

Transcript: Partnerships and innovation to defeat malaria: an interview with Dr David Reddy

Camilla: My name's Camilla Burkot. I'm a Research Officer here at the Development Policy Centre, and it is my pleasure to be sitting down with Dr. David Reddy, who is the CEO of the Medicines for Malaria Venture [MMV]. Welcome. Thank you.

David: Thank you for inviting me.

Camilla: I thought perhaps we'd just start – if you could just tell us a little bit about MMV in general, what role MMV is playing in combatting malaria.

David: MMV is what's called a product development partnership. So we work between both the public and the private sectors, and our role is to facilitate discovery, development, and delivery of new anti-malarial drugs.

Camilla: Fantastic. So one of the first things I wanted to ask you is about this business of drug discovery and drug development, which is a notoriously risky exercise. You start with many different compounds, and ultimately only a very few become treatments. Partly as a consequence of this, it can be very expensive.

So I was hoping you could give us a little overview of MMV's investment strategy. How do you decide where to invest donor funds, and how do you ensure that they're spent effectively?

David: Well the first thing is that we have a strategy of syndicated investment, so we get donor funds from governments, including the Australian government, the Bill and Melinda Gates Foundation, Wellcome Trust and others.

And we use that funding to assemble a drug pipeline, a portfolio of compounds. What we do is we strategically work with groups like the WHO and others to define the key medical gaps and what types of drugs we need.

A great example is drugs that are active against drug-resistant forms of malaria. We then actively seek partners who can contribute to that effort. And then we invest in the development of drugs which actually meet that profile.

We also have an independent expert scientific advisory board that at particular milestones in the drug's development, they look at that drug and compare it to others and determine which is the strongest and which should progress. And in that way, by managing a large portfolio of drugs, we're able to weed out those that really don't make the mark and focus all of the investment on the ones that will really be transformative.

Camilla: So you just mentioned drug resistance, and antimalarial drug resistance, in this region, the Southeast Asia and Pacific region, is something that is a major issue. And it's something that the Australian aid program has recently highlighted in its new 'Health for Development' strategy.

As you said, MMV has been working on tackling resistance for some time now. How would you characterise the severity of antimalarial resistance at the moment? And

how might partners best work to stall resistance while MMV is working on developing these new drugs?

David: In terms of how would we characterise the resistance, I think the first thing to say is that for a number of years we've been talking about resistance to the artemisinin class of drugs. But what has recently emerged, and I partook in a discussion last week out of Boston where we were looking at the new resistance data, we now have multi-drug resistant parasites.

This is a real issue, because both the artemisinin class of drugs and the partner drugs that go with them are now failing. So we urgently need new strategies. The way this is being tackled at the moment is to combine more drugs, so actually try and have even more drugs in the regimen and then treating patients for much longer.

But ultimately what we need is drugs that attack the parasite in a totally different way. And those are the drugs that we're bringing through in the MMV pipeline today. So there is promise, but clearly we need to accelerate our efforts to bring these drugs through.

Camilla: So I guess my next question relates to that. There have been efforts to eliminate malaria for quite a long time, and it's been quite a challenge. And today there are a lot of players in this game, in dealing with malaria.

How would you say MMV fits into this quite complicated space and this continuing push toward elimination?

David: I think the first thing to say is if we want to achieve elimination, it's not just going to be a drug-based approach. We need drugs. We need the vector control, so strategies that reduce the population of malaria-infected mosquitoes. And so you need both vector control and drugs.

Our role, MMV's role, within this is a focus on drugs. We currently are managing 60 per cent of the global portfolio of malaria drugs. And that portfolio is the richest it's been at any point in history. But the key issue that we face is that we can't develop single compounds anymore. We need to mix these into combination drug regimens so that the next generation we bring through can both beat the resistant parasites that are out there, but also increase the hurdle so the parasites can't develop resistance to the new drugs.

So we're doing that in combination with partners. And just to give you a flavour for what that means, we're working with 130 active partners currently in 47 countries around the world – 28 pharmaceutical companies, 13 biotech companies, and numerous academic and research institutes.

Camilla: Great! That's fantastic, actually. I didn't know there were quite so many partners. That's really good to hear.

So as I understand it, MMV was established in 1999. So over the lifetime of the organisation, there's been quite a few shifts in how intellectual property rights [IP] are regarded in public health.

We had the Doha Declaration in 2001, and increasingly with the TPP [Trans-Pacific Partnership] we're hearing there may be shifts as well. So I was curious to know how MMV goes about negotiating this challenging issue of intellectual property when you're dealing with so many different partners, who may have different interests at stake.

David: There's two parts to the answer to this question. I think the first is, what's our experience to date regarding IP and access? And the second is, what is our strategy around this?

So if we look at IP and access, currently in working with pharmaceutical companies, we haven't seen that IP has been a barrier at all to developing the drugs that are needed and getting them out to the patients that need them. And I think a good example is our collaboration with Novartis, where we co-founded and co-developed a drug which is used for the treatment of children with malaria and indeed that has now been distributed to 250 million treatment worldwide at around cost of goods.

So to treat a child, it's probably in the region of \$0.60 for a three-day course of treatment. So really we haven't seen a barrier.

But our approach to intellectual property is probably an interesting one. And that is, we see IP in three ways. The first is that we actually do file patents ourselves as a protection strategy, because then it gives us the freedom to operate on the compounds. The second is that we use it to attract partners, pharmaceutical partners to then engage in the research, because there may be cases where there is a dual market. For example, travellers who are going abroad. And there might be therefore a commercial market.

So it allows them to take that market and make money out of it but then pursue a not-for-profit basis in the treatment of patients in the developing world. So it can actually be a tool to help us engage pharmaceutical partners.

The third element is actually really interesting, because there may be cases where you actually do want to prosecute a company. And that would be if somebody was producing a sub-standard version of your drug, it may be a way to get them out of the market, because you could go back to that country of origin and prosecute. And we would only ever consider doing that if it was a sub-quality drug.

At the end of the day, MMV's role is to facilitate access, not stand in the way of it. But we see IP as a critical tool to help us do that.

Camilla: It's interesting that you say that, because there's things in that are quite different from how people tend to think about IP and public health. And it's refreshing to get that slightly different view.

And that leads into my next question, which is about innovation – this massive buzzword, especially in the aid program here, but also in development more generally. People are always talking about innovation and thinking differently.

And MMV is frequently described, I've read in many places, as an 'innovative organisation'. So I was curious to know, in your experience, what are some of the

factors that enable organisations to innovate successfully and keep innovating, if you like?

David: There's a number of words I could use here. I think the first is that we have something of a philosophy within the organisation where we say 'we own everything and we own nothing'.

What's meant by that is, by everything, we own the mission. And so when we develop drugs our role is to get them out to partners as rapidly as possible so they can pick up the manufacturing, the local registrations and ensure availability. And we have a very strong contractual framework whereby they have to price at certain very affordable levels and make the drugs available in malaria-endemic countries.

And if they do that, they're fulfilling the mission. And then we can let go of it and move onto something else.

I think we're also very opportunistic. What we look at is impact. So innovation comes in many forms. It can be ways of partnering, for example, with Newcrest Mining on some of their initiatives in Lihir Island [in PNG], which is now leading to a joint malaria elimination program on the island.

Or it can be the fact that we will work with whoever are the best in the field – academic institutes, pharmaceutical companies – to bring forward the products that are needed. And in that light, I think it's really important to spell out that half of the most promising compounds that are in the portfolio today come from academia and not from industry.

So I think one of the key things we do is we look for where the expertise, the talent, and the breakthroughs lie. We don't necessarily go back to the same well all the time to drink.

Camilla: So again, innovation is coming from those different partners and being very flexible.

David: Absolutely.

Camilla: Really bringing everyone into the fold. Fantastic. So one other thing that I wanted to highlight, because it's something that interests me personally, I was interested to read on the website about some of MMV's efforts to build research capacity and to build or improve facilities of local partners at this network of clinical trial sites that you have all over the world.

I was wondering if you could tell me a little bit more about those efforts.

David: So firstly, to do the clinical trials, we need to go to where malaria is, so malaria-endemic countries here in Southeast Asia, Africa; we're also working in the Amazon. So we work with local investigators, and I think that's one of the key things about MMV. We're a small organisation. We're 60 people. Primarily scientists, physicians, with malaria expertise.

And so what we do is we work with local institutes, local hospitals on the ground, but we need to ensure that the clinical studies are done robustly and they're done to

the types of standards where the data can be accepted by the TGA here in Australia, the US FDA.

So we will supply and facilitate training and support, and ensure that both the infrastructure and the capabilities are in place before we take our studies. And what that means is that once these facilities have been built up, then we've actually seen that they've been followed by vaccine trials with other groups, and trials with other disease areas. So it becomes a resource that can be used more widely in the global health field.

Another element of this is that we've also began working with researchers in some of the African countries, for example in South Africa. And we now have a compound that was jointly discovered at the University of Cape Town, and that's being co-funded by the South African government.

I think a final element that's worth mentioning is that we've also taken a very unusual step in innovation. And that is open innovation, in that we've selected a group of compounds, the types of chemicals that we know are active against the malaria parasite, and we've made these available along with all the structural information, all the pharmacokinetic information, and we've made that available to any researcher in the world that wants it.

And we distribute this free of charge, and it allows them to do research on other neglected tropical diseases. The only requirement we have is that they have to publish the data. And one of the partners that got this has actually discovered that some of these compounds are active against other parasites, human parasites, visceral leishmaniasis, and sleeping sickness.

And so what it means is that we can move, through this innovative open-source approach, we can move the technologies we've got out into other areas and hopefully impact some of the other neglected tropical diseases.

Camilla: Oh wow! That's fantastic. That's really good to hear. Perhaps this may be one of the things you mentioned, one of my next questions. I was curious to know since you've become CEO of MMV in 2011, which of MMV's accomplishments are you most proud of?

David: I have to say three. The first is that when you go into the field and you see the impact of the drugs you're developing, particularly on young children, that is what inspires everyone within the organisation.

I think the next thing is that if you look here in the Asia-Pacific area, the issue is relapsing malaria. And you've got a big problem that the relapsing form of malaria hides in the liver in a dormant state, and then it comes alive periodically. We don't know exactly why. And you get malaria relapses.

The current treatment for that is 14 days of treatment. We've just now moved with our partners GlaxoSmithKline a drug into Phase III clinical studies, so they're big confirmatory studies. This drug can be taken once. It's one pill, instead of 14 days of treatment, and that drug is called Tafenoquine.

This is a drug that the development is also being supported by a grant from the Australian government, and it could be completely transformative. In fact, the United States FDA has just given it breakthrough status, which reflects how meaningful this drug could really be.

The final thing I'd like to highlight again is from here in Australia, and that is the QIMR institute [Queensland Institute of Medical Research] in Queensland have developed something in collaboration with MMV that again is changing the way we look at drug development. So it's a human challenge model where healthy volunteers get injected with a very small amount of blood with malaria parasites in it.

And then the parasites multiply in their body, but they're never allowed to go up to a level that would ever make them ill. But we're able to give them some of our research drugs and actually see how the drugs work. And that allows us to determine, are those drugs active against the parasite in humans? Roughly what's the dose that we're going to need to go into patients with?

And after that they then receive a fully curative drug and they leave and they've got no parasites in their body. But what we leave with is enough information that it can accelerate our drug development timelines by two years. And so for us this is completely transformative. It lowers cost. It accelerates the development of new drugs and drugs that can be active against the resistant forms.

Camilla: Wow! To shave two years off is pretty impressive, because I think it usually takes about 10-15 years to produce a new drug?

David: It does. But also the key thing here is you're not putting investment into drugs that aren't going to work. And you don't have to wait until you're in patients to find that out. We know a lot earlier.

Camilla: That's fantastic. So that's about it from me. You've highlighted a few really interesting things that I'm sure we'll be hearing more about going forward. And I want to thank you very much again for taking the time to speak with me today.

David: You're very welcome. Thank you.

Camilla: Thank you.

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