSHTM

DID YOU KNOW?

Malaria was present in 108 countries and territories in 2008.

Information Systems & Tools portfolio (continued)

Malaria Decision Support System (MDSS):

MDSS

The effective control of malaria within a region requires programme managers to have access to the most up to date information on the disease in order to best direct interventions against mosquitoes. The Malaria Decision Support System (MDSS) is a computer package that collates data on disease incidence, vector populations (including density and insecticide resistance) and intervention activities and presents this information in a web-based, real-time geographical format.

The MDSS development is a collaboration between the Medical Research Council of South Africa, the National Malaria Control Programmes in Malawi, Mozambique and Zambia, Liverpool School of Tropical Medicine, and Colorado State University. Field data collection is taking place in Malawi, Mozambique and Zambia.

The MDSS brings together all the key indicators needed for effective vector control into one bespoke system customised for the needs of the country or region. The ability to view the outcome of interventions in a number of environmental settings and differing operational challenges further increases the usefulness of the MDSS to programme managers looking to optimise their system.

Sentinel sites have been established in Malawi, Mozambique and Zambia. This is combined with survey, clinic and spray data to provide the full data set needed for the operation of the system.

The MDSS IT infrastructure will be completed in 2010, and in-country testing has been carried out.

The MDSS is being developed alongside, and wherever possible, in collaboration with initiatives from other key players including the Malaria Control and Evaluation Partnership in Africa (MACEPA), the President's Malaria Initiative, the Centers for Disease Control and Prevention and the World Health Organisation.

Project Leader: Mike Coleman, MRC SA
Partners: NMCPs Malawi, Mozambique & Zambia. LSTM. CSU
Contact: mcoleman@liverpool.ac.uk

Dengue Decision Support System (DDSS):

DDSS

Dengue is the most common mosquito-borne viral disease in tropical and subtropical areas of the world. More than 50 million cases of dengue fever and several hundred thousand cases of the more severe dengue hemorrhagic fever are estimated to occur each year.

Because a vaccine against dengue virus is still lacking, control of the mosquito vector is the primary option for disease prevention and control. Currently employed vector control strategies have, however, not been adequate to combat dengue and novel tools and approaches are desperately needed.

One key aim of the Dengue Decision Support System (DDSS) project is to create, optimise and distribute a system which will provide up to date information on all aspects of mosquito vectors and dengue to enable control programme managers to implement, evaluate and refine locally appropriate disease prevention and control strategies.

The DDSS will provide capacity for collection, management and analysis of vector and dengue data in a standardised way. Data will be displayed in intuitive formats (e.g. maps, graphs, charts) to support the implementation of locally appropriate vector/dengue control programme strategies and evidence-based decision making. A framework for the DDSS has been developed and software to enable its operation is being developed. We expect the software development to be completed in late 2010.

DID YOU KNOW?

50 million cases of dengue infection occur worldwide every year.

Aside from the DDSS itself, the project is developing novel strategies for proactive vector and dengue surveillance and control, including:

- Use of Google Earth™ to display DDSS generated data on an image of the physical environment
- 'Casa Segura' – a 'safe house' proactive vector control approach based on use of long-lasting insecticide-treated materials within the home as window curtains and door drapes
- Syndromic surveillance for rapid detection of dengue outbreaks to enable a quicker, more focused vector control intervention.

The DDSS project is an international collaboration including academic partners in the United States and Mexico. Field testing of elements from the DDSS system has been carried out in Mexico, and a major Casa Segura field trial began in 2009.

Project Leader: Barry Beaty, Colorado State University (CSU)
Contact: bbeaty@colostate.edu

Dengue Model (DM):

DM

Current efforts to reduce dengue burden largely focus on prescribed vector control guidelines that fail to consider variations in dengue transmission dynamics between seasons and among different locations.

Quantitive models are the best way to account for inherent variation in dengue transmission and to predict how fluctuations in local dengue mosquito vector populations will impact the incidence of disease among humans.

The IVCC is supporting the development of a user-friendly computer model for simulating populations of the dengue mosquito vector *Aedes aegypti* and dengue virus transmission based on location-specific data; specifically, climate, mosquito biology and behaviour, virus factors, human demographics and immune status. Various control interventions, such as insecticide space spraying, removal of mosquito development sites, insecticide-treated materials and vaccines can be introduced into the programme to assess the relative impact of individual or combined disease control strategies.

The newly-developed Windows™ version of the programme has undergone extensive evaluation to confirm full functionality.

Simulation results have been compared to field-derived data collected in the Amazonian city of Iquitos in Peru by the University of California at Davis and the United States Naval Medical Research Institute Detachment. Work also continues to improve the functionality and usability of the system. The validated programme will be translated into languages other than English.

Our goal is to make the programme freely available as a component of the Dengue Decision Support System, so that at a variety of different levels (eg national, regional or local) public health, vector control or government officials can contrast and select surveillance and control options that are best for their particular circumstances. The simulation programme will aid vector control programme managers, public health officials and policy makers in the development of more effective public health goals, control targets and disease reduction strategies.

Work on the integration with DDSS will begin in 2010. Field testing will also be undertaken by us and by third party collaborators.

Project Leader: Thomas W Scott, UC Davis
Contact: twscott@ucdavis.edu

MDSS: A personal perspective

Miguel Orlans is a systems analyst and project manager who joined the MDSS team in 2009 and is playing a pivotal role in shaping and building the system.

Miguel Orlans, MDSS Systems Analyst

Here he describes how he became involved, the challenges the team faced as the complexities of what they were building unfolded, and how despite having contracted malaria twice, he was largely unaware of the importance of vector control until his involvement with IVCC:

After graduating in electronic engineering and working for a technology company in Belgium, I moved to South Africa and worked in several IT roles for a leading technology group. I left some years later to develop a business as an independent consultant, focusing on business analysis and project management related to IT systems, mainly for global financial institutions.

My initial involvement with the project was a workshop in December 2008 to define the strategy for the further development of MDSS.

After this, it was clear that a detailed functional specification for the system was required, which I agreed to write, along with a project plan. As the project unfolded it soon became clear that the configuration and flexibility of the system that everyone wanted to build made the management of the project much more technically involved, requiring specialised IT experience.

I joined the team as assistant project manager, interfacing with the development team to deliver a system capable of the operational functionality that was being planned by Dr Marlize Coleman. When Marlize went on maternity leave, I took on full responsibility for the delivery of the working system.

Much of this project has broken new ground as nothing like it has ever been done before. The subject matter expertise was abundant and the software development team were very dedicated and competent, but no one was experienced in project managing something so big and technically demanding.

DID YOU KNOW?

In heavy-burden countries, malaria accounts for up to 40% of public health expenditure and up to 50% of inpatient hospital admissions.

"The biggest thing for me personally will be when MDSS is fully established and is saving lives. The software is only a small part of a much bigger picture but it's enough knowing that I have contributed to something that will make a mark on the million lives lost each year to malaria."

We began with a good understanding of the scope of work but as we fleshed out the specification it became apparent that although the functionality was agreed, the amount of flexibility and configurability that was required to make the MDSS a system that could be accepted in any target environment massively increased the volume and complexity of work.

However, we still had our budget limits and our deadlines to meet. We had to produce a working system within six months and after four months we were still working on complicated technology concepts. The first phase delivered a proof of concept for the system but it was a great relief to the team that a follow-on project was agreed for an additional six months, where we could clean up what we had and add a huge amount of value building on what we had developed in phase 1. I was working up to 12 hours per day and due to the eight hour time difference between South Africa and Colorado, where the project was 'happening', I found myself working until 3am most days, so that I could respond to email traffic in real time.

However, we all understood the challenge and the magnitude of what we were doing, and we worked as a dedicated team. I believe we can all be truly proud of the product that is now ready for roll out.

I had little knowledge of vector control before I started work on this project. Although I have contracted malaria twice, my only experience of a control intervention before I joined had been when the guest house I was staying at in Malaysia was 'fogged' with insecticide after another resident contracted dengue. But after dealing with subject matter experts for more than a year and writing the specification, I now have a fair idea of vector control and how it all ties in to each other, breaking the cycle of disease transmission.

Working in vector control is hugely rewarding. What I enjoy most is the dedication of everyone involved. Unlike financial services, it's not about self-worth or financial gain, it's about achieving the goal and working together with a team, supporting each other rather than pointing fingers and laying blame.

All the pressure and stress is self-imposed, trying to do the best within time and budget. The attitude here is "this is what we want to do, how can you help us?", whereas I was used to "this is what we demand, deliver the impossible or suffer the consequences." I have sacrificed blood, sweat and tears on a project that will actually do some good in this world rather than just financially benefiting a client and I've learned to feel good about what I'm doing.

The biggest thing for me personally will be when MDSS is fully established and is saving lives. The software is only a small part of a much bigger picture but it's enough knowing that I have contributed to something that will make a mark on the million lives lost each year to malaria. It is a momentous project and I'm proud to be a small part of it. I'm now looking forward to the challenge of applying what we've learned to a dengue system, and hopefully in time to other diseases.

IVCC Finance

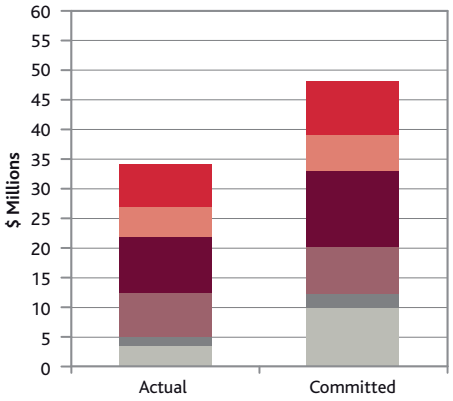
IVCC Funding History

Current Commitments

The level of research activity increased substantially within the IVCC during 2009. This is reflected in the increase in expenditure from $22m at the end of 2008 to $34m by the end of 2009. The levels of committed spend increased marginally from $45m to $48m over the same period.

This reflects the IVCC's risk averse policy and tightly managed processes and ensures future commitments are not made without additional funding secured. As the level of activity remains high the initial funding of $50m for the development of new insecticides and tools will be fully expended towards the end of 2010 and the beginning of 2011.

Actual and Committed Spend 2005-2009

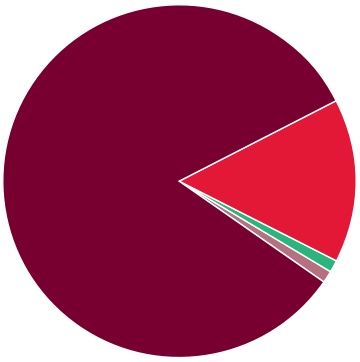


Key	Projects	Spend to 2009 ($)	Committed ($)
	New AI	3,440,076	9,792,069
	Formulation	1,549,826	2,197,994
	Kits	7,421,913	7,936,488
	Information systems	9,233,353	12,710,664
	Project related	4,980,267	6,100,649
	Core	7,178,260	8,889,528
	Total	33,803,695	47,627,392

Management & Administration

During 2009 management and administration costs were consistent with previous years and remain at around 14% of overall expenditure. ESAC and governance costs fell significantly from $432k in 2008 to $174k in 2009. Fewer governance issues following the company's incorporation and more efficient meeting planning has largely led to this reduction. Efficiency savings are actively pursued and it is envisaged that this level of expenditure will continue during 2010 and beyond without any substantial increase.

Expenditure 2009 ($)



Key	Expenditure Analysis	Total Spend ($)
	Project Expenditure	10,587,865
	Management & Administration	1,834,502
	ESAC & Governance	174,231
	Communications	151,055

Projects Completed

2009 saw the first of several projects completed since the IVCC was conceived in 2005. A total of seven projects finished during the year at a cost of just over $2m. These were all completed to time and with an overall financial saving of 18% over the original agreed budgets. It is expected that 2010 will see a substantial number of projects completing at an approximate total cost of $22m. Information Systems and Tools projects accounted for 90% of these, with the remainder part of the insecticide development program.

Future Funding Needs

In the current economic climate, securing additional funding is challenging. All PDP organisations face similar problems over the next few years as many donors scale back their charitable donations.

IVCC's strategic budget requirement for the next five years to deliver pipelines adequate for three new AIs, optimisation of the insecticide re-purposing opportunities, development of a consumer paradigm and extension of the Information Systems and Tools can be seen in the table.

External funding efforts have been focused on support to the Information Systems and Tools projects in 2009 and $18.8m in grants were mobilised from a wide variety of sources (NIH, Wellcome trust, TDR, Saudi Arabia and others). Future fundraising efforts will focus on support to insecticide development.

IVCC Strategic Budget Requirement (All funding sources)

Type	2011	2012	2013	2014	2015	Totals	%
New AI	6.44	8.30	25.96	32.39	39.37	112.45	73%
Formulation	2.55	2.96	2.07	0.89	1.02	9.49	6%
New Paradigms	1.00	2.07	2.14	2.22	2.30	9.72	6%
Information Systems and Tools	2.00	2.00	2.00	2.00	2.00	10.00	6%
Management & Admin	2.44	2.53	2.62	2.67	2.73	12.99	8%
Totals	14.43	17.86	34.78	40.17	47.42	154.66	100%

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