Addressing Questions of Governance and Accountability in Neglected Diseases: The Case of Malaria

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1. Introduction

Neglected diseases of the developing world

This report offers an analysis of the governance and accountability challenges posed by interventions in neglected diseases of the developing world. It begins by introducing neglected diseases and approaches to governance and accountability. Subsequently, the report offers an analysis of policy interventions in neglected diseases and a detailed study of the specific case of malaria.

It is argued that only 10% of global medical research is devoted to conditions which account for 90% of the world's disease burden (POST, 2005). Much of this disease burden is focused in developing countries. These are known as neglected diseases (see DNDi, 2006). The disease burden in the developing world is primarily based on forms of communicable disease according to the World Health Organisation (WHO). Respiratory infections, HIV/AIDS, infections at birth, diarrhoeal disease and tropical diseases (for example Malaria) account for most deaths in developing countries (WHO, 2004). This is in contrast to developed countries where cancer and heart disease have greater prevalence. It is claimed that in the developing world existing treatments are not always used effectively, interventions are ineffective or non-existent, and there is insufficiently widespread knowledge of diseases (POST, 2005). It is said that engaging with this disease burden requires medicine, education, infrastructure and health systems. So what kinds of interventions have been attempted?

Intervention in the disease burden

A broad variety of organizations have been engaged in attempts to alleviate the disease burden of developing countries. The WHO, World Bank, European Union, Oxfam, UNICEF, amongst many others have attempted to provide impetus into the development of programmes of action to alleviate the disease burden of the developing world. This has led to the development of various initiatives, for example:

- South African Aids Vaccine Initiative (SAAVI, 2006)
- International Aids Vaccine Initiative (IAVI, 2001)
- Global Alliance for Vaccine and Immunization (GAVI, 2006)
- European Malaria Vaccine Initiative (EMVI, 2005)
- Medicines for Malaria Venture (MMV, 2006)
- European Public Health Alliance (EPHA, 2006)
- European and Developing countries Clinical Trials Programme (EDCTP, 2003)
- TB Alliance (2006)
- Drugs for Neglected Diseases initiative (DNDi, 2006)
- Initiative on Public Private Partnerships for Health (IPPPH, 2006)

Each of these initiatives involves multiple stakeholders, sources of funding and particular goals. These initiatives tie into one aspect of the UN's Millennium Development Goals to combat HIV/Aids, malaria and other diseases.

However, alleviating the disease burden is not straightforward. For example, just as the vaccine industry is resurgent (The Standard, 2006), organisations within that industry are uncertain as to the risks posed by movements into the developing world and benefits likely to accrue (e.g. organisations face financial risk in developing vaccines which may never come to market, may work but have few markets which can afford to cover the development costs, patents are relatively short, organisations are unsure that they can deliver the right vaccine, to the right people, with guarantees that the vaccine delivered is the one required, will be used in the right way and will alleviate the problem targeted). Also, the initiatives listed above involve many stakeholders, so co-ordination and funding are complex issues. In response, various developed country governments have attempted to stimulate research by introducing means which should aid organisations in more effectively engaging in reducing the disease burden of the developing world. The UK government, for example, has proposed a combination of public private partnerships, a proposed international finance facility, advance purchase commitments (ensuring developers know that a certain amount of a vaccine or treatment will be purchased, prior to production), extensions of patents (meaning a company could, for example, make cheaper drugs by gaining income over a longer period, making drug research and development more attractive) and research and development tax credits to stimulate industry interest (POST, 2005).

Many of these interventions are said to pose governance and accountability challenges. Addressing these challenges is said to be the primary way in which the burden of neglected diseases could be alleviated (see, for example, Buse, 2004; Nishta, 2004; Widdus, 2003; Garner, 2005). This report will, first, outline what is meant by governance and accountability (see next section). Second, it will provide an analysis of the current policy landscape for interventions in neglected diseases and the questions of governance and accountability introduced by these interventions. Third, the report will focus in on the specific case of malaria, attempts to intervene in the disease and issues of governance and accountability provoked and resolved. The second and third sections of the report draw on interviews with policy makers, scientists, consultants, research funders and pharmaceutical firms involved in neglected diseases. The report will conclude with recommendations on ways to engage with governance and accountability issues.

Approaches to Governance and Accountability

In a general sense, governance relates to those structures in place whereby an organisation steers itself (Buse, 2004) or is encouraged to steer itself, and accountability relates to those occasions where some particular feature of activity is made available to be assessed. However, in practice there are a variety of approaches to governance and accountability. The report will briefly outline these approaches by drawing together work from sociology, development studies, management research, science and technology studies, anthropology and philosophy. These approaches can be organised into four areas of: face to face, metric, transparency and engagement-

based forms of governance and accountability. Although in practice these often overlap, they are separated out here for ease of presentation. In subsequent sections the complexity and blurring of these approaches in instances of governance and accountability will be highlighted.[1]

Face to face forms of governance and accountability relate to the sense in which forms of interaction are occasions of accountability. For example, conversations might involve one speaker providing an utterance to be held to account by a second speaker whose subsequent response is then available to be held to account by the first speaker (Garfinkel, 1967; Luff and Heath, 1993). This approach treats accountability as a pervasive phenomenon, constitutive of everyday forms of interaction (constitutive in that through holding each other to account, more or less mutual intelligibility is accomplished). However, the form of accountability outlined can be characteristic of professional as well as everyday settings (Lynch, 1998; Suchman, 1993). In professional settings, the ways in which face to face interactions operate as moments of accountability are tied into structures of governance (for example, meetings are held as opportunities for parties to hold each other to account and those meetings form part of the governance structure of the organisation as they are timetabled, minuted and their existence becomes an expectation amongst organisational members). Face to face forms of governance and accountability are characterised by more ad hoc, less systematic forms of interaction than other areas of governance and accountability. This can be both advantageous (in that problems with for example, metric forms of governance and accountability are easier to avoid) and disadvantageous (governance and accountability of this form can sometimes appear less organised or rigorous). An important principle of face-to-face forms of interaction is mutual accountability – each gets to hold the other to account. This is less apparent in other modes of governance and accountability.

Metric forms of governance and accountability relate to those systems of assessment where an organisation is measured according to certain principles, expectations, standardised measures, benchmarks, performance indicators and so on (see Power, 1997; Baxter and Chua, 2002). The metrics form the focus for accountability. The metrics are also a feature of the governance of the organisation in that the aspects of the organisation to be measured, operate as principal ways in which the organisation steers itself and through which its members come to prioritise certain types of activities and organisational goals (Miller, 1992; Miller and O'Leary, 1994; Rose, 1999). Metrics are often tied into further forms of accountability such as external auditing whereby organisations are expected to be able to demonstrate that they have adhered to certain measurement standards and practices. A drawback of this approach to governance and accountability can be that the areas of activity to be measured do not remain as measures, but instead become targets to aim toward. In this way, the metrics can be consequential for the types of activity that the organisation carries out (see, for example, Strathern, 1999; 2000; 2002). For example, when the UK

[1] An alternative taxonomy of governance is available from Hagendijk and Kallerud (2003).

government set out to measure Universities, they developed the Research Assessment Exercise which was a publication based metric. However, in place of measures of publications, came a nation of University academics all trying to publish in certain journals, in a certain time-frame; the publications became a target to aim toward. This has led to a skewing of academic priorities towards publications (in order to succeed in assessment) and away from other areas which would not come under scrutiny but might still be valuable (such as the extent to which academics have engaged in work of practical consequence). Such an approach to governance and accountability is fine for as long as the metrics are considered appropriate and their potentially narrowing consequences are considered manageable.

Transparency[2] as a mode of governance and accountability refers to those actions understood as carried out, usually by an organisation, on behalf of an often unspecified mass audience. This includes, for example, company accounts made available for the public good or in the public interest. In effect these 'publics' tend to be fairly narrow and specialised (those who are interested in and have the time and skill to read reports, accounts and other ephemera made available by organisations; that is they are not, in practice, often noted as members of the general public; for more on transparency systems, see Gray, 1992). This form of accountability includes calls for organisations to make certain types of information available and for (sometimes publicly funded) organisations to demonstrate their value for money, responsibility (social, corporate) and ethical standards. Demands for transparency are made in relation to, amongst other things, the media (Media Transparency, 2003), global political campaigning (Transparency International, 2003) and corporate organisations (Shaw and Plapinger, 2001). Like metric approaches, transparency becomes a form of governance as organisations are actively encouraged to adopt particular protocols on making information available for assessment and, indeed, for public organisations their funding can depend on an ability to demonstrate that they have adhered to these protocols. Problems with this approach to governance and accountability involve questions regarding whether or not information made available matches internal organisational activity, whom information is made available to, what sense is made of information made available (see Wall, 1996) and how information is used (often, making information available becomes the end goal, a box to tick to demonstrate adherence to a principle rather than for any clear practical benefit; Neyland, 2007).

Engagement-based forms of governance and accountability relate to those structures which actively invite audiences external to an organisation to participate in an aspect of the organisation (for an overview, see Irwin, 1995; Kleinman, 2000; Kitcher, 2001). This is not the same as members of an organisation holding each other to account face to face, or metrics and

[2] Transparency has been considered from a number of different perspectives in poetry (Gordon, 1969), post-modernism (Vattimo, 1992; Baudrillard, 1993), philosophy (Westphal, 1986), political analysis (Wall, 1996), psychology (Tagiuiri et al, 1955) and studies of accounting (Humphrey et al, 1995; Gray, 1992; Zadek and Raynard, 1995; Sikka, 2001; Canning and O'Dwyer, 2001; Drew, 2004).

transparency standards and protocols being used as a means to make information available. Instead, engagement-based forms of governance and accountability revolve around particular set-piece moments where those external to an organisation are offered an opportunity to enter into interaction with (an aspect of) the future direction of that organisation. This can involve citizen juries, deliberative, democratic decision-making, participatory budgeting, public involvement in new scientific developments and so on. The means of engagement becomes an opportunity for accountability and for assessment of the appropriate way forward for a particular area of organisational activity. This engagement also becomes an important area of organisational governance; the organisation and its members are steered by an awareness of the need for engagement, make decisions about appropriate areas of engagement and look to use engagement as a means for steering future activity. Problems with this approach relate to the means of engagement (what would form an appropriate structure for outside involvement in an organisation's decision-making, what sort of information should people be provided with, how to handle, for example, market sensitive information), who gets to engage (that is who is invited – which can be a broad-based invite to the general public – and who turns up – which can be a problematically narrow group with a specific agenda, such as those who may wish to protest against an organisation) and with what outcome (in a similar manner to transparency based governance and accountability where information availability becomes the end-point, in these activities engagement can become the end-point with no clear consequence).

Having outlined four approaches to governance and accountability, this report will now provide a succinct summary (next section) of the policy options available for engaging with the area of neglected diseases. The issues of governance and accountability which arise in relation to these policy mechanisms will be given consideration.

2. Neglected Disease Policy Options

What counts as effective intervention?

It is claimed by a variety of organisations involved in neglected diseases that the problems faced in the developing world are incredibly complex (see for example, Oxfam, 2003). For example, ensuring that medicines are affordable involves negotiation between government and drug companies, the development of, for example, tax breaks to encourage development in this area, the regulation of the production of the medicine (to ensure its quality) and regulation to ensure that the promised prices are met. However, affordability, although complex in itself, does not guarantee a reduction in the disease burden of developing countries. Affordability needs to operate in tandem with further complex processes to ensure that medicine is available. Availability involves transport issues (can the medicine get to the right place), infrastructure issues (is there a location for the delivery of treatment), education (is there a large enough body of people able to deliver the treatment) and a willingness and knowledge on the part of the local population to receive treatment.

In order to address these issues of availability, infrastructure and education, a variety of interventions have been proposed. Each of the interventions raises questions of governance and accountability which are set out below.

Tax breaks

A principal problem invoked regularly across debates regarding diseases of the developing world is the lack of financial incentives for big pharmaceutical firms and biotechs to bring to market vaccines or drugs for diseases 'of the poor.' The claim is made that although millions of people suffer with TB or malaria, for example, these people are too poor to be considered a sufficiently viable market for a drug or vaccine that the corporation's costs will be recouped. The UK government (amongst others) has looked into providing tax breaks for firms doing research into 'poor' diseases. However, the UK government is clear that tax breaks alone are insufficient to provide remedies to all the problems of neglected diseases (drug or vaccine development, delivery, health infrastructure, health education, etc). Introducing tax-based incentives would require a governance system held together through accountable, mutual obligations to gain tax breaks and provide sufficient research and development in return for those breaks. However, this raises a problematic question: How would a narrow focusing of governance and accountability relations around financial incentives (tax breaks) stimulate interest across the problems of neglected diseases: scientific development, delivery, health infrastructure and health education? Would tax breaks enable a form of mutual accountability with an active role for developing country organisations? Are tax breaks of interest to private industry?

> Interviewee 10 (UK-based senior vaccine scientist)
> I think they are of no interest to companies is the short answer. They've been looked at ……. they're far too far down the stream…… tax breaks are irrelevant to biotech companies, their numbers don't add I think on the tax breaks.

> Interviewee 14 (Neglected disease consultant)
> The thing is though, how we've been so stuffy and conservative with the way we develop incentives, and it's all based in this fixed notion of academic innovation followed by handover to a big company, because only a big company can do trials in Africa. Most of them have never done a trial in Africa.…
>
> I think it's the same with the UK tax break. You guys have got a tax break in place now to pay people to motivate them to do something they're already doing, and the big companies will just take it because who's not going to take a few million pounds. It's a great idea. I would take it … But it's completely, the incentives were put in place based on a notion that no-one was doing anything, then a report comes out that says no, look, there's a lot of activity, it's just that you don't support it. But people still kept all the incentives.

Discount Treatments

Several initiatives have attempted to intervene in the disease burden faced by developing world countries by focusing on discounting treatments. For example, in 2000 a US pharmaceutical firm offered to reduce the cost of its AIDS retroviral treatments from $10,000 per person per year to $2,000. This was combined with an offer from the US government that developing country states could take out a loan to purchase these treatments with a repayment interest rate of 7%. Orbinski (2001) suggested that "What is needed is not apparent solutions that consolidate and protect existing monopoly commercial interests," (2001: 226). Orbinski (2001) argues that such treatments could be made available profitably for as little as $250. Instead Orbinski looks to developments in intellectual property rights, public-private partnerships (PPPs) and further exploration of 'forgotten' illnesses for which treatments are available (such as African sleeping sickness) as the way forward. Providing a discount scheme would require a governance system to assess, regulate and account for which countries would qualify for discounts, payments made, treatments delivered and any loan adjustments required (Orbinski, 2001). Such governance and accountability relations would involve questions regarding the kinds of commitments built into this discount system: how far below the market rate will discounts be set, at what interest rate will loans operate and what happens if developing countries cannot make repayments? On what terms would developing countries be able to participate in this system or would they be incorporated as beneficiaries? In short, what would be the consequences of governance and accountability commitments for developing countries under discount schemes? Participants in this research were less than enthusiastic about discounting schemes.

> Interviewee 7 (Neglected disease scientist)
> You hook people onto taking it and then you've got them and they have to find the money to support it – like giving cigarettes to children.

> Interviewee 14 (Neglected disease consultant)
> And in drugs what happens is, if companies make a lot of profit in the US, then they provide them at close to cost price for poor countries. That's what they do with AIDS drugs. But with vaccines, I think we're constructing an approach where they make a profit everywhere, a big profit in the US and publicly subsidised profit in developing countries as well

Even if discounts were well managed, other interviewees identified problems further downstream:

> Interviewee 17 (US-based neglected disease research funding body)
> …we're going to have new malaria drugs coming down the pipeline, and maybe a lot of them… depending on the patterns of malaria resistance to different drugs, you might want to have different drugs being introduced in different places at different times. It becomes quite a complex problem to solve, and you need actually a health system that's able to deal with it that right now can't even deal with delivering one product. You need a health system that's going to be able to deliver new products on a pretty regular basis. Once every two, three, four, five years. They're going to have a new product they're going to have to introduce because the old one is now, you know, malaria has developed a resistance to that and they need to move on to the next thing.

Patents

Krattiger, Kowalski, Eiss and Taubman (2006) suggest that "Throughout the developing world, intellectual property (IP) constraints complicate access to critically essential medical technologies and products," (2006: 67). Given the apparent absence of a ready (i.e. profitable) market for neglected disease vaccines and drugs, extended patents might mean a pharmaceutical corporation can make a viable, but smaller income per dosage over a longer period. However, Lanjouw (2006) argues, it is not clear that this is definitively the case. Lanjouw (2006) points out arguments can be made equally vociferously for stronger or weaker patenting. Lanjouw suggests that weaker patenting could mean wider access to the intellectual property behind vaccination developments, leading to a broader range of further scientific developments, a broader number of competing corporations in the market place and a lower price for vaccines. Alternatively, longer patents could seduce big corporations into investing in vaccines which they could control for longer. The problem in this latter scenario, in line with the work of Blume (2005), is that vaccine programs can get locked in around a single candidate. In Blume's (2005) analysis of polio vaccination it was not necessarily the most medically effective vaccination which was taken up, but one around which routines, publicity, various political assumptions, funding and so on were focused. The relationship, Blume argues, between evidence-based argument and socio-economic processes changes over time (for more on this, see Stanton, 1999; Lehoux and Blume, 2000; Blume, 2006; Blume and Geesink, 2000).

Lanjouw (2006) suggests a way out of this patenting mire would be to look at tailored patenting. "Those patentees would effectively be required to choose to make use of their patent protection either in rich countries or in poor countries, but not both. Because the profit potential in rich countries is much greater, owners of patents related to global diseases will naturally choose to relinquish protection in poor countries. Thus, the policy would lower prices in poor countries where greater incentives are not needed… At the same time it would keep intact patent-based incentives for diseases such as malaria that are specific to poor countries, where there is a clear argument to be made that new incentives are warranted," (2006: 110). Although an interesting proposal, policing health tourism (where patients would move to get cheap drugs) or drug tourism (where drugs would move to more profitable markets) would be difficult and there would be few guarantees that the most optimal drugs would be developed.

Patents are effectively focused on stabilising the future around a particular product and have been imposed on developing countries seeking engagement with the World Trade Organisation (and in WTO patent tailoring is covered by TRIPS). Patent tailoring requires a complex governance and accountability system to assess which countries could justify tailoring and to ensure that pharmaceuticals and/or patients did not cross borders to access cheaper pharmaceuticals. Pharmaceutical firms have questioned patent tailoring: Could a system of governance, designed to control and account for the movements of people and pharmaceuticals, be enforced? Further questions include: Are IP interests primarily focused on pharmaceutical firms rather than developing countries? This raises a broader subsequent question for this report: if pharmaceutical firms are not interested (due to perceived weaknesses in proposed governance structures), is there a viable alternative focus for neglected disease research and development?

> Interviewee 17 (US-based neglected disease research funding body)
> [There is a need for research][3] on building the capacity of publicly funded research institutions in the developing world to manage intellectual property in local public/private R&D partnerships, and also layering onto that the idea, it's something that PDPs [Product Development Partnerships] have pioneered which is sometimes called Public Interest Intellectual Property Management or Humanitarian Licensing Practices, good stewardship of IP and so on. So there are creative ways to deal with intellectual property

> Interviewee 15 (US-based neglected disease Consultant)
> I actually think that most of the PPP's are managing it [IP] pretty well. They are accepting that there's a system there, they're accepting that in order to be regarded as doing things professionally by commercial collaborators they need to handle IP.

> Interviewee 19 (UK-based neglected disease research funding body)

[3] Comments in square brackets are author's addition for clarification

> …we would and do take a position on licensing of patents. You may have heard this from other organisations but when [we have] some kind of say or some kind of power to exert pressure on patent holders that maybe we perhaps fund or are involved with, we would feel strongly that the licensing conditions should be such that say PDP's or other organisations that would be developing these products for use in developing countries would be able to do so and there would be nothing in the licensing agreement that would prevent that. And even furthermore, some of the licensing agreements that have been designed partly by [us] or encouraged by [us] have set criteria for making potential end product available in developing countries.

> Interviewee 4 (European based PPP)
> Why do you want to invest in a patent? There is no likelihood that that investment will come back. At the end of the day, malaria vaccines for those who need them most, the African children, will have to be paid for by the donors, the traditional donors, including DIFID and others, and the World Bank and the Gates Foundation nowadays… But you should not count on that they want to pay a large amount to you on your investment in the patent intellectual property right.

Pharma's markets

Glennerster, Kremer and Williams (2006) suggest that one way forward for the development of vaccines and drugs for neglected diseases would be to construct markets for neglected diseases. Their proposal advocates Advanced Purchase Commitments (APCs) which would act as pull factors to entice pharmaceutical firms into developing vaccines for otherwise less attractive (i.e. less lucrative) diseases. They suggest: "One proposal to incentivize private sector R&D investments in products for diseases concentrated in poor countries is for sponsors (rich-country governments, private foundations, or international organizations such as the World Bank) to undertake 'advance purchase commitments' for desired products, such as HIV vaccine… If no vaccine is developed, no donor funds would be spent" (2006: 67). They argue that this approach is cost effective, involving an outlay of $15 per life year saved.[4] They also argue that APCs are particularly useful for product development Public-Private Partnerships (PPPs or sometimes PDPs such as IAVI and MVI, see next section). The cost-effectiveness of this approach is tied into broader arguments that vaccines are effective as they have fewer infrastructural needs than on-going medical treatments. Glennerster, Kremer and Williams (2006) argue that there are precedents for these pull factors such as the US Orphan Drug Act which encourages the development of drugs for rare diseases by offering longer than standard market exclusivity. They claim that since the Act in 1983, 200

[4] Developing country populations are usually considered good value anything up to $100 per life year. Glennerster, Kremer and Williams (2006) argue that: "the US cost-effectiveness threshold is estimated to be as high as $50,000 to $100,000 per life-year saved," (2006: 74).

orphan drugs have been developed. Before the Act, only 10 were developed.[5]

The details of the APC proposal are as follows: a group of credible sponsors provide a legal contract, which sets out the total potential market for a vaccine (around $3b). The sponsors then underwrite a price (say $15 per dose). This price is guaranteed for a certain number of doses (up to $3b). Countries which will be eligible are also established at this stage. After this fixed price, the developer (who will have covered their costs by this point) must guarantee to sell doses at a cheaper price (say $1 per dose). Sponsors would pay more than recipient countries of the initial $15 dose (say $14 and $1 respectively). Subsequent products would also be eligible for guaranteed price; if a better product comes to market, recipients could switch to another product. The proposal suggests an independent adjudication committee oversees the agreement.

APCs are not without criticism. The work of Farlow (2004; 2005; 2006; and with Light, Mahoney and Widdus, 2005) suggests that the APC "model for these vaccines [HIV, malaria, and TB] is unworkable, inefficient, and inequitable towards the wide range of potential developers and suppliers of such vaccines." (Farlow, Light, Mahoney and Widdus, 2005: 2). Farlow (2005) argues that there seems to be a "set of literature that severely downplays the problematic side of APCs for early-stage vaccines, and that instead paints a picture of a 'simple,' 'straightforward,' and 'powerful' new tool, even though APCs have never been used for anything before," (2005: 2). According to Farlow (2005) these tools will struggle to replicate market conditions. Furthermore: "The case for APCs for early-stage vaccines was not helped by the early decision to trivialize the science of HIV and malaria vaccine development to one that is 'linear,' fixed, simple and static, when for early stage vaccines it is instead highly complex, and dependent on feedback loops, collaboration, and comparison of results and sharing of information," (Farlow, 2005: 4).[6]

For Farlow, further problems with APCs involve questions of the size of the market (why would $3b be correct?), how to encourage further innovation instead of further sales of the same thing, how to figure out minimum standards of quality or effectiveness for these vaccines, whether or not APCs would damage PPPs (see next section), how non-eligible countries would react to these APCs, what the cost of running the systems would be, how firms will lobby to influence APC committees and how IP issues would be resolved. Farlow remains unconvinced that APCs would do much to

[5] In some cases APCs have a slightly different emphasis in comparison with Advanced Market Commitments (AMCs). The former are focused on putting in place an agreement to purchase a near-market product, the latter involve producing an agreement to purchase a theoretical future product once available, effectively (attempting to) stimulate general market competition to produce such a product. However, on occasions in the literature, APCs and AMCs seem to be used interchangeably.

[6] Farlow (2005) argues that later stage vaccines require different considerations: "For currently existing and near-market vaccines, purchase commitments are all about creating stability of demand, incentives to invest in production capacity, the tailoring of an already existing product to new users, the creation of low product prices, and access to vaccines," (2005: 3).

resolve other areas of vaccine problems (such as infrastructure and education) and raises concern that authors advocating APCs have not consulted people from or working in the developing world. Orbinski (2001) is more damning, suggesting that discussions of whether or not there is a market for TB vaccines are "little short of obscene," (2001: 231). Farlow, Light, Mahoney and Widdus (2005) suggest that more investment in PPPs "would be better at unlocking the constraints of developing and emerging economy biotech firms, releasing their innovation potential," (2005: 22). In sum, questions have been asked of APCs in terms of: Will APCs replicate a market? Do they make simplistic assumptions about the complex science of vaccine development, availability and infrastructure issues? Importantly for this report, are there ways of governing APCs so that they are equitable, workable and efficient? Do the accountability relations built into APCs stimulate future improvements or instead lock in the first available vaccine? Are developing country organisations able to play an active role in holding others to account?

> Interviewee 9 (UK government agency)
> …you need to have both push and pulls. My own personal opinion is that people haven't thought through enough who the AMC is aimed at. I mean I think on paper the AMC is a really interesting idea but we need to have a more detailed analysis of who will actually respond to developing potential vaccine candidates for neglected diseases and very often that's smaller bio-tech companies rather than big pharma so the incentives of an AMC are in the wrong time-scales for bio-techs and my view although I'm not an economist and I could be completely wrong – the timescales of AMCs is missing the most innovative part of the industry. I've talked to bio-techs and they're trying to take things forward more quickly than big pharma so we need a more nuanced approach more than just we'll promise to buy all this in 20 years time. We need intermediate milestones which will give the right incentives to the right companies at the right time in development. That's my own view which some others share, but I don't know how widely held that view is.
>
> If you've got a guaranteed market for something which is good enough but not very good what's the incentive for making something really good? If you get something that's good enough that you can work on to make better it would be the small companies that might take it up – so you need the IP right to make that happen.
>
> Interviewee 10 (UK based senior vaccine scientist)
> …the idea behind the Gordon Brown initiatives is that if you put a big enough pot of gold at the end of the rainbow that suddenly private companies will invest in these diseases.
>
> …that's an untested idea. The initial problem with it is… by and large vaccines are made by very very very big companies. 80% of the world vaccines are sold by six companies. These companies are interested in products that earn at least a billion dollars a year, not a third of a

> billion dollars a year, and the malaria vaccine and TB vaccine might hit peak sale of half a billion a year. But by and large they are under the threshold. They're not blockbusters.

> Interviewee 14 (Neglected disease consultant)
> I think largely because it was designed in the US and they have a strong pro-market preference, so all their incentives start with we need to make a market, because that will stimulate people. But in practice, I always say to them are there a lot of people in America have colds, of course there are, there's a big market for a common cold but there's no treatment for it. Why is that? It's because for some things it's not the market, it's the problem is we don't know how to do it.

Public-Private Partnerships

Public-Private Partnerships (PPPs) have been under development over the last ten years in a variety of guises. Broadly speaking, PPPs draw together private pharmaceutical firms, bio-techs and other private interests with public bodies such as UN agencies and state governments and sources of public and philanthropic funding. According to Buse and Waxman (2001) PPPs can involve solving previous, seemingly intractable problems engaging multiple countries and conditions. PPPs can be distinguished through partnerships managed by intergovernmental agencies (e.g. GAVI) and those managed by a separate legal entity (e.g. IAVI). Sundaran and Holm (2006) suggest PPPs should aim to reduce global disparities through new drugs, better access to drugs, enhancing the quality and viability of vaccine markets and by putting health at the centre of developments. They suggest PPPs usually involve: shared objectives, governance or advisory bodies of public and private members, new combinations of skills, expertise and resources and the use of cross-sector techniques to achieve goals.

Although most PPPs focus on drug or vaccine development and distribution, some focus on health education. Several PPPs have an independent legal status, while others operate more like an informal collaboration. Walt (2001) outlines three main types of partnership: Product Development Partnerships (or PDPs; e.g. new vaccines), systems/issues partnerships (e.g. based on advocacy) and product based partnerships (e.g. donation programmes). Nishta (2004) further suggests that PPPs can be owned by the public sector but with private partners or hosted by an agency/NGO or orchestrated by a company (i.e. Action TB), or be legally independent. Nishta (2004) suggests partnerships can be focused on: product development (IAVI), improved access to healthcare products (Accelerated Access Initiative), global co-ordination mechanisms (GAVI), strengthening health services (Multi-lateral Initiative on Malaria; MIM), public advocacy/education (Alliance for Microbicide Development) or regulation and quality assurance (Pharmaceutical Security Institute). PPPs also offer opportunities for managing risks.

> Interviewee 9 (UK government agency)

> We like PDPs because they are a good way of managing risk because of their portfolio of activities and their scientific expertise… we don't have that scientific expertise to manage all those tasks. Because they're managing a portfolio they're able to distribute their risk across different candidates.
>
> …going forward with one product is a big risk and we're not keen on those and as a donor you bear the expense yourself.

Furthermore, PPPs have become a recognised way to incorporate industry.

> Interviewee 15 (US-based neglected disease consultant)
> I think one of the things that people are starting to recognise is that …. I think they [PPPs] are potentially very good ways of getting industry in, I think there's a lot of bilateral donors, Northern European donors, Scandinavians that I still think are a bit suspicious of PPP's. They don't see that industry actually brings more to the table than they are paid to do. Most of these PPP's actually get a lot of pro bono contributions from industry that you probably couldn't get if you simply paid for it. Industry wanted to do the right things and PPP are a way of helping them do it.

According to Hanlin (2006) "PPPs are seen as mechanisms that reduce transaction costs, increase collaboration and build trust in a way that will provide a mechanism for vaccines to be developed," (2006: 20). Chataway, Hanlin and Smith (2005) suggest that PPP's "are seen by some as a way of overcoming the crisis of 'neglected diseases' and the fact that 90% of the world's spending on health related research benefits only 10% of its population." (2005: 1). Advocates argue that in the PPP pipeline are: 8 diagnostics, 45 new drugs, 8 microbicides and 50 vaccines in development. It is said PPPs also contribute to local health and research infrastructure and help make progress toward Millennium Development Goals of health for all (see 'Open Letter to the G8,' 2005). Taking on these viewpoints it would appear that PPPs offer a way forward that incorporates an active role for developing country organisations in forms of mutual accountability (particularly in face-to-face partnership meetings). However, Chataway, Smith and Wield (2005) argue that PPPs only offer the potential for advantageous developments if they operate and are understood in particular ways. They suggest, for example, that PPPs should focus on a broad range of innovations, not just the science of vaccines. Innovation for PPPs should also include capacity building, ways of working in developing countries, establishing local centres of expertise, ensuring efforts are sustainable and relevant beyond the BRIC countries (Brazil, Russia, India and China) which usually receive attention.

Further concerns are raised regarding the nature of the 'partnership' implicated in PPPs. Widdus (2003) suggests: "True partnership is really about combining different skills, expertise and other resources – ideally in a framework of defined responsibilities, roles, accountability and transparency – to achieve a common goal that is unattainable by

independent action." (2003: 3). However, Buse (2004) raises concerns regarding inequality between partners, with developing countries bringing populations of sick people to the table (who are not considered a resource) and large pharmaceutical companies bringing expertise, possibly the means of distribution and possibly finance to the table. Both Hall, Bockett and Taylor (2001) and Sundaram and Holm (2006) look to the use of terms such as interactions, alliances or collaborations as an alternative to partnership. Yet such a change in terminology does not address the issue of unequal partners if it is perceived as a problem in PPPs (Buse and Waxman, 2001). Indeed the ways in which developing world 'partners' have been incorporated into PPPs raises problems for Hardon (2001) who suggests PPPs involve: "reinforcement of donor dependence, a skewing of health programs, a large emphasis on creating markets, the weakening of UNICEF's independence, a lack of sustainability for traditional vaccine suppliers and technology transfer, greatly reduced transparency, and limited involvement by developing countries and consumers," (2001: 21). Hayes (2001) further suggests that "there are huge differences in the quality, sustainability and power relationships of the types of co-operation now all being labelled as 'partnerships'," (2001: 4). Rundall (2001) argues that private partners in PPPs "aggressively advertise their links with charities and good causes in order to counterbalance bad publicity," (2001: 23) building surplus good publicity in case of a crisis ahead.

Further problems for PPPs are noted by Nishta (2004) who suggests that challenges include: a lack of global norms and principles shared between partners, private firms may re-orient public sector health care, the possibility that local state care will be withdrawn in anticipation of PPP outputs, a conflict of interest between partners, international efforts may ignore specific local issues, health systems may be fragmented (as PPPs chase easy wins, such as easily accessible segments of the local population), there may be a need for common goals and there might need to be a focus on outcome (not just how to work). Sundaram and Holm (2006) suggest more research is required on PPPs, while Chataway, Smith and Wield (2005) argue that research assessment (such as the UK's RAE) acts as a disincentive to UK researchers to pursue practical research on PPPs' effectiveness (as the RAE stresses academic publications and development journals are not considered highly).

Oechler (2004) warns PPPs are not a "magic solution," (2004: 32). In Caines and Lush's (2004) research, the participant countries showed: no capacity to assess IP; limited involvement of health policy makers in trade negotiations; little support from international organizations on IP issues; lack of capacity to register/enforce brand drugs; little trust between government and pharmaceutical companies; confusion over whether one policy (say discounting) ruled out another; little means to secure best prices on existing drugs; little means to compare effectiveness of drugs; and limited information from international organizations on prices, quality, sources, and utility of different drugs. However, they conclude that excluding private firms is unrealistic as a way forward in drug development.

If PPPs remain the most appropriate way forward for engaging with neglected diseases, how might some of these issues be tackled? Buse (2004) suggests that developing countries should have reserved seats on PPPs (as is the case with GAVI) and that: "Access to timely and relevant information about decision-making is essential to enable stakeholders to hold an organization accountable and to enable participants and representatives to make meaningful contributions to the deliberations," (2004: 236). To understand governance, Buse argues we need to develop further insights into: legitimacy: particularly is governance considered legitimate by those subject to it; representation and participation: notably are those governed involved in decision making?; accountability: are those involved in decisions and outcomes available to be held to account; transparency: "the extent to which information pertinent to decision- and rule-making is freely and readily available to those affected," (2004: 230); are governance arrangements sustainable?; and do governance arrangements operate in a particular context (most PPP secretariats are 'based' in Geneva or the US and questions are raised regarding the importance of these locations in shaping development issues, perhaps underplaying the local detail of developing country contexts). Buse (2004) suggests we need to understand PPPs' "authority, representation, accountability, transparency and oversight," (2004: 226).[7] In sum, the fluidity and complexity of PPPs has led to questions of governance (who is in control of partnerships, are partners equal, what should be the ethical principles of PPPs and how should they work?) and accountability (how should PPPs be measured, what would count as an effective partnership, how can they be rendered transparent?). Even where metrics are in place to hold a partnership to account, further questions can still be asked.

> Interviewee 15 (US-based neglected disease consultant)
> It's very difficult because, one of the things I put to them earlier, you can have a PDP that is moving things down the pipeline that is having a lot of success with process indicators, and they may be doing the wrong things. They may be not paying attention to the delivery issues, product design, whether people are doing the right thing as well as making progress has to be part of this evaluation. Whether they frame the question correctly… accepting that it will take a hell of a long time to get to performance measures that are based on delivery of health impact is one of the things that maybe PPP's have oversold themselves a little bit on.

And, in partnerships which incorporate developing country organisations, there remain challenges.

> Interviewee 5 (EC representative)

[7] Buse (2004) is not alone in voicing such governance and accountability concerns. Similar points are made by Nishta (2004) and Widdus (2003). Garner (2005) goes a step further in suggesting that we need to develop "consistent, transparent and workable policies and criteria for closing down partnerships that are unlikely to succeed" (2005: 7).

> In [a European PPP] there has been substantial involvement from developing countries. There is a developing countries committee of prominent scientists from developing countries – so they have an equal say in the priority setting for what kinds of new research and capacity building should be supported. The problem as I see it, the European representatives are more or less official representatives of their countries. The same cannot be said for African participants – it is very difficult to get official commitment and support for this process. It is mainly Africans involved at this stage are just talking for themselves. The reason is that the research agenda has a very low priority in most African countries.

Summary

Problems for effective intervention in the disease burden of the developing world are multiple. Research suggests this involves issues of:

- Vaccine and drug development (some diseases have no vaccines or effective drug treatment, some have drugs or vaccines, but price and quality is difficult to control)
- Education (sometimes effort is required to provide a sufficient number of administrators, sometimes a local population requires convincing of the value of vaccination or treatment)
- Finance (for the development and purchasing of drugs or vaccines)
- Infrastructure (for local delivery, for local, sustainable research initiatives, for administering vaccines and treatments)

Various interventions have been attempted, but each of these interventions is said to involve further questions of governance and accountability:

- Tax breaks are designed to encourage pharmaceutical firms to invest in research and development, targeting diseases of developing countries. However, holding pharmaceutical firms to account for the promises they may make in return for tax breaks provides a narrow perspective on neglected diseases which does not cover many of the problems outlined above.
- Discount schemes are designed to make existing drugs treatments available at a price affordable to developing countries. However, governance and accountability questions arise in relation to loan systems (which may lock developing countries into expensive debt), levels of discount and how promises of discounts would be met (held to account by what means?).
- Extended patents are intended to enable firms to distribute their profits over a longer period reducing the cost of each dose, while short patents are designed to open up access to IP. Patent tailoring is proposed as a compromise. However this might fix governance and accountability measures around a single product, doing little to enhance further innovation in the same area, may lead to lock in around a sub-optimal treatment and there appears little interest amongst pharmaceutical firms in a change in patent governance.
- APCs would introduce a new system of governance and accountability based around guaranteeing a contractually agreed price for particular

vaccines up to a certain maximum value, providing a market for less marketable diseases. However, it is argued that this governance and accountability focus on pre-agreed contracts, problematically simplifies the science of vaccinology, markets and problems faced in providing vaccinations and may face enforcement difficulties in relation to next generation products.

- Momentum seems to be with PPPs which draw together private firms with public bodies to work together, in a long-term, sustainable manner, addressing a broad range of issues. Partnerships may enable management of risks and offer developing country organisations the opportunity to participate in accountability. Yet governance questions of control, inequity, ethics and ways of working, and accountability questions of measurement, effectiveness and transparency, continue to come under scrutiny. However, PPPs are the only intervention potentially offering governance and accountability face-to-face (through partnership meetings), in metrics (through performance measures and indicators developed by funders), through transparency initiatives and forms of engagement (which could offer opportunities for accountability beyond the narrow membership of a partnership).

How might this range of governance and accountability questions be addressed and what other difficulties arise in specific instances of practice? The next section of this report will provide a succinct analysis of options addressed in the case of malaria.

3. The Specific Case of Malaria

Background

This section features an analysis of issues of governance and accountability raised in relation to interventions in the specific neglected disease of malaria. In line with the preceding section, it draws on research and arguments presented in the malaria literature and on interviews carried out with individuals in the field.[8] It is claimed (Bayer, 2006) that between 300 and 500 million people contract malaria each year. It has also been claimed (VOA, 2005) that half the people who have ever lived have been killed by malaria and that 3 children a minute continue to die from the disease. Somewhere between 1 and 2 million people are said to die each year from malaria and around 90% of these deaths occur in Sub-Saharan Africa, with 90% of those deaths occurring in children under the age of 5 (National Geographic, 2007; Gates Malaria Partnership, 2006). It is said (GSK, 2005) that malaria costs Africa $12b a year and accounts for 40% of public health spending in sub-Saharan Africa.

When infected female Anopheles mosquitoes bite humans they inject a sporozite into the bloodstream through the mosquitoes' saliva. The sporozite enters the liver where parasites multiply before being released into the body via red blood cells. Malaria can then spread through the body, causing fever, vomiting, coma and death. Adults can build immunity to malaria through successive attacks of the disease. However, adults can lose immunity (for example in pregnancy), can suffer from on-going mild attacks of malaria even with immunity, can suffer from neurological damage (as parasites might attach to the brain) and children under 5 have little chance to build up immunity. Other mosquitoes biting the human after infection can then become carriers of malaria and infect others. In different regions of the world, there are different mosquitoes (Anopheles gambaie and Anopheles arabiensis in Africa and Anopheles stephensi and Anopheles culicifacies in Asia). It is said that only one species of mosquito (Anopheles gambaie) prefer humans to livestock (FARM-Africa, 2005). There are also different strains of malaria (plasmodium falciparum, p. vivax, p. malariae and p. ovale), with p. falciparum being the most lethal and most commonly found in Sub-Saharan Africa. In the body these parasites are said to be able to mutate in response to obstacles (such as immune responses) presented by the human body. Despite all these claims, statistics and scientific models, there is a frequent refrain that malaria retains significant unknowns (National Geographic, 2007; VOA, 2005).

Attempts to alleviate the disease burden of malaria in Africa have involved educational initiatives (for example based on promoting the use of bed nets), malaria management drives (through, for example, attempts to reduce mosquito populations) malaria treatment (through the provision of medicines to people who have developed malaria) and vaccine development programmes (co-ordinated by, for example, the Malaria Vaccine Initiative

[8] 34 interviews were carried out with research funders, university researchers, consultants, policy makers and pharmaceutical firms involved in malaria. Quotes from these interviews are clearly labelled in this report and have been anonymised.

(MVI) a PPP involving Gates Foundation funding, GSK pharmaceuticals and University researchers amongst others). Each of these activities has run into complex problems. Firstly, malaria differs by region in terms of its prevalence and seasonality. Some areas have low levels throughout the year, some areas are characterised by seasonal upswings in the number of mosquitoes and rate of malaria infection (for example, during the rainy season) and some areas have high malaria prevalence year round. Significant problems also arise in attempts to predict where and when epidemics of malaria might start in regions characterised by sporadic outbreaks (Gates Malaria Partnership, 2006). Secondly, malaria differs by region in terms of the symptoms suffered by patients (for example, the likelihood of coma). Third, provision of equipment such as bed nets have cost implications and insecticides in bed nets only work for a certain period. Fourth, attempts to manage mosquito populations can be costly and cause local pollution (although this is still a matter of debate). Fifth, the provision of medicine to malaria sufferers can be expensive, requires sometimes lengthy treatment which requires a medical infrastructure and requires that patients are diagnosed correctly and treated appropriately and swiftly. Sixth, malaria is a parasitic disease and the parasite may be able to adapt swiftly to, for example, vaccines introduced into the bloodstream to combat the disease. Indeed the Walter Reed Army Institute of Research in the US point out: "There has never been a vaccine against an organism this complex; there has never been a successful human vaccine against a parasitic disease," (VOA, 2005: 1).

Malaria PPPs

Each of these initiatives to combat malaria – education, disease management, drug treatment and vaccine development – has involved a Public-Private Partnership (PPP). These include educational and advocacy initiatives such as Roll Back Malaria (RBM) PPP, malaria treatments and the provision of medicine involving Medicines for Malaria Venture (MMV) PPP, a combination of both of these activities through the Global Malaria Programme (GMP) and attempts to develop a range of different malaria vaccines under the stewardship of Malaria Vaccine Initiative (MVI) PPP.[9] Looking in detail at each of these areas of activity can provide us with insights into the problems and possibilities posed by work to combat malaria.

Educational and equipment initiatives

The Roll Back Malaria (RBM) PPP involves WHO, UNICEF, the World Bank and UNDP along with state agencies and private enterprise in a variety of attempts to alleviate the burden of malaria. RBM identify as one of their key activities raising awareness of issues relating to Malaria in order to get the disease into various policy, funding and state political discussions (RBM,

[9] There is also the smaller European Malaria Vaccine Initiative (EMVI) amongst several other initiatives. These include: European Alliance Against Malaria, Malaria Consortium, Malaria R and D Alliance, Malaria Research and Reference Reagent Resource, Multilateral Initiative on Malaria, South African Malaria Initiative, VOICES for a Malaria Free Future, Walter Reed Army Institute of Research, Massive Effort.

2004). They identify the principal causes of malaria as poverty, conflicts and natural disasters and the ability of mosquitoes to elude straightforward treatment. The RBM strategy involves helping to promote various measures to aid prevention of the disease. Insecticide Treated Nets (ITNs) are promoted by RBM as "one of the best ways to prevent mosquitoes from biting people and infecting them with malaria," (2004:8). However, simply providing nets is insufficient to guarantee protection against malaria; RBM attempts to deliver nets alongside "social marketing and education, setting technical specifications and development of new technologies (such as long-lasting insecticidal nets)," (2004:8).

An important challenge perceived by many involved in these educational issues is to counter local myths regarding malaria, for example that it is caused by "excessive sun exposure, eating too many mangoes, being rained upon or, in severe malaria, possession by evil spirits," (GSK, 2003: 4). RBM do not limit these initiatives to providing nets and educating populations about their use. They are also involved in spraying insecticides in people's homes (discussed more fully in the next section). Private pharmaceutical firms (such as Bayer, 2006) are also involved in these net initiatives, looking to build local manufacturing capacity in developing countries for the provision of such equipment. However, ITN based initiatives involve complex questions regarding the cost implications of nets (they could be given for free, but this would not build a sustainable local business, they could be sold, but not everyone would be able to afford a net. Instead, some advocate voucher systems, but this requires infrastructure only accessible to those in towns not rural areas and may still lead some to use discount vouchers to purchase the cheapest, not the most effective nets), the length of time insecticide lasts (for some new long-lasting nets, it remains unclear how long exactly the insecticide will last as the nets are relatively new developments), who gets access to a net (some rural populations find access more difficult than urban populations, but rural populations are more likely to be affected by severe malaria) and the role of nets in eradicating malaria (insecticides can kill mosquitoes, reducing malaria, but if someone sleeps under a net, they will not build up immunity to the disease meaning they may be susceptible to severe malaria when bitten). There is also some evidence of mosquitoes developing immunity to insecticides used in nets (for more on insecticide immunity, see next section).

> Interviewee 13 (Senior scientist in neglected diseases)
> I fear a lot of the subsidy – which is about the same as if you bulk purchased free nets is going to people in urban areas who only need protection against nuisance mosquitoes not malaria – it's not at all targeted. Just about no-one uses a voucher to buy a long-lasting net, they pay less to get whatever they can. A torn, untreated net is no better than no net at all. Regular annual retreatment is obsolete now. Even if [insecticide treated] long-lasting nets are torn they're still useful because before the mosquito finds the hole, they've picked up insecticide.

> Interviewee 18 (Malaria PPP)

> Well I think that when you look at clinical trials of bed nets there's about 30% efficacy, which is pretty good in terms of value, and it's about what we think the vaccine is, so you start adding these things together.

Managing malaria

Initiatives to manage malaria, involving inputs from the Global Malaria Programme (GMP) and Roll Back Malaria (RBM) amongst others, look to reduce the number of cases of the disease by controlling the population of mosquitoes. These activities include attempts to: breed mosquitoes which can not carry the malaria parasite and which are more likely to breed successfully and survive than existing mosquitoes (ABC, 2007); introduce mosquito-larva eating fish to water sources where mosquitoes breed, a form of larvicide (GMP, 2007); spray outdoors (Wall Street Journal, 2006) or indoors (WHO, 2006) with insecticide; and control livestock which may be involved indirectly in increases in malaria incidents (BBC, 2001; FARMAfrica, 2005; HHIAD, 2006; WHO Bulletin, 2001). Unlike drug treatments (see below) which may not reduce the number of cases of malaria, but simply provide a means to treat cases as they arise, these mosquito management strategies aim to cut the cycle of disease. By reducing the number of ways in which mosquitoes come into contact with humans, the chances of delivering malaria parasites to the body are reduced and, as a consequence, the chances of another mosquito picking up those parasites and infecting another person are also reduced. Historically, these management strategies have proved a success in the US where malarious swamplands were transformed through environmental management and in southern Europe where the population of malaria-carrying mosquitoes was eradicated (National Geographic, 2007).

However, it should not be assumed that these management strategies are without problems. Firstly, breeding resistant mosquitoes is scientifically complex and there appears no clear rationale for why these insects should flourish at the expense of existing mosquitoes. Secondly, managing water sources is complex as the sources can dry out during dry season (requiring management of larvicidal fish stocks) and new water sources can appear all the time (keeping abreast of all likely mosquito breeding grounds becomes difficult). Thirdly, spraying may have an impact on the local environment, damaging crops, or on local people (however, as arguments over DDT have demonstrated, this is not always agreed upon, Wall Street Journal, 2006[10]). Also if spraying reduces mosquito prevalence for a time and then they return with malaria in numbers, cases of severe malaria may increase as the population's immunity to the disease may have decreased during the lull in attacks. It has also been suggested that in certain parts of the world mosquitoes are developing immunity to insecticides. However, the case has been argued that spraying could have been pursued more vigorously in certain developing countries to reduce malaria (GMP, 2007) and that some contemporary spraying programmes are producing good results (RBM, 2007).

[10] There are emotive claims that banning DDT may have killed 20m children (National Geographic, 2007).

Fourthly, control of livestock and the exact relationship between incidents of malaria and, for example, movement of cattle, remains a point of contention (e-mail exchange with malaria scientist). These efforts to manage the disease appear to remain on the margins of malaria intervention:

> Interviewee 7 (Neglected disease scientist)
> You need good intervention to stop it getting into the liver, to stop it getting out of the liver and to treat it once it's out. So the focus has been on drugs, bednets and now vaccines. Things like spraying is worth exploring a bit, but it's unstable. Environmental control doesn't stand a chance because Anopheles is fantastic – it can breed anywhere in sub Saharan Africa. Even in a hoofprint. So it might work elsewhere in the world.

Treatment of malaria

Treating malaria can be an expensive process which can take some time, requires a healthcare infrastructure, requires access to swift and appropriate treatment and a supply of relatively expensive drugs (relative to the (lack of) wealth of the population requiring treatment). For these reasons, a malaria vaccine is heralded by some as the most appropriate way forward in place of treating people with malaria (as it is claimed a vaccine would be easier to administer, require less infrastructure and could perhaps be cheaper than drugs required for treatment; see next section). However, the problem remains: there is as yet no malaria vaccine (although see next section) and around 500 million people per year contract malaria.

The Medicines for Malaria Venture (MMV) PPP including university scientists, GSK pharmaceuticals and biotech firms have been involved in attempts to produce cheaper and more swiftly effective medicines for malaria. However, this is not primarily a charitable concern. GSK suggest the "primary responsibility for addressing this problem rests with governments, but all stakeholders, including the pharmaceutical industry, have important contributions to make," (GSK, 2005:13). GSK are also concerned about the marketability of their work; "Pharmaceutical companies must be profitable to sustain their business and to continue to develop new medicines… Unfortunately, because of the lack of resources in endemic countries, there is limited profit to be made," (GSK, 2005:14). GSK see PPPs like MMV as the only viable way forward, with funds provided by development organisations or funders like the Gates Foundation, a significant research contribution coming from the academic science sector and GSK providing "clinical, regulatory and manufacturing expertise," (GSK, 2005:14). This combination, they suggest, should enable treatments to be delivered at affordable rates. However, GSK are clear that they are opposed to patent tailoring through TRIPS which may make existing treatments available at lower rates to developing countries by opening up the patenting and intellectual property rights of particular medicines to local producers who can then provide cheaper generic versions of drugs. Firstly, they enter into "anti-diversion measures," to prevent any drugs discounted from moving from the country where they have been made available cheaply to elsewhere (GSK, 2005:20).

Secondly, they state: "GSK believes that widespread use of compulsory licences [TRIPS] will undermine the intellectual property framework and be counter-productive in the long term. R&D into new treatments, especially where commercial markets exist… depends on protection for intellectual property," (GSK, 2005:21). It remains questionable if malaria provides a viable drug market. However, attempts to make malaria 'profitable' through initiatives such as APCs can also run into problems.

> Interviewee 14 (Neglected disease consultant)
> …one firm actually said to us if there was a profit in this we would leave, because what we're getting out of it now is the good guy benefit, and if we're making money we don't get that and it's not worth it, we just go back to blood pressure. So I think it was very, very clear that they wanted to partner, it wasn't about profits and the incentives were set wrong.
>
> …it's funny, because when the economists reviewed our work they said it's, the funniest thing is that governments appear to be, there's a lot of not-for-profit activity being done by companies in the drug field and governments are now trying to monetise it in a sense, and move them to doing it for-profit what they now do not-for-profit, and it's really hard to see why you would do that.

Concerns regarding the intellectual property and difficulties of providing medicine cheaply without undermining pharmaceutical firms' markets are not the only issues involved in delivering treatment to patients. Firstly, despite the efforts of MMV, treatments are only available to some in areas where there is a healthcare infrastructure and, even in these areas, these treatments are dependent upon an accurate diagnosis of malaria. For example, Gates Malaria Partnership suggest: "In moderate and low transmission settings over 90% of all anti-malarials were given to people where the clinician had requested a malaria test and received a negative result," (Gates Malaria Partnership, 2006:22).[11] Secondly, even where drugs are available and delivered to people in a timely manner, there remain uncertainties regarding the effects of malaria treatments on specific members of the population. For example, although those living with mosquitoes year round tend to develop a certain amount of immunity from severe forms of malaria, as suggested previously pregnant women appear to lose this immunity. However, it remains unclear the extent to which existing malaria treatments such as artemisinin-based derivatives, have negative impacts upon women in pregnancy and their unborn babies (New Scientist, 2006:27).

Thirdly, treatment of patients takes time and can require repeat visits by patients to clinics. There is often insufficient infrastructure in place to

[11] This issue of diagnosis is a general problem for making claims about the prevalence of a particular disease in a particular part of the world. Further examples of this problem include claims regarding the pervasiveness of HIV/Aids in, for example, Kenya when only 10% of the population actually know their (positive or negative) diagnosis (GSK, 2005:22).

ensure that patients are reminded of the necessity of re-visits to surgeries. One means to treat patients is through Intermittent Preventative Treatment (IPT) where those in high prevalence malaria areas are given anti-malarial treatments as a protection against future infection. In this case, drug treatment operates like a proxy vaccine. However, drop out rates from this treatment regime can be high. In one study patients dropped out due to perceptions that the local scientists were taking too much blood from children being treated, suspicions about the content of the drinks offered to participants after treatment and concerns that the device used to measure children's height for demographic information (which required children to lay down) were measurements taken in preparation for the building of a coffin (as prone bodies were only commonly measured for coffins in villagers' experience; Pool et al, 2006).

Fourthly, it is not clear that academic medical scientists who are heavily involved in the treatment of malaria patients are primarily interested in engaging in the politics of medicine availability or health care infrastructural problems. For example, one scientist suggested in regard to treating patients with malaria: "It is not that interesting… My main thing in life is to learn new things," (New Scientist, 2006:31). Another pointed out that: "Our clinics cannot replace a failing public health system… We're here to do research," (New Scientist, 2006:35). Fifthly, the malaria parasite appears to be able to develop immunity to treatments it encounters in the human body by mutating. These mutations can then be picked up by other mosquitoes and can infect other people leading to an escalation in cases and severity of malaria (as people's immunity is rendered less meaningful). One way to combat these problems has been to combine different drugs into combination treatments. This appears to reduce the chances of immune parasite development. A downside of this approach is that the more active ingredients that are combined into a single drug, the higher each treatment costs and the greater the likelihood of more IP issues arising (as each ingredient might be 'owned' by a different company; immunity is also an issue for vaccines, see next section). Sixthly it appears that there are further infrastructural issues which require attention in relation to malaria drug treatments.

> Interviewee 7 (Neglected disease scientist)
> In the drug world there are certain products that people are going to have to choose between and it's become a competitive shimbling shambling mess. Ministries have no idea what they're supposed to be doing and WHO are proving no help. I imagine the same thing would happen if there was more than one vaccine product.

> Interviewee 17 (US-based neglected disease research funding body)
> …there is very little work being done yet to get the Ministries of Health of the developing world ready for the concept of the introduction of new products on a regular basis into their malaria programmes.

Vaccine development

Malaria, like most other diseases found predominantly in the developing world, does not have a market – a population or state insurance system sufficiently affluent to hold out the promise of profitable returns if investments were made by pharmaceutical firms in research and development aimed at producing a malaria vaccine. However, vaccines are presented by some as the most effective way forward to reduce the burden of malaria. Vaccines may require less healthcare infrastructure than medical treatment (as vaccines may not involve on-going treatment), may be administered to children and may last a long time, and may reduce the population of malaria-carrying mosquitoes (as mosquitoes will have fewer infected bodies to feed on and fewer opportunities to carry malaria).

> Interviewee 1 (Clinical trials manager, sub-Saharan Africa)
> [the leading malaria vaccine candidate] has shown reasonable protection against the amount of malaria kids get. 30% less malaria that children get in a season following the [a dose of the leading candidate] vaccine. And it shows 60% less severe malaria in children. So it's encouraging but it's not brilliant. The 30% figure is quite important because we see about a 30% reduction in malaria in children sleeping under bed-nets. So what we're looking at at the moment is a vaccine that's about as effective as sleeping under a mosquito net. So is it worth it? Lots of people say no, but if you vaccinate kids then it's done and that's less than having to educate populations about bed-nets making sure they haven't got holes and so on.

This positive picture of the potential for a malaria vaccine is dependent on the theory that a vaccine will have reasonable efficacy, be deliverable in one dose (or at most a few doses), last a long time, and operate in the liver stage of the disease (thus reducing malaria in the bloodstream and breaking the disease cycle). Each of these areas is a matter of discussion as subsequent debate will demonstrate. For some, a malaria vaccine is a feasible way forward.

> Interviewee 3 (US government agency)
> We also know, based on the … experience [of the current leading malaria vaccine candidate], that here you have a novel synthetic vaccine that gives you at least partial immunity and so, you know, if you take all of these things together, I think that the overwhelming impression is that technically it should be feasible to come up with a malaria vaccine.

While for others, a malaria vaccine may not be worth pursuing.

> Interviewee 2 (Senior neglected disease scientist)
> I see malaria vaccine as taking money away from areas that we know work to something which is entirely speculative. I'm just a bit cautious about that… It's a really serious issue…. [The current leading

> malaria vaccine candidate] will never achieve anything at all in Africa.

Others suggest that the absence of vaccines for diseases of the developing world provides a physical embodiment of inequality between developed and developing countries; a form of vaccine poverty.

> Interviewee 6 (Sub-Saharan Africa based PPP scientist)
> …a child born in the USA now has access to 16 vaccines OK? A child born in Africa today has access to 6. So the gap has got bigger. The rich have got better off and the poor has stayed the same. Talk about developing new vaccines, there's a lack of access to already available vaccines. Some of those are not so expensive and are maybe not a priority.

The Malaria Vaccine Initiative (MVI) PPP (managed through Program for Appropriate Technology in Health – PATH) is involved in overseeing around 15 vaccine development projects. The Gates Foundation has contributed $257m to MVI. Although this is a potentially beneficial funding source, choices are still required between different vaccine candidates, different areas of the world for testing, different possible means of combining candidates with other substances, different ways of administering candidates (as one off or on-going programmes) and so on. For pharmaceutical firms like GSK, PPPs become the only viable way forward as GSK are accountable to their shareholders (who it is claimed by GSK will not look favourably on highly risky investments in research and development for products with no markets). PPPs take on the financial risk of trials for vaccine candidates, with pharmaceutical firms contributing expertise. PPPs also take on the reputational risks involved in trials meaning that no single organisation (such as a pharmaceutical firm) has to take on all the issues resulting from a trial failure (from being associated with failure through to liability issues).

For university scientists involved in much of the early stage research work in vaccines, PPPs are a viable way forward too as they provide research investment, and also hold out the promise of taking up discoveries made in early stage vaccine testing and putting these into development sometimes in partnership with pharmaceutical firms (something which university scientists do not always have the infrastructural capacity to achieve). University scientists are mostly held to account through forms of peer review of published articles in well respected journals (which can be achieved more effectively according to scientists through multiple publications on early stage vaccine research than through tying oneself into one or two long-term testing projects) and are under some pressure to bring in research funding. Having PPPs take on promising vaccine candidates for trials, enables academics to meet these targets. This suggests PPPs are a useful way forward for vaccine development. However, funding is only one obstacle on the way to producing a successful vaccine: there are also problems with complex science, with vaccine trials and questions regarding appropriate focal points for activities. Attempts to hold vaccine developments to

account through PPP funders, have involved a focus on clinical trials (which must adhere to procedural standards) and attempts to measure the success of PPPs (based on vaccine efficacy, project milestones, agreed management plans and go- and no-go-points). These accountability processes have proven complex.

> Interviewee 4 (European based PPP)
> We've also learned from … trials that it's enormously difficult on a scientific basis to define the outcome, what do you want from your vaccine? What is it you expect from your vaccine? Now if you are an industrialist and seasoned in the game, you're having one or two objectives and then you have 25 exploratory objectives because then you will always hit something. So it was one of the exploratory objectives that satisfied the criteria when [the leading malaria vaccine candidate] moved on, it's not the original objectives. So it's a lesson for all of us how difficult it is. It is a difficult area.

Despite the continued focus on accountability through measurement and outcomes, the complexity of figuring out likely outcomes in advance, has led to the development of numerous possible goals being the likely focal point for assessments of success.

> Interviewee 3 (US government agency)
> …in the [recent] trial, because it was a larger trial that involved something like 1,600 children, it had the opportunity to look at severe disease as a secondary endpoint. So the study was not actually powered based on that. So it wasn't that they necessarily set out to look at that as a primary endpoint and that he had enough participants to do that, but, as it turned out, they were able to achieve a statistically significant, or demonstrate a statistically significant reduction in the incidence of severe disease of around 58% that was, you know, that was not, as I said, it was not a primary endpoint but it turned out to be statistically significant.
>
> The obvious question with that is, is this a statistical fluke? Will it hold up in subsequent trials if under similar epidemiologic settings? And will it hold up in different epidemiologic settings?

This fluid approach to outcomes has partly stemmed from the complex and uncertain science of malaria vaccinology. One approach taken to producing a malaria vaccine has been focused on a prime-boost strategy. This involves stimulating people's antibody responses to malaria through focusing on the malaria sporozite. Although Gates Malaria Partnership tested a variety of these prime-boost vaccine candidates, the results were disappointing; "it did not provide any protection against clinical attacks of malaria" when tested (Gates Malaria Partnership, 2006:26). This emphasises a central problem with the science of vaccine development: promising vaccine candidates can involve high costs (in terms of testing, trialling, in different places at different times of year, with different mosquitoes and so on; MVTR, 2006), a great deal of time (due to the variety of tests required and

the necessity of gradual technical adjustments which can take 10 to 20 years; BBC, 2004) and there is insufficient funding and scientific capacity to pursue all possible candidates. Hence choices to fund one possible candidate rather than another involve significant commitments. These choices are not made blindly; early 'challenge' testing is used as a means to figure out appropriate ways forward. However, the effectiveness of candidate malaria vaccines is never 100% (that is, candidates never provide 100% coverage against all attacks for all people), so further decisions have to be taken regarding adequate efficacy. Efficacy claims for the current leading malaria vaccine are around 30% (see above interview quote and, for example, Guardian, 2007). Although the latter sounds low, reducing malaria by 30% for 500 million malaria sufferers per year would be an achievement and the trial demonstrated around 58% efficacy in children aged 0 to 5. However, appropriate efficacy levels have been a matter of dispute.

> Interviewee 4 (European based PPP)
> But there is no vaccine in the world, none whatsoever, which has an efficacy that's below 80%, most of them 90%, so why should you go for a 30% efficacious vaccine for the poor in Africa? That's simply a double standard, you can't do things like that, that's immoral in my view. I dare not say it loudly when the [pharmaceutical firm] board member is around but I whisper it in his ear from time to time.

> Interviewee 6 (Sub-Saharan Africa based PPP scientist)
> How do you assess something that can really save people's lives? In business sense something that's 60% effective is of course better than something that's 30%, but if you've got nothing at the moment then 30% is good enough. You can't pre-determine an efficacy rate based on say animal data. The only time you'll know is at a big phase three efficacy trial. You know you're testing it out in the world and then you can't say a vaccine has got to be 70% efficacy. That sounds like a good figure but 50% efficacy is a humungous leap from a public health perspective, but it might not make much sense from a financial perspective.

> Interviewee 18 (Malaria PPP)
> …our ability to be able to make a 100% vaccine is probably non-existent. And the reason for that is that even people who get infected are never immune. They don't get clinical malaria because they have enough antibody to prevent the side effects, but they get parasites in their blood and it has effects in terms of their immune system, etc. So it's a different kind of situation than a viral disease where if you get one bout of it you're done with it for life, and you can make a vaccine just, you know, a limited number of, or maybe a single protein, and that's not true for malaria as far as we know because the parasite's used to, it's evolved to live in the blood so it has very, very extensive escape mechanisms.
>
> But …all diseases are not the same in terms of making vaccines in terms of their complexity. Most vaccines in the past were made by a

> kind of an opportunism; you just try something and it works. We're trying to be a little bit more directed about this but, to a certain extent, we're still doing the same thing with a much more complicated organism.

Further decisions have to be taken regarding the length of time any candidate vaccine provides protection. This ties developments into time commitments in relation to testing the on-going efficacy of candidate vaccines (and involves further questions of what counts as adequate temporal efficacy). In a similar manner to drug based IPT, it is not clear how long vaccines will boost immunity. These temporal problems are said to be exacerbated by malaria's parasitic nature. The parasite can adapt to the conditions presented by the body and effectively develop immunity to the vaccine candidate. Subsequent mosquitoes attacking the body hosting immune sporozites can then go and infect other vaccinated bodies whose defence against malaria will have been compromised. It has been suggested that vaccines (like drugs) might need to combine promising candidates in order to reduce the chances of immunity developing in malaria parasites.

> Interviewee 15 (US-based neglected disease consultant)
> I think sophisticated science, you know, putting the vaccines together, different types of parasites, different stages, different promoters, it's sophisticated science but only needs to be done once or twice. Sophisticated science can mean, but doesn't automatically mean that the price will be very high to manufacture it.

These scientific complexities involving decisions over what to pursue, what to combine with what, how to deliver a vaccine into a host body, how to decide on adequate efficacy and how to combat shifts in the nature of the parasite under attack are not the only difficulties involved in developing malaria vaccines. According to the Malaria Vaccine Technology Roadmap (MVTR, 2006) there are further problems in: the lack of standardization of research protocols making comparison between initiatives difficult; a need to use state of the art equipment to identify host-parasite relations (which still remain somewhat unclear); a need to share information between different initiatives to foster learning; figure out ways to prioritise certain vaccine candidates; establish the means to scale up development capacity for malaria vaccines; establish and broaden good clinical practice in vaccine trials; have more country level discussions on vaccine policy; secure financing for future vaccine procurement; and figure out novel regulatory strategies to speed up approval for vaccine candidates (due to problems in both US and EU regulatory bodies' attitudes to licensing vaccine candidates for elsewhere, established and tested elsewhere). These complexities introduce more questions of accountability. For example, beyond vaccine efficacy, what else should be measured, made a priority and held to account?

> Interviewee 1 (Clinical trials manager, Sub-Saharan Africa)
> …what I often say to MVI is 'where's your marker of success?' because you can get a product registered but actually getting it used and

> bringing down the burden of disease is the real thing that should get measured. But that's much harder to measure and that takes 20, 30 years. So all the celebration will happen on registration and then there's no incentive for 2nd or 3rd generation vaccines to come through.
>
> Whoever makes the first one has got an easy run because they've got nothing to measure against.

In sum, a significant challenge for addressing malaria is uncertainty over the most appropriate way forward. Interviewees in this research produced a range of possible outcomes in relation to the current leading malaria vaccine candidate ranging from it being a waste of time through to it being a major breakthrough.

Outcome 1: There will be diminishing interest in malaria because the leading vaccine candidate does well and takes the PR prize
Outcome 2: There will be diminishing interest because the candidate fails to live up to expectation (after 20 years of development and is far ahead of the next viable vaccine)
Outcome 3: The candidate only does reasonably well, but still dominates the field (due to using up PPP funding and the complexity of future trials)
Outcome 4: There is an increase in malaria as funding is switched to the candidate
Outcome 5: There is enhanced interest in neglected diseases from pharmaceutical firms because the leading candidate shows pharmaceutical firms have low costs and spin-off benefits
Outcome 6: There is enhanced interest in neglected diseases because the product development partnership shows a useful way of working
Outcome 7: There is enhanced interest in malaria because the leading candidate does well or is an acceptable failure and provides hope for the next generation of vaccines

Given that there is no way to accurately predict which of these outcomes is more or less likely, the conclusion of this report will turn attention to ways of dealing with governance, accountability and uncertainty in interventions in neglected diseases.

4. Conclusion

The positive advantages of Public Private Partnerships

Public Private Partnerships (PPPs) appear to offer the principal way forward in tackling neglected diseases. They attract the most funding, are a focal point for drawing together organisations and manage to engage across the complexities of neglected diseases. In the specific case of malaria there are complexities around availability issues (developing a vaccine and drugs, getting existing treatments or bed-nets to people), infrastructural issues (having the transport and medical infrastructure in place to deliver treatments and, at some point in the future, vaccines, and figuring out ways to initiate environmental controls) and educational issues (around, for example, diagnosis, bed-net use and insecticidal spraying). This has led to suggestions that PPPs offer the most suitable way forward through having a varied field of activities. PPPs offer opportunities to pursue a variety of different practical interventions.

> Interviewee 3 (US government agency)
> I think that one way to think about it is that, you know, in malaria we really have multiple different objectives: we want to prevent infection; we want to prevent disease; and we want to prevent transmission, or we want to control transmission. So if you think about it from the standpoint that we have at least three different objectives here, some of which are linked and overlapping, we may need more than one tool to accomplish that objective.

Alongside practical interventions, PPPs also offer opportunities for managing other policy interventions. For example, PPPs could be the focal point for managing APCs or specific Product Development Partnerships developed as part of a PPP could be the focus for managing patenting/IP issues or tax breaks or getting agreements on discounts (although this research did not find great enthusiasm from any party for tax breaks or discounting). In terms of funding, PPPs appear to have been useful in drawing in funding to neglected diseases and putting specific neglected diseases on the policy agenda (through for example advocacy partnerships such as Roll Back Malaria) and in providing a focal point for the management and distribution of funding (through, for example, Malaria Vaccine Initiative and Medicines for Malaria Venture). In sum, PPPs offer opportunities for managing three forms of risk:

Financial risk – PPPs can be focal points for drawing together and managing a range of different financial sources (from state funding, philanthropic sources and contributions from pharmaceutical firms, even if those contributions are in kind). This can mean that PPPs are not dependent on a single source of funding (although Gates foundation funding is substantial for some partnerships and is not always yet matched by state funding). PPPs can also take on the responsibility for assessing which projects to fund through scientific advisory boards, enabling an informed distribution of funds.

Reputational risk – for vaccine and drug development, it has been suggested in this research that pharmaceutical firms might be put off engaging in neglected disease research due to concerns about their reputation (ranging from being connected with failures as the science of, for example vaccines, is uncertain through to liability issues arising from trial failures). PPPs offer an opportunity to manage these risks by spreading the reputational burden across several organisations and by establishing complex liability issues up front.

Opportunity risk – PPPs (as suggested above) can be developed to tackle a disease from multiple angles simultaneously. This is notably the case in malaria with PPPs focused on environmental controls and education (RBM), drug development and delivery (MMV) and vaccine discovery (MVI). Having a broad field of PPPs avoids problematically narrowing the field of activities in an uncertain area and enables limited funds to be focused on practical disease management (getting things done now) and the development of future solutions (such as vaccines).

Challenges for Public Private Partnerships

Although PPPs appear to have the greatest momentum in the neglected disease field, significant questions have been asked of their operation, direction and usefulness. In terms of their operation PPPs face challenges in the nature of the partnership at the heart of their activity, whom is included, on what terms and to what effect. In terms of their direction, PPPs have been questioned according to what their goals should be (practical engagement in what works now or risky research with uncertain future outcomes) and who is setting the agenda (the largest contributors of finance, pharmaceutical firms, developed country governments or developing country organisations? The latter always appear to play a minor role in direction). In terms of usefulness, questions are asked of PPPs about whether they are the optimal way of managing limited funds, whether or not they will produce anything significant (such as an HIV/AIDs or malaria vaccine) and how they could ever be assessed on returns for money invested (particularly as, for example, vaccines can take 10 to 20 years to produce and make available).

Many of these challenges relate to questions of governance and accountability which form the focal point for this research.

Face to face accountability. The principal means by which partnerships enable face to face accountability would be through partnership meetings. However, these pose several problems. Firstly there are questions regarding who ought to be a member of the partnership and what role they ought to play. Having a representative from every organisation connected to a partnership involved in the practical running of the partnership would be an administrative burden. Instead, a smaller executive group and secretariat run partnerships with larger set-piece meetings forming occasions where a broader set of interested parties have opportunities to have their say and find out information on what a partnership is doing (i.e. they get to hold the partnership to account). These occasions are, broadly speaking,

opportunities for developing country organisations to participate in partnership meetings. These occasions do not resolve the problem of who should participate in these larger meetings – questions can still be asked about whether or not the members of the meeting are appropriate and whether or not developing country organisations ought to have more significant involvement in partnerships.

Secondly, questions can be asked about the kinds of information made available to this broader membership and whether this enables the membership to hold the partnership to account (this will be taken up in the 'transparency' section below). Thirdly, the members who are invited to take part in the meetings are not always in strong positions to represent a broader constituency in these moments of accountability. It has been suggested in the research that developing country organisation representatives are often just talking on behalf of themselves and there is a sense that these representatives are disconnected from, for example, African health ministries. Given that many participants in the research suggested that close relationships with such ministries were vital to the future development, delivery and availability of drugs and vaccines for neglected diseases, it appears that strengthening the accountability capacity of these representatives would be important.

Accountability metrics – There are many calls in the literature and from participants in this research for greater accountability of PPPs through measures, indicators, benchmarks and other metrics. The basic rationale for these arguments is that, first, in order to assess whether or not a PPP is delivering value for money, successfully achieving agreed deliverables and is in a position to make information available to external parties (see next section on 'transparency'), metrics are essential. Second, it is argued that standard metrics across partnerships would enable cross-comparative accountability assessments between partnerships. Problems with the first aspect of this metric rationale are that the introduction of measures has consequences and these are not always considered in advance and the purpose of the accountability metric are not always analysed in depth. The consequences of measures can be that organisations begin to re-orient their actions in line with the principles of the measurement process particularly if funding for the organisation is tied into metric success. The kinds of things to be measured then require careful consideration as they are consequential for the actions of PPPs; questions need to be asked of what should be measured, by what means, for what purpose? (Further issues regarding the quality of information produced are dealt with in the 'transparency' section below).

Problems with the second area of this metric rationale are that introducing standard measures across partnerships may stifle innovative ways of working, moments of discovery outside the parameters of measurement (which appear important in an area of scientific uncertainty, but may not be pursued if they are not going to be measured) and the rationale appears based on a quest for comparison which may be at odds with the basic goals of intervening in neglected diseases. If an advantage of, for example,

malaria partnerships is that they can carry out multiple activities and spread their opportunity risk, encouraging diversity might be a useful way forward. Encouraging standard measures of standard practices might then both limit this diversity and also produce measures for comparing across unlike entities (i.e. it might attempt to introduce an assessment comparing an advocacy partnership like RBM which attempts to get malaria on the political agenda and a vaccine development partnership like MVI. Such a comparison on the grounds of effectiveness, value for money (etc) would appear limited as the partnerships are trying to achieve completely different goals). Engagements with neglected diseases may benefit from fewer attempts at cross-comparative performance metrics.[12]

Accountability through transparency – Calls for PPPs to be 'transparent' most often relate to suggestions that the organisation should provide particular forms of information to external parties in order to demonstrate that they are a responsible organisation, which provides value for money, adheres to all relevant protocols and has clearly structured and suitable ways of working. However, transparency can prove a problematic principle to enact. First, in line with accountability metrics, demands regarding what kinds of information should be made available can be consequential. If funders are looking for information to be made available on developing country participation in PPPs this may lead PPPs to re-structure their actions in order to be able to provide further information on this participation (PPPs may even do more to encourage developing world participation as a result of demands for participation-based transparency). This may not be problematic in itself, but the choice of what should be made transparent needs to incorporate an analysis of these consequences. Second, transparency processes often assume that they are opening a window on internal organisational activity. However, the quality of information and the kind of picture of internal organisational activity it portrays requires consideration. For example, how closely information made externally available matches internal organisational activity should be a matter of concern. Third, producing calls for transparency has become common in a range of different organisational fields. PPPs are subject to calls for transparency just like many other areas. This fashion for transparency, however, should not mask complex questions that need to be asked: what should be made transparent, by what means and for whom or for what purpose?

Accountability through engagement – This form of accountability is more limited than face to face accountability where members of an organisation are invited to hold each other to account (through, for example, meetings) where they can assess the extent to which they have fulfilled their promises and obligations. This form of engagement accountability is more narrowly focused on a specific issue or a limited number of issues around which a particular opportunity for accountability is built. For example, specific PPPs might hold occasional open meetings, addressing a specific area of work and

[12] This suggestion does not include standards for such areas as ethics in clinical trials, but is limited to those efforts to introduce standardised performance metrics to compare partnerships.

advertise these to anyone who is interested in engaging in discussion of this particular area of the work of PPPs. These forms of engagement occur in certain local and national government settings (such as citizen juries, participatory decision-making and occasions of consultation). The advantages of this mode of accountability are broad-based participation, generating community participation and a greater sense of ownership of the issue, and helps anticipate problems which might occur further down the line (such as a community backlash). The problem for PPPs is that these forms of engagement do not appear to be on the agenda as ways of engaging with, for example, developing country participants/populations. There are various practical reasons for this (taking the example of malaria: where in sub-Saharan Africa or other developing countries should engagement take place, on what issues, on what terms, with what consequences, and who would be able or likely to engage?). However, greater thought given to local and regional forms of engagement could enhance PPP involvement in developing countries and enhance the accountability capacity of developing country organisations.

Suggestions

If forms of accountability continue to be heralded as the problem to be solved and the way forward for Public Private Partnerships, the following suggestions could prove useful in order to address some of the issues PPPs have faced:

- Calls for more accountability need to take into consideration complex questions such as accountability for whom, by what means, for what purpose.

- The mode of accountability to be employed requires consideration (and this could involve a combination of face-to-face, metric, transparency- and engagement-based forms of accountability).

- Modes of accountability have consequences both for the organisations to be held to account (such as PPPs) and those invited to carry out accountability measures. These consequences require consideration.

- If calls for developing country organisations to take a greater role in PPPs are to be taken seriously, then more work is required in enhancing the accountability capacity of both developing country organisations and their representatives (so that a representative is representative of a relevant constituency, has access to the means of accountability and has some consequential input) and organisations such as PPPs (so that they provide relevant information and have in place structures through which developing country organisation representatives can engage in accountability).

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