vector control

saving lives

ANNUAL REPORT 2014-2015

IVCC

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Ten years ago, in October 2005, IVCC signed its first funding agreement with the Bill and Melinda Gates Foundation. This launched IVCC on the trail of new vector control tools—especially new insecticides to combat insecticide resistance in malaria transmitting mosquitoes.

In 2006 IVCC employed its first staff, and began operations. All that has been accomplished over the past 10 years (see page 14) has come out of the relationships formed with a great group of committed partners and funders.

Over the past 10 years our industrial partners evaluated over four million potential insecticide compounds and narrowed them down to nine classes of novel active ingredients.

Several new insecticides are now within sight. This is no mean achievement when you consider that the last new public health insecticide was introduced more than 30 years ago.

The importance of vector control in controlling malaria is now well documented. The new insecticides we are developing with our partners are essential if the impressive gains in malaria control of the last 15 years are to be maintained.

MEASURING PROGRESS

Dr Pete Gething.
Associate Professor, University of Oxford.
Head, Malaria Atlas Project.

Recent work by the Malaria Atlas Project has provided new insight into the impact of vector control on malaria across sub-Saharan Africa

Our results provide the most compelling evidence yet that ITNs and IRS have been enormously effective at preventing malaria infection and illness for hundreds of millions of people

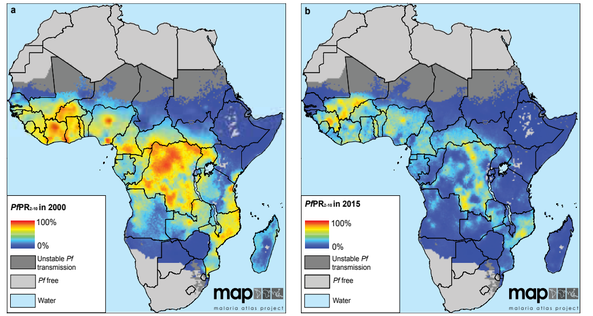
Since the year 2000, investment in malaria control in Sub-saharan Africa has grown twenty-fold. These funds have allowed the provision of vector control interventions—primarily insecticide treated bednets (ITNs) and indoor residual spraying (IRS)—on a scale never seen previously anywhere in the world.

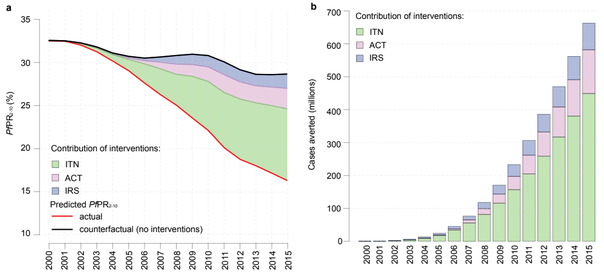
The rationale for deploying these tools on such a massive scale was built on solid foundations—a multitude of cluster randomized trials demonstrating the protective efficacy to both those sleeping under the nets or inside sprayed households and the wider community. But malaria is a complex disease, transmitted by a complex vector. What works in one location may, for reasons only partially understood, not work in another. The necessarily idealised conditions of a randomized control trial may not fully predict how an intervention will perform across the great diversity of malaria transmission settings of sub-Saharan Africa.

Over the last two years, the Malaria Atlas Project team in Oxford has been working to evaluate the impact that vector control and antimalarial drugs have had in reducing transmission since the year 2000. Rather than base our estimates on an extrapolation of control trial results, as earlier impact assessments had done, we opted to ignore those data and look for evidence of impact in an entirely different way. Our idea was to first assemble every line of data we could find that reported on levels of malaria endemicity or bednet coverage in communities across the continent at different points in time. We used these to generate detailed maps that reconstructed the changing landscape of malaria risk in Africa, and how these changes related to the way intervention coverage had been scaled up across the continent.

This approach allowed us to measure just how much malaria transmission has fallen: comparing the map of infection prevalence in the year 2000 with that of 2015 (*see Figure*), we see dramatic declines in many (although not all) endemic regions of Africa. Overall we estimated infection prevalence had dropped by 50% over the fifteen year period and the incidence of clinical malaria disease by 40%. Showing these declines was important: many in the malaria community were familiar with local success stories, but the profound shift in malaria endemicity across wide swaths of the continent had not been described this clearly before.

Perhaps more important was unpicking the relative contributions of different interventions (along with other factors like climate or urbanisation that may also have driven trends in malaria risk).





We estimated that ITNs alone had averted around 450 million malaria cases since the year 2000, with IRS (which is in less widespread use) averting a further 66 million (*see Figure*). Together, vector control was responsible for about 80% of the overall decline in infection prevalence across the continent.

These striking headline figures conceal substantial geographical complexity - we found the impact of ITNs and IRS to vary from place to place. It is also well known that, even where highly effective, these measures will rarely be enough to completely interrupt transmission on their own. Locally appropriate intervention mixes and innovative new tools, guided by robust data, will inevitably form part of any successful long-term approach.

Nevertheless, our results provide the most compelling evidence yet that ITNs and IRS have been enormously effective at preventing malaria infection and illness for hundreds of millions of people. This impact has been achieved with coverage levels still well below international targets, and the prospects for even greater reductions in transmission are clear if coverage continues to rise. Conversely, if enthusiasm for these more established approaches begins to wane, and if the growing threat of pyrethroid resistant anopheles mosquitoes goes unchecked, then it is almost inevitable that the impressive gains we describe will be eroded.

We estimated that ITNs alone had averted around 450 million malaria cases since the year 2000

MUCH TO CELEBRATE

IVCC is celebrating its tenth anniversary this year

In the next five years we face three major challenges. The first is to shorten the regulatory approval cycle

With our funders, our industry partners, scientific advisers and all of the IVCC team, we have much to celebrate. The basis of the truly seminal five year initial grant of $50 million from the Bill and Melinda Gates Foundation was the determination to find three completely new insecticide molecules so that the world could fight the deadly resistance which was building against the decades-old workhorses of insect vector control which had been, and remain, the backbone of the battle against malaria.

The use of insecticide treated bed nets and spraying of house walls with insecticides are estimated to have contributed over three quarters of the over 600 million cases of clinical malaria averted in the last fifteen years. The continuation of this progress is severely threatened by resistance and so, after screening over four million compounds, the success in identifying with our industrial partners several new compounds that overcome resistance and provide cover for the three new compounds needed is a real cause for celebration.

The first ten years has also seen the transition from a start up with a concept and a concrete target to a partnership with the challenge of bringing real products to delivery. They have also seen the transition from an organisation led by Professor Janet Hemingway, rooted in science but building partnerships with industry, moving to an organisation led by Dr Nick Hamon with his long industrial experience focussed on bringing the products through the licensing procedure to deployment in the global public health market.

Along the way the organisation has grown by recruiting new staff, many with industrial backgrounds and experience, while continuing to build on the essential science of our Expert Scientific Advisory Committees which is so freely given and of such value.

In the next five years we face three major challenges. The first is to shorten the regulatory approval cycle and have three of the suite of compounds which have been identified licensed for the market in endemic countries. If we follow the usual well-trodden regulatory path through different trials and regulatory agencies in various organisations and jurisdictions, this is a process that could take more than twelve years.

Resistance is building in a way that models show could, in a few short years, lead to over one hundred thousand additional deaths, climbing even further as existing methods fail, so such a delay is clearly unacceptable. None the less, society needs reassurance that the products are safe and do not carry concealed threats.

Thus all the actors in the regulatory process, from companies and trial sites through international organisations to national regulators need to come together to remove overlaps and redundancies from the process with the aim of at least halving the time required. IVCC will be a key participant and convener in this process.

Secondly there is the issue of funding. The Bill and Melinda Gates Foundation repeated their initial $50 million grant for the second five years; this was supplemented by grants from DfID (UKAID), USAID and the Swiss Agency for Development and Cooperation so that some thirty five or forty percent of funds now come from other donors.

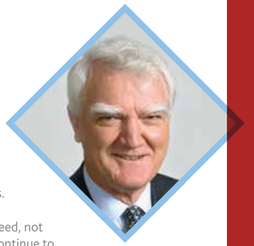
As we go into the next ten years we need, not only to convince existing funders to continue to fund this effort that is delivering such concrete results, but also to widen the range of funders.

These two challenges are complicated by a third challenge, which is to forge agreements between our industrial partners that in future the products must be rotated and used in such a way that the growth of insecticide resistance can be prevented.

The invaluable contribution of our commercial partners is not just access to their facilities and chemical libraries, but also their expertise in science and manufacturing, and the opportunity cost of diverting outstanding researchers from the commercial activities which are their lifeblood.

If we are successful in meeting these three major challenges we will be able to focus more attention on the mosquito vectors that do not simply bite at night, but during daylight and out of doors.

This, and the challenge of malaria prophylactics and treatment need to be addressed, and if malaria is ultimately to be eradicated all of these tools are necessary. Such eradication, even on a national scale, has to be the ultimate goal.



Sir Mark Moody-Stuart
Chairman, IVCC

COMPLETING THE MISSION

Getting new vector control tools quickly and efficiently to market will save more lives

Dr Nick Hamon
Chief Executive Officer
IVCC

IVCC is 10 years old, so we should allow ourselves a brief moment to celebrate and reflect. We have grown dramatically in scope and funding in the past few years, but growth 'per se' is not our goal. Businesses are judged on growth in market share, turnover and profitability, but IVCC is not a business and nor do we want to emulate one.

Our task is to work with partners to deliver life-saving vector tools and solutions to those that need them most, the intervention implementers and vulnerable people living in malaria endemic countries. Inherent in our mission is to contribute to the eradication of malaria and other neglected tropical diseases through vector control. Success will mean we eradicate ourselves as an organisation.

At this point in our lifecycle, IVCC has to grow in funding and expertise to deliver on the core mission; three novel insecticides with modes of action new to public health. Novel insecticides are needed where insecticide resistance is a growing threat, primarily to replace synthetic pyrethroids in long lasting insecticide treated nets (LLINs) and to provide alternative indoor residual spray (IRS) products.

More than 70% of IVCC's effort and funding is directed at active ingredient development, and this will have to grow significantly over the next five years if we are to take these chemistries through to market. Once we are confident of delivering three novel insecticides that can be used effectively in rotations or combinations where insecticide resistance is challenging performance, there will be no IVCC pipeline of novel chemistry.

There is a high cost to supporting the development phase of novel chemistry, but that cost is modest when measured in lives saved rather than sales growth or profits.

The process of taking an insecticide through development to market is much like that of a drug or vaccine. A new active ingredient needs to go through nearly 200 different studies over four years to demonstrate it is efficacious as well as safe for humans and the environment. We will have to learn how to formulate it, how to manufacture it cost-effectively, how to apply it, alone and in combinations and alongside other interventions such as drugs and vaccines as part of an eradication program. It then has to complete a regulatory review and WHO approval process before being available for use.

Existing insecticides used in LLINs and IRS were developed and registered first for agricultural use, so a great deal of pioneering work is going on in IVCC and across the stakeholder community to optimise the pathway to market, making novel insecticides available in the 2020-2025 time frame. This pioneering work is part of a major initiative called Innovation to Impact (I2I), designed to encourage innovation, improve efficiency and guarantee quality of vector control products.

In the next 10 years we expect to make available a full toolbox of technical solutions, and our focus will have shifted to delivery, access and optimising impact. For malaria eradication we need to be able to detect the human reservoir of infection, eliminate the parasite, and block transmission.

There is substantial evidence that LLINs and IRS have been extraordinarily effective at blocking transmission, preventing hundreds of millions of cases of malaria worldwide since the ramp-up of their use in 2000.

In addition, the importance of malaria vector control as a partner in Mass Drug Administration (MDA) is now well documented. In September 2015 a technical report for the WHO[1] concluded : 'The removal of vector control led to a sudden and large increase in all-age prevalence, and the subsequent MDA programme did very little to reduce this shift even in the short term. We predict, therefore, that an MDA programme of this type is insufficient to totally replace vector control, even at high levels of coverage'.

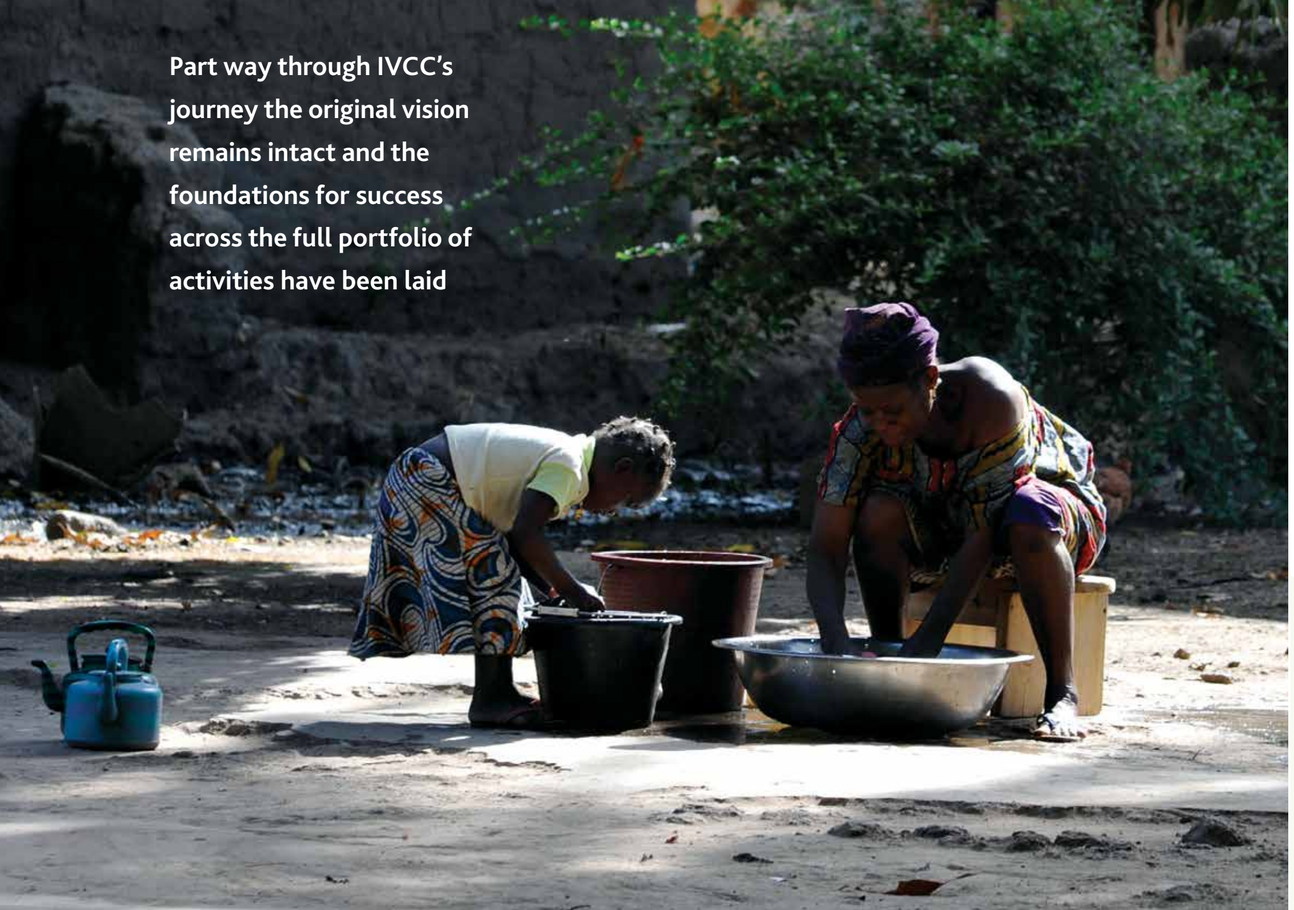
Without tackling the temporal transmission gaps (times during the evening when vulnerable people are not sleeping under a LLIN) or spatial transmission gap (locations where people are not sleeping under a LLIN, are outdoors or not protected by IRS), malaria eradication will be challenged. IVCC is working with funders and other stakeholders to identify technologies to 'mind the gap' and manage residual transmission.

What do we need to complete the mission? We need industry partners to stay the course, all stakeholders to work towards removing barriers preventing new products getting quickly and efficiently to market, and funders to increase their support, particularly over the next five years. If we can do this, we will have a robust vector control toolbox not only capable of supporting malaria elimination and eradication, but also available to tackle other vector borne neglected tropical diseases.

Vector control is a small and not particularly attractive market for research-based crop protection companies. However, contributing to the eradication of malaria represents an unparalleled opportunity for a company to demonstrate that it is not just 'best in the world' but can also be 'best for the world'. Agricultural science and technology will continue to save millions of lives. Some may argue that is priceless.

[1] *Consensus modelling evidence to support the design of mass drug administration programmes Malaria Policy Advisory Committee Meeting, 16–18 September 2015*

The high cost of supporting the development phase of novel chemistry is modest when measured in lives saved rather than sales growth or profits



Part way through IVCC's journey the original vision remains intact and the foundations for success across the full portfolio of activities have been laid

ROOTS

Two perspectives on the journey from IVCC's beginnings in 2005

Professor Janet Hemingway
Director
Liverpool School
of Tropical Medicine

The concept of IVCC was formulated in 1998. I was working with the late Brian Sharp monitoring the baseline susceptibility of Anopheles funestus in the cross-border malaria programme in South Africa, Mozambique and Swaziland. It was clear, as pyrethroid resistance was rapidly selected and caused a resurgence of malaria in South Africa, that had a number of diagnostic, data management and intervention tools been available, greater sustainable reductions in disease could have been achieved.

Brian and I formulated a proposal to develop these tools with input from academia, control programmes and industry and submitted a proposal to the Gates Foundation. Independently, Barry Beaty and Tom Scott approached the Foundation requesting support for a dengue vector control and virology programme.

Rick Klausner, then the Executive Director of Global Health for the Foundation called Barry and I to a meeting in Mexico in 2003, where he asked us to work together to combine the two proposals, focus them down onto vector control and resubmit a single proposal. A few months later Rick also suggested that Brian Greenwood from the London School join this initiative, as they had submitted a follow on proposal for vector control from work originating from their Gates Malaria grant. Two years of intense negotiation with the Foundation followed, refining the programme and educating the Foundation on vector control.

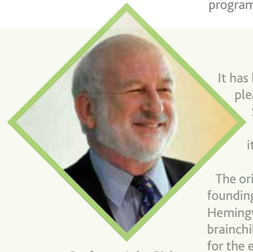
In mid 2005 Kate Aultman joined the Foundation and was tasked with working with me to finalise the submission. In December 2005 the Foundation approved an initial investment of US$50m. This came with a number of conditions.

In the first 6 months we had to start the diagnostics and data management projects, establish the consortium structure and legal framework under which the academic partners would operate, establish expert scientific advisory panels that would assess and advise on all project proposals and demonstrate that we could get appropriate industrial engagement to populate the new insecticides and formulation portfolio.

We successfully achieved all these targets and were formally given the approval to proceed with the programme and start to employ full time staff to take the consortium forward in 2006. As industrial engagement strengthened and products started to emerge in both the diagnostics and insecticide arms of the consortium, IVCC transitioned from a consortium grant to the Liverpool School of Tropical Medicine into a separate legal entity.

I have been fortunate as the Founder and initial CEO of IVCC to see it grow and flourish as a vibrant product development partnership for malaria and NTD vector control. Many individuals, companies, institutions and funders have contributed to this success. Ten years on we have already delivered new insecticide formulations into operational use for indoor residual spraying, data management systems that are being used by malaria and leishmania control programmes and diagnostics that are in operational use for quality assurance of spray programmes.

IVCC was originally envisaged as a 25 - 30 year programme for it to deliver all its objectives. Part way through that journey the original vision remains intact and the foundations for success across the full portfolio of activities have been laid. A success for which all involved can be proud.



Professor John Pickett
Chair of IVCC ESAC 1

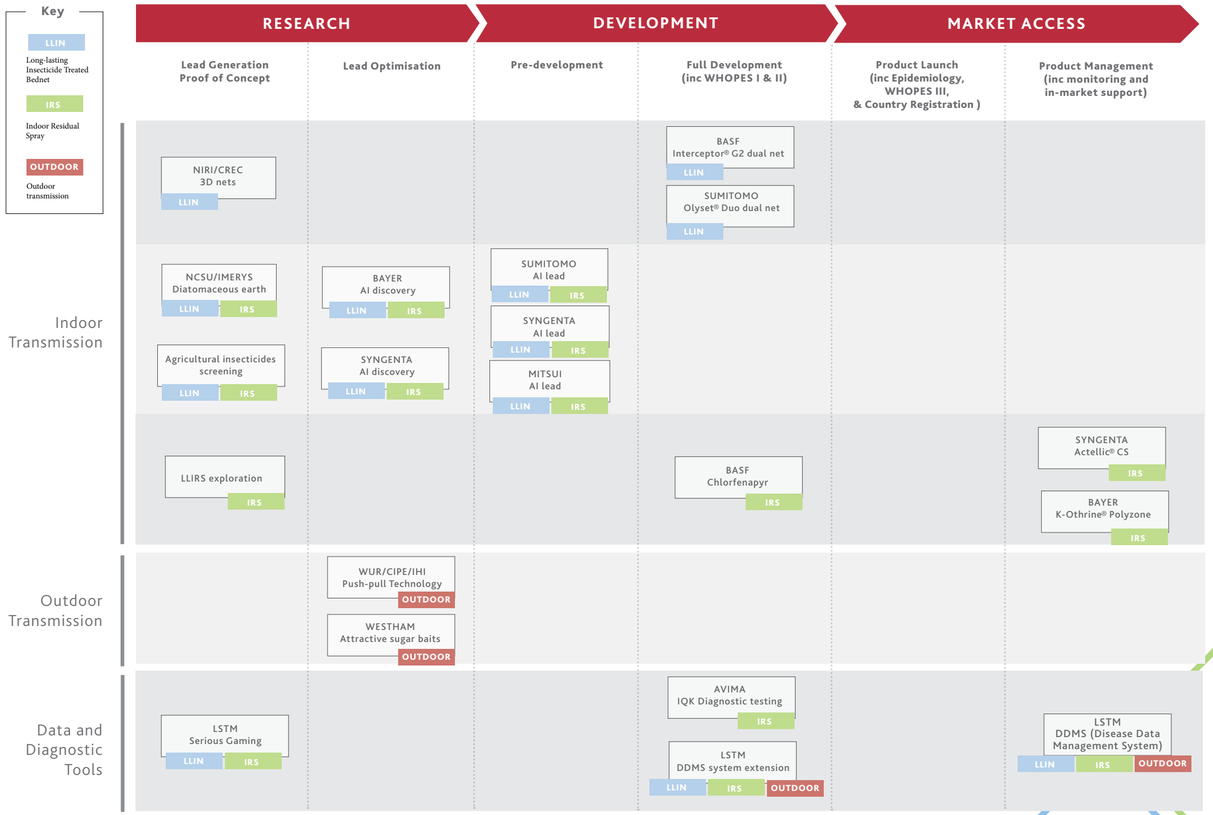
It has been a very great privilege and pleasure to Chair IVCC's Expert Scientific Advisory Committee 1 (ESAC) more or less since its inception back in 2006.

The original IVCC team and its founding Director, Professor Janet Hemingway FRS, whose original brainchild this was, was a great leader for the early and formative days.

I remember expressing both positive and negative comments arising from the assessment of the ESAC knowing that they would be assessed by a very astute team.
I think the earliest satisfaction was seeing that the advice the ESAC gave, and the way it was received and acted upon by IVCC, could lead rapidly to developments towards new active ingredients against pathogen vectoring insects.

I personally enjoyed working with the representatives of the BMGF, particularly Janice Culpepper and now Dan Strickman. It is crucial that our advice relates to the needs of the overriding funding agency, and that our critical assessment of what might generate a new intervention against human pathogen vectors impacts realistically on the aspirations of the agency.

IVCC PRODUCT DEVELOPMENT PORTFOLIO



MOVING PRODUCTS ON

The introduction of new chemistries to the market must be carefully managed

Sarah Rees
Portfolio Manager

Moving products on into full development will mean significant investment

Insecticide resistance is widely reported across Africa to all classes of public health insecticides approved for use today. This makes the development of new insecticides for vector control increasingly urgent, as well as important.

During 2014-2015 IVCC continued to develop its public health portfolio of new active ingredients for public health insecticides for indoor use, either as residual sprays or for long lasting bed nets. As well as supporting the discovery of new insecticides, IVCC also evaluates the repurposing of insecticides that have been developed for agriculture but not yet applied to vector control.

Discovery of new insecticides
The portfolio of new insecticide leads reaching pre-development is impressive. Our industrial partners have worked with a rich diversity of chemistries, and leads have been selected based on ability to kill insecticide resistant mosquitos. Cost effectiveness and safety are paramount.

The leads for vector control product development come from all three of IVCC's long-standing collaborations with industrial partners, Bayer, Sumitomo and Syngenta. All the most advanced leads are likely to be developed exclusively for the vector control market. This has advantages for resistance management because agricultural use will not compromise efforts on resistance management.

It does, however, come at a cost since the safety studies and the manufacturing process cannot be offset against a range of market opportunities beyond vector control.

Moving products on into full development will mean significant investment. This will be recommended only if there is strong evidence that the product can successfully navigate the rigours of the development process, and if it is likely to establish a strong position in the market place.

Rigorous process
We use a rigorous stage gate process to manage IVCC investment choices that addresses all aspects of product development:

- Is it effective for field control of insecticide resistant mosquitoes?
- Can it be made at a bearable cost and scale?
- Will users understand it to be cost effective and attractive to use?
- Will it be used in a way that prevents insecticide resistance occurring?
- Will it provide a return on investment over the long term?

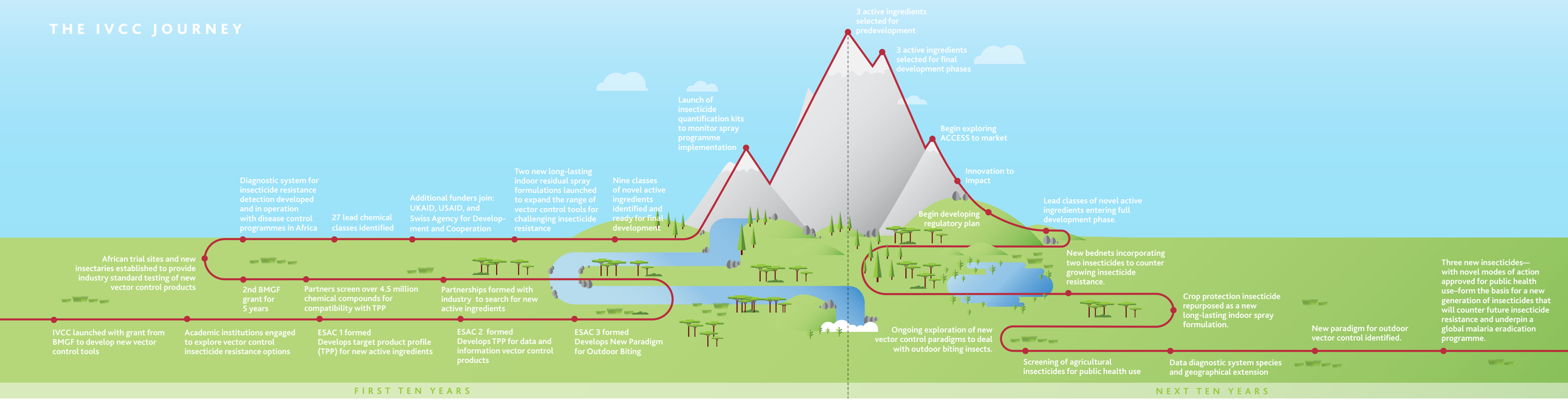
The introduction of new chemistries to the market must be carefully managed if we are to avoid wasting the investment in discovery and product development through the untimely development of resistance to new insecticides. For this reason, the development of mixtures of more than one chemical class is important, and particularly for bed net use where it is expected that a bed net will last for up to 3 years. Exposure of a single chemistry to many successive generations of mosquitos over 3 years creates a situation with a high risk of resistance occurring. This may lead us to consider combinations of different chemistries.

Key focus
The development of combination insecticide treated bednets is a key focus of IVCC's partners with access to currently registered insecticides. In 2015 IVCC is supporting projects with BASF and Sumitomo that are already being evaluated in WHOPES. In addition IVCC is working with BASF on the development of a chlorfenapyr-based long lasting indoor residual spray.

The considerable work required to deliver new vector control products for its essential role in eliminating malaria could not be achieved without the support of partners and funders alike. The substantial reward is measured in the number of lives saved and malaria cases averted.

The portfolio of new insecticide leads reaching pre-development is impressive

THE IVCC JOURNEY



ACHIEVEMENTS

2005

IVCC is launched with support from the Bill and Melinda Gates Foundation to develop new vector control tools.

2007

Academic institutions engaged to explore vector control insecticide resistance options.

Partnerships formed with industry to evaluate over four million potential insecticide compounds.

2010

African trial sites and new insectaries established to provide industry standard testing of new vector control products.

2013

Diagnostic system for insecticide resistance detection developed and in operation with disease control programmes in Africa.

Two new long-lasting indoor residual spray formulations launched to expand the range of vector control tools for challenging insecticide resistance.

2014

Launch of insecticide quantification kits to monitor spray programme implementation.

Nine classes of novel active ingredients identified and ready for final development.

2015

Three lead active ingredients in pre-development.

Ongoing exploration of new vector control paradigms to deal with outdoor biting insects.

Begin exploring ACCESS to market.

2017

Crop protection insecticide repurposed as a new long-lasting indoor spray formulation.

New paradigm for outdoor vector control identified.

2022

Three new insecticides— with novel modes of action approved for public health use–form the basis for a new generation of insecticides that will counter future insecticide resistance and underpin a global malaria eradication programme.

FOCUSED ON DELIVERY

Overcoming the barriers to Access

Dr Tom McLean
Head of Access

In the face of the diverse challenges that Product Development Partnerships (PDPs) face in achieving access to the products they develop, the PDPs have developed a community of expertise in resolving them and their work can be seen at *www.PDPAccess.org*

Often the actions required to deliver impact fall outside the capability of the PDP and the role of PDPs in addressing these has varied from doing, to facilitating, to advocating for others to take action.

Barriers to Access

There are four potential major barriers to rapid and sustainable access to the new vector control products, and specific targets within those challenges where IVCC could have optimal impact.

Firstly, there is a need to minimise time to market and maximise optimal coverage of the new products. This will involve engaging with the regulatory processes that govern new insecticides, and analysing potential markets to provide suitable interventions where appropriate.

Secondly, there is a need for supporting evidence and impact based deployment of innovative vector control technologies. Evidence of impact and cost effectiveness needs to be created, together with tools and data to enable robust decision making at country and global levels. This will facilitate making the case for a global funding stream for Insecticide Resistance Management.

Thirdly, we need to ensure that there is effective management of the new vector control products. This is essential in order to prevent insecticide resistance to the new products from developing. To make this work will require sustainable Target Product Profiles (TPPs), something already written into IVCC's development projects, and it will also require supporting the creation of policy, guidelines and Standard Operating Procedures as part of supporting the development of IRM capacity at country level.

> "Access" refers to a coordinated set of activities needed to ensure that the products developed will ultimately have an equitable public health impact.

The fourth target is more directly related to product development. For the vector control successes to continue there will need to be incentives for continuing innovation in vector control, probably in the form of sustainable access agreements and facilitating stable markets for new products.

Engaged

IVCC is already tackling some of these challenges. For example, we have been working to minimise some of the constraints on using the new long lasting non-pyrethroid IRS developed by Syngenta in collaboration with IVCC. Although this product has been shown to be highly effective the price is higher than previous products, there is only one supplier, and the small size of the market discourages other manufacturers from entry.

What is needed is robust evidence of impact and cost effectiveness to support the policy recommendation process and encourage national malaria control programmes (NMCPs) to use new products for IRS. A further complication is that demand forecasts for new products are unreliable resulting in increased manufacturing costs and long lead times.

Partnership

Each market shortcoming reinforces the others, creating negative feedback that inhibits progress. To resolve this IVCC is assembling a partnership to remove each of the obstacles to the effective use of the new products.

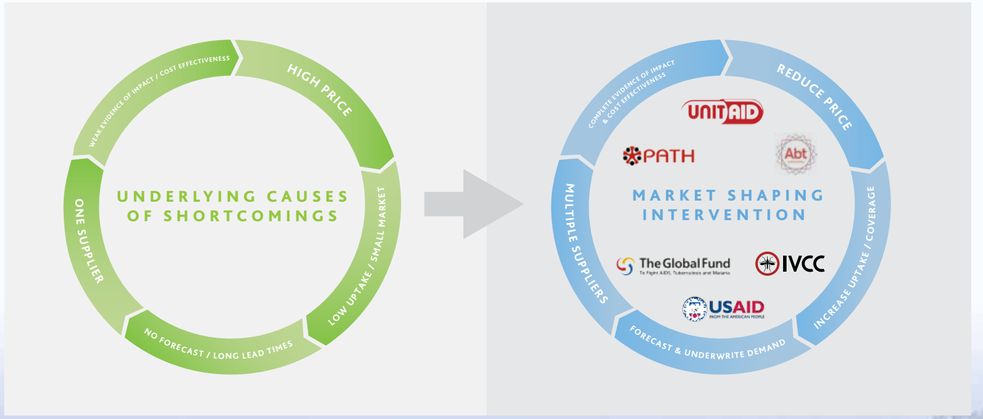
The partnership, with planned funding from UNITAID, will be made up of IVCC, President's Malaria Initiative (PMI), Abt Associates (PMI's implementation partner), PATH Malaria Control and Elimination Partnership in Africa (MACEPA) and The Global Fund to Fight AIDS, TB and Malaria (Global Fund, GF).

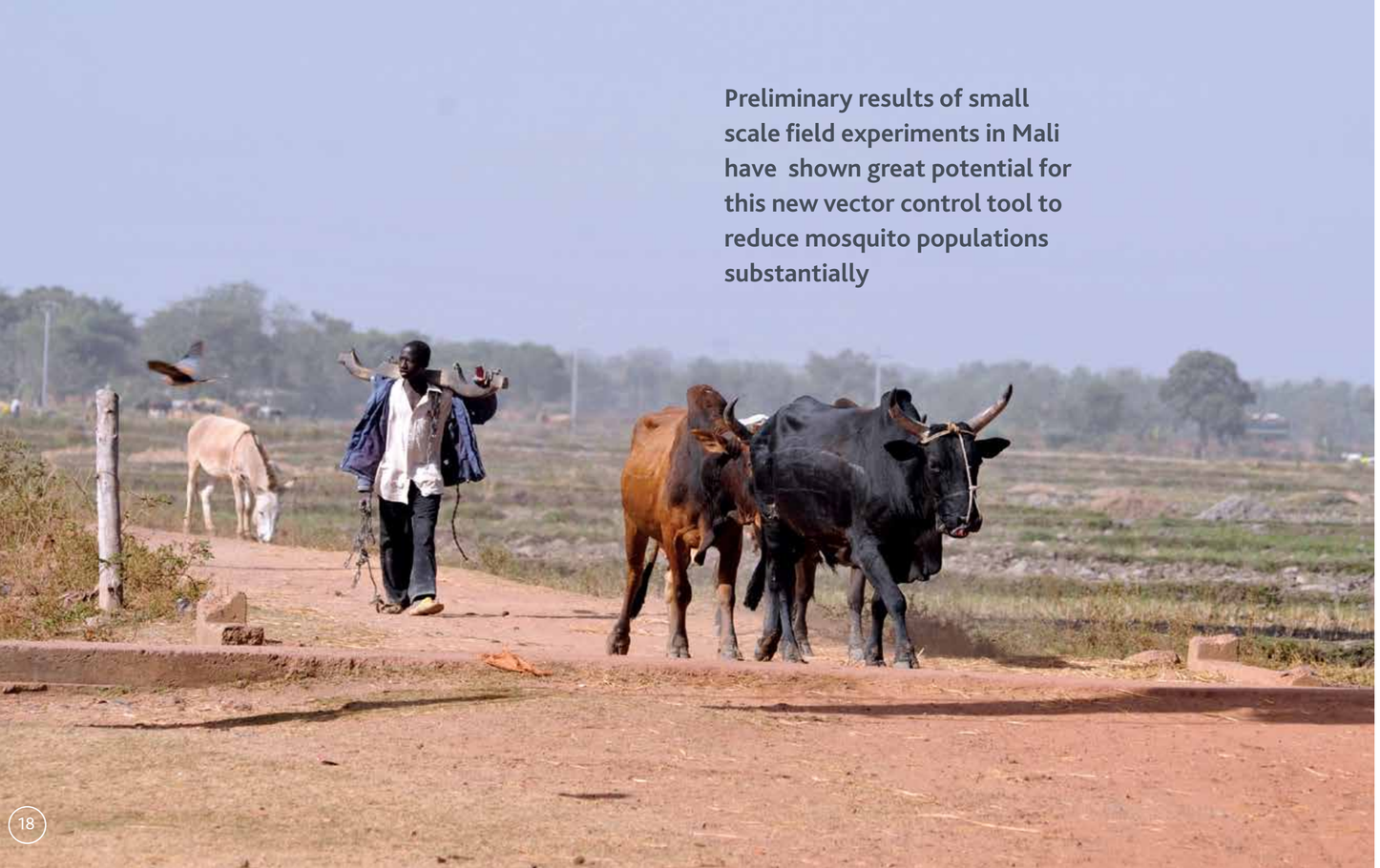
The partnership aims to increase the size of the market by introducing co-payment to increase the number of countries using new products and increasing the scale at which they do so. There will be an improved system for forecasting of demand, which will be underwritten in return for price reductions.

Development of alternate products from the high quality supplier base will be accelerated, together with negotiations to reduce the prices of all products in the marketplace.

In addition to these activities, sustainable demand generation will be driven through evidence of impact and cost effectiveness of these interventions and dissemination widely to control campaigns.

To resolve the market shortcomings IVCC has assembled a partnership to remove each of the obstacles





Preliminary results of small scale field experiments in Mali have shown great potential for this new vector control tool to reduce mosquito populations substantially

NEW PARADIGMS FOR VECTOR CONTROL

Addressing the challenges of Outdoor Transmission

Dr Silas Majembere
Senior Scientist

Current malaria vector control relies almost entirely on killing malaria-carrying mosquitoes that have come into a house to feed or rest. Spraying houses, schools and other buildings with insecticides, and wide distribution of insecticide-treated bednets have been highly successful at reducing deaths and sickness from malaria.

But not all mosquitoes bite inside. Some species of mosquito prefer to bite their victims outdoors when they are unprotected, or early in the night before they are protected by nets. These outdoor or early biting mosquitoes provide a route to continuation of transmission that prevents elimination. Sometimes this becomes the dominant source of new malaria infections.

New tools
To address this challenge, new vector control tools are needed for three overlapping ecological contexts: where people are away from the house for occupation or necessity, like rubber tappers, forest workers, miners, night guards or displaced persons, where mosquitoes bite early before people use nets, and where biting mosquitoes transmit malaria outside the house but still within the community.

The key to bringing a new class of intervention tools (often referred to as new paradigms) to wide and effective use, is to validate the effectiveness of the Target Product Profile of that class of products. This is done by testing prototypes in the field to demonstrate the technical requirements of the products and the settings in which they work.

Evidence
Clear evidence is required to show that these new tools are epidemiologically effective. This is necessary to support policy recommendation and large scale intervention funding.

IVCC has published a guide to the type and scale of evidence, supporting activities and technology development that would be required in order for new ideas to grow efficiently from concept to established intervention.

'A framework for validation of new intervention paradigms and product categories in vector control interventions', covers issues of user acceptance, manufacturing sustainability, economics, and technical and epidemiological evidence.

Proposals
Last year, IVCC issued a call for proposals to respond to the challenge of outdoor transmission. A good number of interesting proposals were submitted for funding, and in the first phase three projects were selected to support partners to develop the necessary evidence for a new paradigm targeting transmission outside of homes.

The first project, "Attractive Toxic Sugar Baits" aims at developing a tool containing a toxic sugar bait placed outside homes to attract and kill mosquitoes that feed on it. Preliminary results of small scale field experiments in Mali have already shown great potential for this tool to reduce mosquito populations substantially. This project started in 2015 and is progressing well.

The second project, "Push-Pull" aims at developing a "Push" system using spatial repellents to drive host-seeking mosquitoes away from homes combined with a "Pull" system using attractants to trap "pushed" or host-seeking mosquitoes. This project is scheduled to begin in 2016.

The third project, "Targeted Swarm Spray" aims at identifying mosquito mating swarms and spraying them directly with insecticides for population reduction. Early studies conducted in Burkina Faso suggest that mosquito mating swarms can be readily identified and tend to use the same swarming sites repeatedly, making it relatively easy to target once identified. This project is scheduled to start in mid-2016.

These approaches will then potentially be further developed for policy recommendation, product development, and broad implementation, provided that they fulfil the requirements of short time to market, and high impact technologies.

Duncan Preston
Finance Director

Financial Audit and Governance

IVCC is a not for profit company limited by guarantee with charitable status in both the UK and the US. The annual statutory accounts of IVCC are audited by Grant Thornton UK LLP and are produced using the Statement of Recommended Practice: Accounting for Charities (SORP) issued in March 2005. This ensures compliance under both the Companies Act 2006 and amended Charities Act 2006.

IVCC benefits from shared accounting and audit arrangements with its host institution the Liverpool School of Tropical Medicine (LSTM). A finance and investment committee made up of senior employees and trustees external to the organization give governance oversight on all financial operations of IVCC and meet 4 times a year. A specialist taxation service is provided externally. The team has extensive knowledge of all major funders within the sector and the expertise to comply with all external funder audit requirements.

All internal audit work is carried by an independent external organisation whose remit is to provide independent and objective assurance to add value and improve the organisation's operations. This is carried out through the evaluation and improvement to risk management, governance and control processes. An audit committee exists to oversee all recommendations made.

IVCC received a clean unqualified audit report for the sixth year in succession and no control issues were identified by either the external or internal auditors.

Value for money is important to IVCC. Following on from the migration of all key documents and contracts into SharePoint during 2014/15, IVCC is reviewing all workflows in the organisations. These will then be migrated into FlowForma, which sits on the Sharepoint platform. This will greatly enhance and automate all workflow processes, improving efficiency and effectiveness, and eliminating the need for paper based document completion and authorization in a safe and secure environment.

A further investment in improving IVCC's business intelligence capability is taking place using Microsoft Power BI and will introduce real time dashboard reporting for budget holders.

Investments

	2015/16*	2014/15	2013/14	2012/13	2011/12	2010/11
Income	£23.23m	£9.91m	£8.79m	£8.30m	£6.07m	£4.31m
Expenditure	£23.03m	£9.61m	£8.25m	£8.30m	£6.07m	£4.31m
Surplus/(Deficit)	£ 0.20m	£ 0.31m	£0.54m	-	-	-

**forecast numbers*

IVCC continues to use a conservative investment strategy using a combination of money market deposits and secure US government and corporate bonds, in line with current unsettled market conditions. Consequently, returns are low on both the sterling and dollar funds held. The total interest received during the year was £21k (£30k: 2013/14) and this will be used to fund future project activity.

FINANCE

Financial Performance

2014/15 saw a growth in program activity, with total spending increasing to £9.6m and an increase in income of £1.7m.

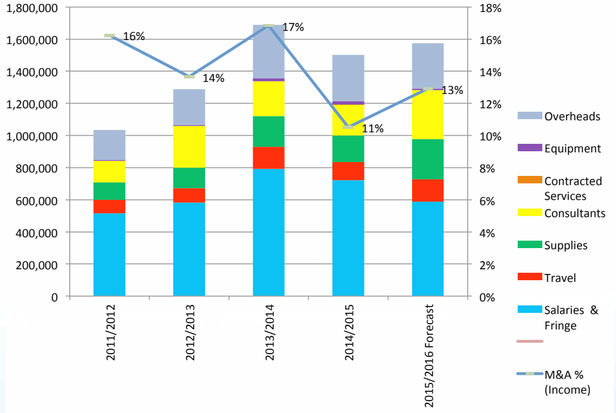
A total of £6.96m was spent on direct charitable project activities with a further £1.2m paid out on project supporting activities.

The new active ingredients portfolio has seen an increase in annual product development costs rising from £3.8m in 2013/14 to £4.7m. A significant increase in costs will happen in 2015/16 as the next phase of development starts, with costs estimated to more than double to £10.8m.

Costs for diagnostic tools and data management systems dropped to £0.2m to fund on-going development work and product testing in the field, but will see an increase to £0.5m during 2015/16 as work is undertaken on the Serious Gaming project and the roll out of DDMS in Zambia.

Spend of £0.4m on outdoor transmission work is consistent with 2013/14 levels, but will increase significantly during 2015/16 to over £1m following a grant supplement from BMGF.

Core administration support costs of £1.5m were also incurred in the year representing 11% of total cash received from donors. This represents a reduction of 6% from 2013/14 levels and emphasizes the increasing efficiencies made in IVCC and improvements in value for money.



FINANCE

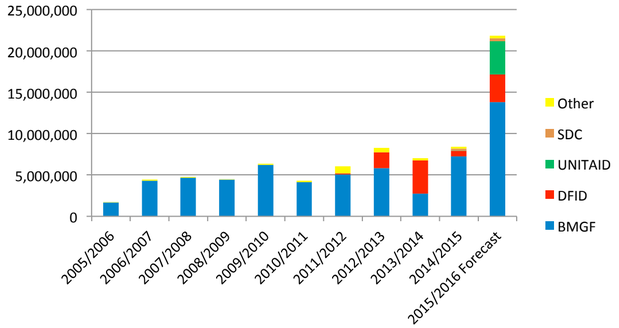
Funding Mix

BMGF provided 73% of the charity's income in the year, up from 31% in 2013/14 but similar to the levels in 2012/13 and prior years. Successful fundraising efforts, in particular with the UK's Department for International Development (DFID/UKaid) and USAID has enabled IVCC to diversify its funding base and reduce its reliance on one main donor.

The remaining 27% of income was split 7% DFID/UKaid, 12% USAID, 5% the Swiss Development Corporation (SDC) and 3% several smaller donors.

It is forecast for 2015/16 that the contribution from BMGF will reduce back down to 64% of the total funding received, with DFID at 15%, USAID 5% and SDC 2%.

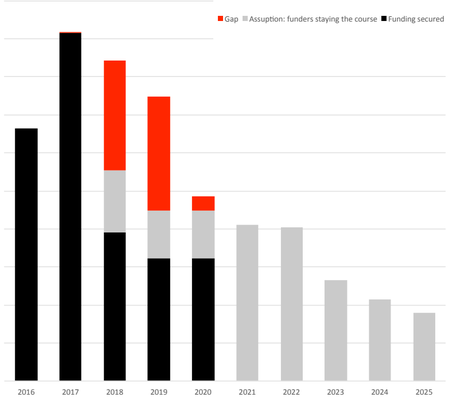
A planned new funding stream from UNITAID would account for 13% of funding, however, this money would be ring fenced for specific implementation work on the Next Generation IRS (NgenIRS) programme.

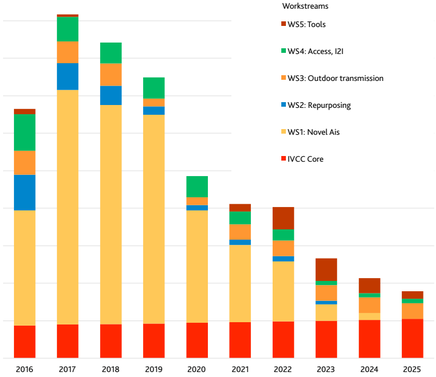


Funding Requirements 2016-2025

Forecasting long term funding and income scenarios enables IVCC to manage its product portfolio more effectively. It provides a base analysis for fundraising activities aimed at financing the portfolio in line with the latest projections and for negotiations with partners more effectively.

The total funding required to enable IVCC to meet all of its current objectives up to 2025 is dominated by the new active ingredients portfolio. Year on year funding has been steadily rising since 2014 and will peak in 2017 before falling over the remaining period to 2025. However, this is only one of several possible scenarios currently being considered by the team.





Phasing of IVCC activities over 10 years

Bridging the Gap

If current funders (BMGF, UKaid, USAID, SDC) sustain their current funding levels, there is still a significant gap to bridge if IVCC is to fulfill its mission. Negotiations are ongoing with funders and other key stakeholders over the next few years to ensure IVCC is able to deliver the products needed for malaria eradication.

INNOVATION TO IMPACT (I2I)

Transforming the vector control ecosystem to save more lives.

www.innovationtoimpact.org

Innovation to Impact (I2I) is an initiative that aims to transform the value chain for developing and delivering vector control products for diseases caused by vector borne pathogens.

I2I was launched in 2013 in response to increased insecticide resistance in vectors and gaps in transmission protection. Given the nature of the change required, the initiative quickly evolved into a multi-stakeholder effort and now includes more than 20 actively participating organisations.

These include manufacturers, The World Health Organization (WHO), The US President Malaria Initiative (PMI), The Global Fund, the US Environmental Protection Agency (EPA), UNITAID, The African Leaders Malaria Alliance (ALMA), IVCC, and representatives from countries and other stakeholder groups.

Over the past two years I2I has matured from a loose confederation of interested parties to an organisation of committed stakeholders determined to work together to change the world of vector control.

This will be managed through six work-streams that will work together to deliver the vision.

The **Industry Engagement workstream** will work with industry partners on prioritisation and investment in vector control in support of malaria and NTD eradication.

The **Pathway For New Ais workstream** will design and finalise a rapid regulatory pathway for new public health Active Ingredients (AIs).

The **GLP Site Accreditation workstream** will develop Standard Operating Procedures, protocols and training for site accreditation, enabling data generation by third parties

The **World Health Organisation Transformation workstream** will implement a faster & more transparent evaluation processes for efficacy, safety & quality, including confidential treatment of manufacturers' data.

The **Procurement Plans workstream** will generate collaborative solutions to enable value-based procurement, and develop a path forward on additional evaluation methods, normative guidance, and expert review panels

The **Country-Level Impact workstream** will accelerate country-level registration and approval by engaging more countries and regulatory teams in the I2I initiative.

To manage the implementation of I2I an independent, sustainable governance structure will be created. There will be an I2I Leadership team that will help the workstreams implement the I2I vision, serve as ambassadors of I2I to the general public, and lead changes in strategy and address stakeholder issues.

The Leadership team will report to an I2I Advisory Board, made up of key leaders and influencers from the different stakeholder groups. It will review progress, set strategic direction, provide thought partnership on topics, risks and actions needed, and apply influence to ensure optimal and timely implementation

To speed up the process of establishing I2I, support and financial oversight will be provided by IVCC's Board of Trustees, who will be responsible for approving the I2I budget and changes in the strategy recommended by the I2I Advisory Board, providing oversight of the grant provided for setting up I2I, and oversee the work of the I2I Director

The IVCC team will provide a home and a ready-made infrastructure, with professional support for logistics, IT, HR, training and technical expertise.

The benefits from I2I are potentially enormous. Transforming the vector control ecosystem to increase innovation, efficiency and quality will save many more lives. This could be a new dawn in the battle against malaria and NTDs.

THE IVCC TEAM

l to r: Mathias Mondy, Nick Hamon, David Malone, Duncan Preston, Sarah Rees, Jed Stone, Lois Rossi, Silas Majambere, Karen Johnson, Tom McLean, Lynn Byrne

Sarah Rees
Public Health Portfolio Manager

Sarah joined IVCC in September, following a 30 year career in agrochemical research and development with Syngenta and its legacy companies. She has held a variety of biotechnology and crop protection R&D roles and has considerable experience in technical management and portfolio leadership in all aspects of product development, from the generation and evaluation of ideas to project management from discovery through to launch. Sarah has a degree in Plant Sciences from King's College, London and a PhD in Phytochemical Insect Antifeedants from Reading University.

Silas Majambere
Senior Scientist

Silas Joined IVCC in September. He is a medical entomologist with 10 years of field experience in mosquito behaviour and control. He worked on malaria vectors during his Masters degree at Wageningen University, before completing a PhD at Durham University, UK. During this time he managed a large project, based in The Gambia, West Africa, looking at the impact of using microbial larvicides for the control of malaria vectors Silas has worked in Tanzania, based at the Ifakara Health Institute (IHI), and supported National Malaria Control Programs in Zanzibar and Burundi.

Alan Magill

The Vector Control community lost a great friend and advocate when Alan Magill, Director of Malaria Programs at the Bill & Melinda Gates Foundation, died unexpectedly on September 19, 2015, at the age of 61.

This tribute, written by the BMGF Malaria Program at IVCC's request, encapsulates our thoughts and memories.

Alan was a great friend of IVCC, and he believed that vector control products have a central role to play in the fight against malaria.

It was this belief that he translated into the Innovation to Impact (I2I) program, which has recently seen real sucess in making the product development process faster, smarter, and more predictable. Alan's background in drug and vaccine development enabled him to learn the insecticide landscape and provide intelligent discussion and guidance.

Alan was a towering intellect, joyful in his desire to learn new things and apply key insights to real-world problems. He often commented that he was a "closet entomologist," fascinated by the complexity of mosquitoes and their rapid adaptation to their environment and to the transmission of malaria parasites.

It was great to sit down with him to discuss vectors and know that this physician would be curious, receptive, and thoughtful. Only a week before he died, he completed a long memorandum to Bill and Melinda Gates describing the vector control component of the Malaria Program, with a long section describing the incredible accomplishments of IVCC.

Alan came to his interest in entomology and support for vector control over many years of experience in experimental medicine at the Walter Reed Army Institute of Research. He was always a champion of vector research and the efforts of its investigators even when higher levels of administration were doubtful.

In one case, he was an essential advisor to the entomology program when it developed commercial dipsticks for the detection of parasites and viruses in mosquitoes, including the creation of a GLP laboratory for the purpose.

In another, he stood behind entomology as it formed a bridge between a shortsighted defunding of leishmaniasis programs and the obvious relevance of this disease during the wars in Afghanistan and Iraq. He definitely brought a fearless, do-the-right-thing leadership style to the foundation.

Alan left us with a lasting legacy on which we will build. His life ended much too early, but we are extremely grateful for the three years he had with us at the foundation. He impacted everyone he touched, from his malaria team to foundation leadership, to our invaluable partners. We are determined to accomplish what Alan most wanted, that malaria delenda est, malaria must be destroyed.

FUNDERS

A very special thank you

None of the lifesaving advances we have made would have happened without the support of our major funders.
Their investment is at the heart of the exciting products in the IVCC pipeline that will accelerate progress towards malaria eradication.

BILL & MELINDA GATES *foundation*

The Bill and Melinda Gates Foundation have had a long-standing partnership with IVCC. The organisation works to tackle critical problems worldwide through building partnerships across the globe. The Global Development Division seeks to help the world's poorest people help themselves in alleviating hunger and poverty, harnessing advances in science and technology to save lives in poverty-stricken areas in the world. BMGF emphasises collaboration, innovation, risk-taking and results, which fits precisely with IVCC's mission and achievements. BMGF recognised the urgent need for new vector control tools to fight malaria and other insect-borne diseases and supported the establishment of IVCC as a product development partnership to bring together the resources to make it happen.

UKaid from the Department for International Development

UKAID is the public face of the Department for International Development (DfID), which is the UK government department with a mission to promote sustainable development and eliminate world poverty. DfID aims to halve the number of people living in extreme poverty and hunger, combat HIV, AIDS, Malaria and various other diseases, and build partnerships across the world to support development. DFID's partnership with IVCC has provided a substantial boost to the practical task of developing effective vector control approaches, such as insecticide treated bednets, that have substantially reduced child and maternal deaths and the overall incidence and death rate from malaria.

USAID FROM THE AMERICAN PEOPLE

USAID is the leading US Government agency, which works to eradicate extreme global poverty, and allow for resilient, democratic societies to realise their own potential. USAID's mission seeks to promote economic prosperity, protect human rights, provide humanitarian assistance in all disasters, strengthen and promote democracy and improve global health. USAID, through the President's Malaria Initiative (PMI), is a strong supporter of IVCC and their investment in the development of new public health insecticides for bednets and indoor residual spraying will help produce the new vector control tools that are urgently needed to combat insecticide resistance.

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Swiss Agency for Development and Cooperation SDC

The Swiss Agency for Development and Cooperation (SDC) is Switzerland's international cooperation agency. SDC's humanitarian aid seeks to reduce global poverty through a variety of methods. This is promoted through fostering economic self-reliance and state autonomies, finding solutions to environment problems, problems in regards to access to education and basic healthcare, and enabling access to resources and services to the greatest number of people. SDC's support to IVCC acknowledges that many of the poorest countries in the world suffer from endemic malaria, which not only kills and incapacitates large numbers of people, but also seriously damages economic development.


RESISTANCE TO PUBLIC HEALTH INSECTICIDES
HAS BEEN BUILDING FOR YEARS.
WE'RE HERE TO
CRUSH
THE RESISTANCE
IVCC