

PDP Support of Country Decision Making: A Discussion Paper¹

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Abstract

Product development partnerships (PDPs) are focused on developing new health products for low income settings. But public health impact from these products comes only after adoption of the product into the health system. This adoption, in turn, relies on an affirmative decision from local policy makers. Here, we describe how PDPs have structured their approaches to support this process of country decision making. These approaches vary, but include country consultations, regional meetings, formation of regional, product-specific committees, road shows, support of local advocates, development of decision-making frameworks, provision of technical assistance to aid guideline revision, and conduct of stakeholder and Phase IV studies. There was no specific pattern in these by intervention type or disease area, although there was a trend towards some strategies according to stage of development of interventions within a PDP. Tactics in establishing a presence in endemic countries vary from the founding of country offices to engagement with part-time consultants or with long-term or ad hoc committees. PDPs prioritize countries for engagement based on burden, prior PDP contact during clinical trials, and other factors. PDPs also have a role in acting as a bridge between international decision making processes and countries influenced by those processes. Other lessons on division of labor (who does what in supporting country decision making) are hard to generalize as the contributions of partners (such as pharma, and global disease partnerships) vary so widely. Very few PDPs have formally defined expectations for their support to decision making, particularly with their pharma partners, which may be an area for future synergies. PDPs have an opportunity to further refine support to national decision making processes by drawing upon lessons from peer organizations.

Objectives

The objective of this paper is to explore the various approaches that PDPs have taken to support country decision making, and why those approaches were taken. After describing some of the basic strategies that various PDPs use, we analyze related issues such as the establishment of a local PDP presence in endemic countries, prioritizing countries for engagement, generating local data, the role of international institutions in country decision making, and the division of labor between different actors in supporting country decision making. Finally, we close with remaining challenges and some activities to support country decision making that PDPs may want to consider.

Strategies: the basic models for building country consensus around adoption into health systems

As the term “country decision making” suggests, it is the country that conducts the central activity of reaching a decision on whether to adopt a product into its public health use. Although the process in any individual country may vary, a country’s own preparation for decision making is generally understood to include the following:

- 1) Obtaining information on the future products that are likely to become available;
- 2) Ensuring a decision-making body is present, active, and has a relevant membership;

¹ Prepared by William Wells (TB Alliance) and Alan Brooks (PATH Malaria Vaccine Initiative), with interviewing assistance from Eric-Marie Dupuy, on behalf of the PDP Access Steering Committee, which is made up of the following organizations: Aeras, Concept, DNDi, FIND, iOWH, IPM, IVCC, MMV, MVI, PDVI, and TB Alliance.

- 3) Defining a timely process for local decision-making in general (in a particular disease or intervention area) and then for adoption of new products specifically;
- 4) Defining the evidence base required for decision making, including local data requirements; and
- 5) Making plans to generate this required local evidence base.

PDPs have a direct interest in supporting this process of decision making in order to maximize impact. PDP activities related to country decision-making fall into two broad categories. The first set of activities – those that are consistent across all PDPs – include:

- 1) Identifying information that is expected to be needed for national decision-making, and integrating consideration of these information needs into R&D activities. This affects, for example, clinical trial planning and development of regulatory strategies;
- 2) Disseminating product and pipeline information;
- 3) Assisting countries to define data needs and gaps, including clarifying if the information should be generated in a country or internationally;
- 4) Gathering and disseminating a standard evidence package for decision making;
- 5) Engaging appropriate stakeholders (with key, consistent individuals including national program managers, WHO country office staff, and local researchers);
- 6) Addressing concerns that are common across countries (e.g., price, ease of use, source and geography of manufacturing, and impact on supply chain). These can be inter-related, e.g., an affordable price negotiated by the PDP results in greater global demand and thus more reliable local supply.

Other PDP activities to support country decision making vary according to certain circumstances. These activities include:

- 1) Investigating disease burden, and sharing information with policy-makers (less need if disease is well characterized and recognized);
- 2) Limiting product introduction activities geographically based on disease burden or resistance patterns (less relevant if disease is widespread and resistance patterns vary little);
- 3) Supporting the establishment of decision-making structures (more need if bridging two fields in public health (e.g., immunization and malaria); less need if strong, defined structures already exist);
- 4) Supporting local advocacy and communications activities to inform policy makers about a disease and/or options for addressing a disease (depends on involvement of others who may undertake this, e.g., pharma partners and/or global disease partnerships);
- 5) Influencing key variables impacting decision-making, such as pricing, supply, financing and regulatory issues, demand estimation, and post-introduction surveillance plan (influence depends on specific role of PDP in a country and in developing the product – see separate papers on most of these topics);
- 6) Generating or compiling local evidence required for decision making, potentially including the funding and/or running of Phase IV studies (depends on clearly defined needs from a country, whether the country can act as a regional or global source of data, and the willingness, local staffing, and available resources from PDP); and
- 7) Supporting countries to make decisions about a complementary mix of interventions (only relevant if other interventions for the disease are widely used or being considered).

Specific PDP models for country decision making activities

The examples below illustrate that PDPs have taken many distinct approaches to facilitating country

decision making. Not surprisingly, the more extensive experience generally lies with the PDPs who have approved products (i.e., the first four PDPs listed below).

PneumoADIP (now IVAC) built on experience with Hib and Hepatitis B vaccine introductions. Decision-making was accelerated by increasing disease and vaccine awareness, and by providing data so that countries would actively seek more information and make a decision. The team used regional meetings, one-on-one interactions with local researchers and advocates and involvement in projects to establish a stronger evidence base. The Hib Initiative also conducted a number of country consultations.

Early adopters (the first to adopt) and early majority countries (those among the first to adopt, but often many years after product availability) have different needs and expectations.² These needs were defined by Pneumo-ADIP and the Hib Initiative via perceptions research (around health priorities and product introduction) and country consultations. When formalized, a *country consultation* was a fact-finding mission with WHO participation in which one-on-one interviews and some group work resulted in a formal report to the government (on availability of data, financing, barriers, etc). These consultations generally occurred only once per country, although some larger countries had multiple consultations, and were carried out before, during and after regulatory approval. Almost always there was no decision during the consultation itself, and WHO was an essential partner to track subsequent country progress.

To address the perceived need for more data on projected coverage and impact, the team helped establish surveillance networks, with annual investigators' meetings to share data between countries and to identify advocates. These investigators and other *local advocates* met with policy makers, advocated for research to cover gaps, organized events, spoke to the press, and helped to write op-eds. They sometimes received small grants to conduct particular events and were recognized in newsletters but not paid or otherwise on a retainer.

Regional meetings were an opportunity to check back in and to move countries to put their decisions and proposed actions on paper, by presenting their conclusions in front of others. The regional meetings usually covered only one or two products and were funded and organized by the project team in collaboration with WHO, rather than relying on EPI managers' meetings, which often covered multiple topics. They included EPI managers, directors of health services, researchers, pediatricians, economists, and sometimes donors and financing people from MoH or other ministries, and were a useful mechanism to support decision-making in countries, particularly those that were not directly targeted through other interactions. WHO was critical to ensure decision-making and engagement in a broader range of countries than could be reached by the project.

iOWH supported studies in India that generated data for advocacy and decision making on Visceral Leishmaniasis (VL) treatment and elimination. They sponsored and collaborated with a research institute of the Government of India to document the incidence of VL, the financial burden of disease, households' willingness and ability to pay, and treatment-seeking behaviors in both public and private sectors.

iOWH sponsored the clinical trials required by the national regulatory authorities for adoption of the drug in the National program. These included Phase 3 and Phase 4 (post licensure) studies. In addition to safety, the Phase 4 study included an effectiveness module that provided training, clinical support, and guidance on pharmacovigilance reporting, and demonstrated effective delivery in public and private

² See *Crossing the Chasm* by Geoffrey Moore.

facilities. The clinical trial investigators formed a core constituency for local advocacy for improved products.

At the national level, iOWH leadership engaged with key stakeholders in the Indian government, World Bank and WHO to inform them of the progress of the studies, identify their key questions and concerns, and address future funding issues. Training modules and community communication models were developed for smooth transfer to the National authorities.

DNDi defines itself as a patient and country needs-driven initiative that develops new treatments based upon needs identified by and with endemic country stakeholders. From the very start of a project, DNDi engages stakeholders via several mechanisms: disease platforms; strong partnerships with founding partner organizations in endemic countries; actions by pharma and other international partners; intervention or field trials; and advocacy and communication.

- *Platforms* were formed with the aim to strengthen clinical research capacity and assist with GCP clinical development around specific diseases in a geographic area, i.e., Visceral leishmaniasis in East Africa, sleeping sickness in West Africa, and Chagas Disease in Latin America. These platforms include country program staff, researchers, regulatory officials, NGOs and WHO and meet twice a year. Platform members became natural partners for country decision making as they gather relevant information on in-country issues, programs, and processes and convey key information to in-country decision makers.
- Certain organizations in endemic countries contributed to DNDi's founding and are represented on its Board of Directors. These *founding partners*, such as ICMR in India, KEMRI in Kenya, and Fiocruz in Brazil play a key role in defining needs and a related Target Product Profile (TPP), and facilitating clinical and intervention trials and, ultimately, national program adoption.
- In some areas, DNDi relies on *pharma and other international partners*. For example, WHO Neglected Tropical Diseases (NTD) department and MSF are key drivers for the adoption of NECT combination for the treatment of sleeping sickness, now used in 6 endemic countries. Sanofi-Aventis (SA), within 18 months of WHO prequalification, has distributed 50 million ASAQ treatments in 24 African countries, and developed a specific package for social interventions and home based management programs; SA is conducting a 15,000 patient pharmacovigilance program in partnership with DNDi and with MMV in Ivory Coast.
- *Intervention or field trials* are essential to demonstrate feasibility and generate necessary data for adoption into national programs. For instance, Brazil conducted a 23,000-subject malaria intervention trial prior to adopting ASMQ for treatment of falciparum malaria in the Amazon basin.
- Last but not least, *advocacy* is a key component of DNDi implementation work, to inform both international audiences and endemic countries, where workshops for instance are conducted prior to launch.

MMV's main focus is on disseminating information through international and regional channels, determining country-specific data needs, identifying local barriers and, in select countries, encouraging revisions of standard treatment guidelines (STGs) when significant advances in treatment choices become available. In other areas, they leverage the role of their pharma partners, particularly in support for training and implementation of best practice workshops for policy makers and implementers. In the past, within 18 months of anticipated launch, MMV has approached targeted countries with "road shows" to increase MMV's and their pharma partners' visibility. Post-launch, the focus moved towards targeted responses to specific financing, supply chain, or policy acceptance barriers for individual

countries. It is not clear that the “road-show” model will be the optimal approach going forward, particularly in light of having two separate but closely-timed partner product launches in 2011. There are, however, numerous country-level dialogues, including once-a-year subregional meetings (of WHO AFRO and Roll Back Malaria) and, in select cases, day-long workshops. These provide opportunities to give product-specific briefings and to reinforce recommendations of normative entities (primarily WHO) in terms of best practice for the development and revision of treatment guidelines. Longer-term programmatic collaborations in specific-countries are very limited; the focus is on initiative (e.g., piloting of an affordable medicines private sector subsidy in Uganda) that address specific access challenges and could serve as guiding lights for policy makers and funders across the larger stage of all malaria endemic countries.

The country decision making approaches of three PDPs that do not yet have products approved are listed below:

MVI began by documenting the shared lessons from recent initiatives to introduce new interventions into malaria and immunization programs in Africa. This led to a 3 year process with countries and WHO to develop decision-making frameworks for 9 individual countries. These frameworks were then integrated into a regional framework, which was validated by representatives from over 30 African countries in a series of 1 day meetings organized together with WHO and Roll Back Malaria (RBM) sub-regional networks. The framework builds upon existing WHO guidelines, and lays out what data are needed from different sources (global vs national), in different thematic areas (disease burden, other malaria interventions, impact, financial, efficacy, safety, programmatic, sociocultural), and at different times (pre-licensure, licensure, and post-licensure); it also notes whether each is essential or nice to have. It provides a similar framework for policy processes. The framework process has and will structure dialogues around malaria vaccines with countries to make it largely technical. In some countries, it has led to the formation of ongoing decision-making structures (e.g., technical working groups – MVI now sponsors three of these). It also helps define what data countries are holding the international community accountable to deliver. The framework helps overcome the distance between EPI and malaria personnel, which needs to be bridged for the adoption of a malaria vaccine. MVI has also held annual, practical, training workshops for approximately 10 African scientists on advocacy, and working with the media and politicians.

The framework approach was adopted based upon the shared decision-making lessons in malaria and immunization, and as a means to plan in advance for eventual decision making so that the groundwork is already in place as a first vaccine becomes available.

TB Alliance is entering an area that has existing products but little analysis of decision making or how new products would be considered. TB Alliance therefore focused on conducting sequential stakeholder studies to increase the knowledge base around preferences and processes in the existing environment including TB drug markets, TB regimen changes and the how TB drug use is integrated in the health system. These studies also served to initiate engagement with local stakeholders, provide opportunities for the promotion of regimen change issues in international fora, and frame conversations with local stakeholders during TB Alliance participation in WHO review missions. Finally, the findings of each study influenced the design and content of the next. The studies addressed the following: the size and structure of the existing TB drug market; what local stakeholders want from a new TB regimen; how the experience with past TB regimen changes can inform future approaches; and what producers and products are dominant in the private sector. TB Alliance selected this approach due to the opportunities and challenges presented by the availability of existing TB treatment regimens and partnerships.

Based on an identified gap in field implementation, IVCC is engaging country decision makers by developing information systems and tools to track clinical and survey data and insecticide resistance (the Malaria Decision Support System, or MDSS). This tool is applicable to a wide range of diseases and supports the effective monitoring and evaluation of vector control programmes, the management of advanced insecticides, and decision making on adopting new vector control products. IVCC has validated the methodology in 3 countries – Mozambique, Malawi, and Zambia – based on existing partnerships with the ministries of health and varied infrastructure and ecological environments. IVCC is now planning wide-ranging implementation of the system funded by the M&E section of vector control grants by USAID, PMI, and GFATM. As a central objective, the MDSS should be adopted and owned by the national malaria control campaign and serve their information needs. IVCC plans that, when the number of implementers reaches a critical mass, the implementing role will be adopted by a spin out company from IVCC, which should be based in Africa. IVCC does not expect to need a permanent presence in every country implementing MDSS.

Strategies for establishing a local presence

If a PDP has staff in an endemic country, there are clear opportunities for improved information flow and closer engagement with local stakeholders. However, PDPs were primarily founded as research organizations, so budgets for an endemic country presence are usually driven by organizational needs such as those related to clinical trials. Aside from MMV's office in Uganda, none of the offices associated with interviewed PDPs were reported as being set up primarily for an access-related purpose. PDPs vary in their in-country presences, with the extent usually increasing as products move further through the pipeline. PDPs within larger institutions such as PATH are also able to leverage staff in multiple offices, who are shared between different initiatives.

The options for establishing a local presence, listed from most to least committed, include:

- 1) Country offices (staff need sufficient standing to deal with government officials). See Annex for examples.
- 2) Consultants on partial retainer. These individuals need disease-specific expertise and the respect of local stakeholders from relevant government, medical and research institutions. They can design and facilitate local research, and the PDP can provide them with support for decision-making activities. [iOWH; MVI]
- 3) Sustained engagement with existing committees or structures (may be formed after prompting by the PDP).
- 4) Strengthening the pool of scientists, who at the same time become stronger advocates within their regions and countries, such as MVI's annual Malaria Vaccine Advocacy Fellowship Program, DNDi's platforms, or PneumoADIP and Hib Initiative's local advocates.
- 5) Engagement with ad hoc committees or structures formed at the prompting of a PDP.
- 6) Ad hoc engagement with existing structures (e.g., regional or sub-regional disease-specific committees or meetings organized by WHO).

In sum, the rationale for the country presence of interviewed PDPs has been driven by R&D or organizational needs, with access activities building upon that presence. This suggests that access teams should seek to be part of decisions on where R&D activities are undertaken. PDPs have also tended to take advantage of less costly means for engaging with greater numbers of countries by working through existing committees and structures (including WHO), developing new structures for sustained engagement where feasible, or otherwise working through ad hoc collaborations.

Prioritizing countries for engagement

PDPs may help to formulate roll-out plans and build early success cases. Prioritizing countries for engagement on access-related issues is not a science – there is no perfect answer. This is true regardless of which approach is taken to establishing a local presence (see list above). Different PDPs use shorter or longer lists of criteria in making such decisions. However, most PDPs consider a number of the following criteria (listed in order from those mentioned most, and most vehemently, to least):

- 1) Prior engagement via PDP-sponsored trials
- 2) Burden of disease (absolute or reflecting specific resistance or age patterns)
- 3) Potential health benefit (e.g., based on drug resistance patterns)
- 4) Political stability
- 5) Capacity of national program to deliver treatment (e.g., focusing new vaccine interventions on those countries with strong EPI programs)
- 6) Existence of local champions and openness to change
- 7) Research capability for a pilot, which would generate evidence for other countries
- 8) Regional importance of country
- 9) Information for decision making is available

Prioritization generally considers two goals, which may or may not overlap: identifying early adopters; and maximizing final public health impact. Prioritization may also reflect an effort to include settings reflecting the full range of epidemiologic patterns of the disease (e.g., for malaria).

WHO regional advisers can also provide prioritization guidance. WHO regional EPI officers helped the Hib Initiative to target efforts and identify where to go: they identified issues and barriers for each country and defined whether country stakeholders were already including Hib in their multi-year plans. Pneumo-ADIP looked at the history with Hep B but its pattern of adoption was not a good predictor of Pneumo and Hib adoption, probably because EPI managers at the country level had differing views for different vaccines (possibly based on the opinions and strength of local champions and experiences in neighbouring countries) plus the person making decisions sometimes changed.

PDP role in generating local data to inform country decision making

Some PDPs devote considerable resources to generate local data; others devote almost none. This variability is determined in part by the earlier gap analysis – local data may or may not exist or be needed. The effort to generate local data is also determined by how novel an intervention is, either within its disease arena (e.g. a malaria vaccine coming into malaria control raises a number of local data questions) or by the existence of a program with clear accountability in the country which is already collecting such data (e.g. TB Programs already hold extensive data on existing treatment regimens). Regardless of the disease or intervention, clarity on which data need to be generated at a local level versus provided from regional or global studies is essential in prioritizing activities. PDP involvement in local data generation should prioritize local capacity building. In addition, PDPs have suggested cost-saving mechanisms:

- 1) A single model can be adapted to generate local data for multiple countries. Examples include IVCC's MDSS (see above) and models that MVI has helped develop to estimate local impact and cost; the inputs are either local data and assumptions or regional and international estimates extrapolated to the country level.
- 2) IVAC and MVI minimized the need to generate local data by (a) uncovering existing local data at

universities (programs and WHO may be unaware of these data), and (b) explaining why certain data were not needed if they would not affect the final decision.

Role of international institutions and their partners supporting national decision making

WHO recommendation is seen as essential by all the interviewed PDPs. In addition, as long as products are already in WHO standard treatment guidelines, MMV reported that there is a pathway for PDP activities to promote uptake at country level. Interaction with WHO at both central (Geneva) and regional levels was reported by the interviewed PDPs as being essential, and strengthening of the PDP links to WHO was mentioned by a country stakeholder as being a priority.

Decision making and processes in international institutions are often precursors to country-level decision making. The need to inform and work with more than one multilateral partner (e.g., WHO and World Bank) separately can slow such international decision making. In addition, processes managed by different partners may not be harmonized. MVI worked with international institutions to develop a policy pathway for malaria vaccines that included the regulatory, policy, manufacturing, financing, procurement, and country steps needed prior to vaccine use. The pathway laid out who would act when, and which processes would happen sequentially or in parallel. It highlighted areas for further work, such as between GAVI and GFATM, and the need to analyze and clarify data requirements and policy processes of WHO technical committees such as STAG for malaria and SAGE for immunization.

The decision-making agenda can also be advanced by international committees that are formed de novo. The Pneumo-ADIP worked with the Sabin Vaccine Institute to support the formation of a single global committee of approximately 20 country and global members (the *Pneumo Awareness Council of Experts (PACE)*) that contributed to strategy and issued a call to action. In addition, the All-Party Parliamentary Group on Pneumococcal Disease Prevention in the UK was also formed with the support of Pneumo-ADIP and was instrumental in influencing the GAVI investment case and AMC. Some low income countries are now using this approach of engaging parliamentarians for Pneumo adoption.

Division of labor

Ultimately, it is country stakeholders who drive the two critical events: defining what evidence base is necessary; and implementing decision making itself. Increasingly, country stakeholders will be faced with choices between interventions in different disease areas. Most external actors (not just those in PDPs) have a focus on a particular disease area, so the best way to support such cross-disciplinary decision making remains to be determined.

It is clear, however, that PDPs have a role in the global processes required upstream of country decision making. At both global and country levels, the PDP can provide information on programmatic implications and perhaps a standardized public health case weighing the evidence for and against adoption. Typically, however, passive provision of this information is not enough to lead to clear country decisions. Financing is a key additional requirement, and there is often a need for an organization specifically responsible for tracking and coordinating all of the activities needed for access, including those needed before decision makers will reach an adoption decision.³ PDPs may either be prominent in this role or largely transfer it to others.

³ Frost & Reich, "Access: How do good health technologies get to poor people in poor countries?" 2008.

An organization primarily responsible for supporting decision-making must interact extensively and directly with country stakeholders, particularly in countries identified as potential early adopters. It may also help gain consensus from the multiple in-country actors that tend to cluster around certain topic areas. However, the number of countries with which a PDP can expect to interact directly is not clear. It seems likely that most PDPs (including, for example, TB Alliance) would interact significantly with at least some early adopters (perhaps 5-8 countries), but many PDPs would then rely on existing multilaterals, NGOs, and pharma partners to reach other countries. A more engaged example is the Hib Initiative, which worked together with WHO to support directly or indirectly 72 countries. This level of engagement was seen to be necessary to implement a global recommendation for use of a long-available product.

Even if PDPs follow the Hib Initiative model of extensive engagement, partnership is essential. PDP access staff can initiate these partnerships by bringing together different parties, such as the scientists and manufacturers. However the rationale behind individual PDP partnering choices is not always obvious. Table 1 describes possible partners and some of their advantages and disadvantages.

Table 1: Partners who can support countries and PDPs in country decision making

<u>Partner</u>	<u>Advantages</u>	<u>Disadvantages</u>
Multilaterals such as WHO	Extensive reach and impartiality	Typically cautious about new interventions; May be overwhelmed by other initiatives and thus lack time and resources to devote to new product introduction
Local academia, researchers and/or professional organizations	Close to in-country processes, needs and data; Credible with local policy-makers	May not have a broad view of a problem; May be influenced by personal research interests
NGOs	Some have specific expertise in new product introduction	Require funding specific to the new product to drive their activities
Pharma and/or manufacturing partners	Product-specific expertise, and in some cases extensive sales networks in some markets	May be seen as a biased source of decision making information; may lack experience in the disease and/or in low income settings

There is a perception that manufacturers may be able to support decision-making and all downstream steps. However, many originator companies may have limited experience of introduction into low income country markets (some Indian and Chinese generics may be more established in these markets). Companies may also be concerned that they could be perceived to be self-serving if supporting decision-making around the introduction of a new product directly in countries. Thus, the initial information sharing and country decision making step will generally require the involvement of other actors, including PDPs.

An interesting example of division of labor comes from Uganda, where PATH and their donors are supporting a demonstration project for HPV vaccines. Before any activities started, PATH signed a Memorandum of Understanding (MOU) with the Government of Uganda (GoU) to specify who would do

what. The GoU committed to provide health services delivery infrastructure, human resources in the districts, and EPI staff for delivery of the vaccine. The two PATH technical staff members, located in the WHO Uganda office, provide technical and logistical support. PATH also provided transport allowances (but no per diems) to health workers in the field and funded local university researchers to conduct the formative research and operations research. WHO and UNICEF participate in a technical advisory committee set up by the MoH to oversee the demonstration project, and also helped with monitoring of vaccination. Pharma (GSK) donated and shipped vaccines to Uganda, but had no other role in the project. UNFPA and other stakeholders provided input on reproductive health issues, and NGOs (e.g., CARE and Save the Children) helped with mobilization in the districts. One further suggestion would be to include GAVI in supporting the demonstration project so that their commitment to funding eventual procurement is solidified.

Country participation and validation

Most interviewees believed it is not realistic to have a complete decision-making process and adoption commitment many years prior to availability. However, discussions with stakeholders about possible adoption decisions are still useful to identify general issues of concern about a potential product. Subsequently, the process of country-specific planning should engage stakeholders in the adoption decision process and build their commitment to it.

MVI is attempting to support countries to take conditional decisions on whether to use a vaccine; this occurs in parallel with the growing body of data from the phase 3 trial. This is intended to reach an objective, agreed with its pharma partner for the anticipated first generation vaccine: *To ensure that robust evidence and financial resources are available to all countries in sub-Saharan Africa, allowing each to take a decision if they want to adopt, defer, or not adopt RTS,S into their EPI and/or wider health systems, within one to three years of legal and physical availability.*

As yet, there are relatively few examples of adopted PDP products (see Annex), and thus few reflections on whether countries found the PDP involvement in country decision making useful or appropriate. MVI's decision-making framework activities were externally, independently evaluated by the funder, including follow-up surveys to dozens of past participants. It validated the approach and called for additional activities. In the GAVI validation of the ADIP/Hib Initiative process, countries said they appreciated that someone was promoting their adoption concerns, such as pushing GAVI to make clearer commitments.

Challenges

- Country decision making is driven by the country, not the PDP. Conveying this idea of public sector policy change to R&D staff and PDP boards can be challenging.
- PDP boards often think that local implementation partners can do it all, so local engagement by the PDP is not necessary. But partners are focused on many other issues, and may not have the full depth of information on a given intervention. [MMV; iOWH]
- For MMV, there are 45 endemic countries and a PDP can't roll out support to all of them. Yet just doing one country right won't necessarily allow replication, as each country is different. [MMV]
- Optimal engagement timelines are unclear. Advance planning is risky as product timelines are uncertain, but without early engagement (e.g. 5 years pre-licensure), country decision making may be delayed and products will sit on shelves. [MVI]

- In the studies used to inform product acceptability, the level of disagreement and variability between countries makes it challenging to satisfy all potential markets and all potential decision makers. [TB Alliance]
- In terms of PDP access budgets, a critical step will be to address the number and cost of Phase 4 studies and who will bear the burden of financing them (e.g., PDPs, donors, countries or some combination). [TB Alliance]

Activities to support country decision making that PDPs may want to consider

Link to clinical trial activities

- Access strategy emerges from engagement at country level during the clinical trial stage. [iOWH]
- Involving local clinical researchers and other endemic country stakeholders in formal committees from the conception of the project and during the clinical trial phase is critical. Doing so allows them to share relevant information for the country and ensure the product developed meets the country needs. They are natural partners in the project. [DNDi]
- PDPs could help to think through strategies for first and early adoption of products by countries. Countries participating in clinical trials or in which phase 4 trials are planned can provide platforms to build country ownership of and familiarity of a product. [DfID]

Identifying advocates

- Local representation of some sort is critical for forming relationships that aid adoption.
- Focused activities in countries provide advocates for global activities. [IVAC]
- Engage local stakeholders who are technically inclined and provide them with the technical arguments they need, rather than engaging other stakeholders who are more interested in political issues (e.g., local manufacturing). [MMV]
- Once local researchers are engaged meaningfully, they themselves (rather than the PDPs) are best suited to present evidence to local decision makers and communicate directly with a government agency. [DNDi; iOWH]

Partners

- Have a mix of scientists and field people on advisory bodies. [DNDi]
- Partner NGOs are essential to help understand issues and burden of disease. [DNDi]
- WHO Geneva and country offices are key implementers in addition to country disease programs. [DNDi]
- Work with global agencies when available (especially for HIV, TB and malaria); neglected diseases may require more country by country engagement in addition to partnering with WHO. [DNDi]
- When working on so many countries at once, it is so important to have the regional WHO officers constantly involved. [IVAC]
- Early in the R&D relationship with a pharma partner, reach an agreement with the partner on the objectives of the access strategy, particularly in the area of country decision making. [MVI]
- PDPs and donors should not aim for a unified approach to country decision making, as there is too much variability in the needs and non-PDP resources available.
- WHO regional offices and sub-regional inter-country teams may be able to act as key partners for multiple PDPs. Therefore, donors and PDPs should consider building their partnering capacity.

Prioritizing activities

- Although countries do vary, deep investment in one country leading to proof of concept is important (especially if it leads to a publication and funding for roll out in further countries). [MMV]

- Access strategies and activities are project specific and based upon identified gaps: an awareness gap requires advocacy (Chagas campaign); an evidence gap requires an efficacy and cost-effectiveness study (VL). [DNDi]
- It is easy for PDP staff to be pulled in multiple directions at once. Therefore, it is important to prioritize strategies and activities by planning over the medium and long-term using a timeline (e.g., a policy pathway) that has clear milestones. [MVI]

Engage with a broad perspective

- Define how the new intervention will fit with, and affect, all aspects of the existing public health environment. [TB Alliance]
- Facilitate the formation of a normative decision making process that covers all interventions in an area, not just those sponsored by the PDP. [MVI]
- Rather than focusing too much on one product, take a holistic disease approach. This is how programs think and it will allow them to engage. A disease approach brings in allies from other areas that might otherwise be competitors (e.g., Innovative Approaches and New Tools sub-working group of the Stop TB Partnership). [IVAC; MVI; TB Alliance]

Timing of interventions

- Financing discussions and commitments should be developed early, or else countries cannot commit to decision making. [IVAC; TB Alliance] In doing this, the PDP should plan for success rather than wait for positive Phase III results.
- Start early with manufacturers so they can understand the plans and steps, and can better communicate with countries about expectations for volume and price evolution. [IVAC]

Annex

A: Individuals interviewed

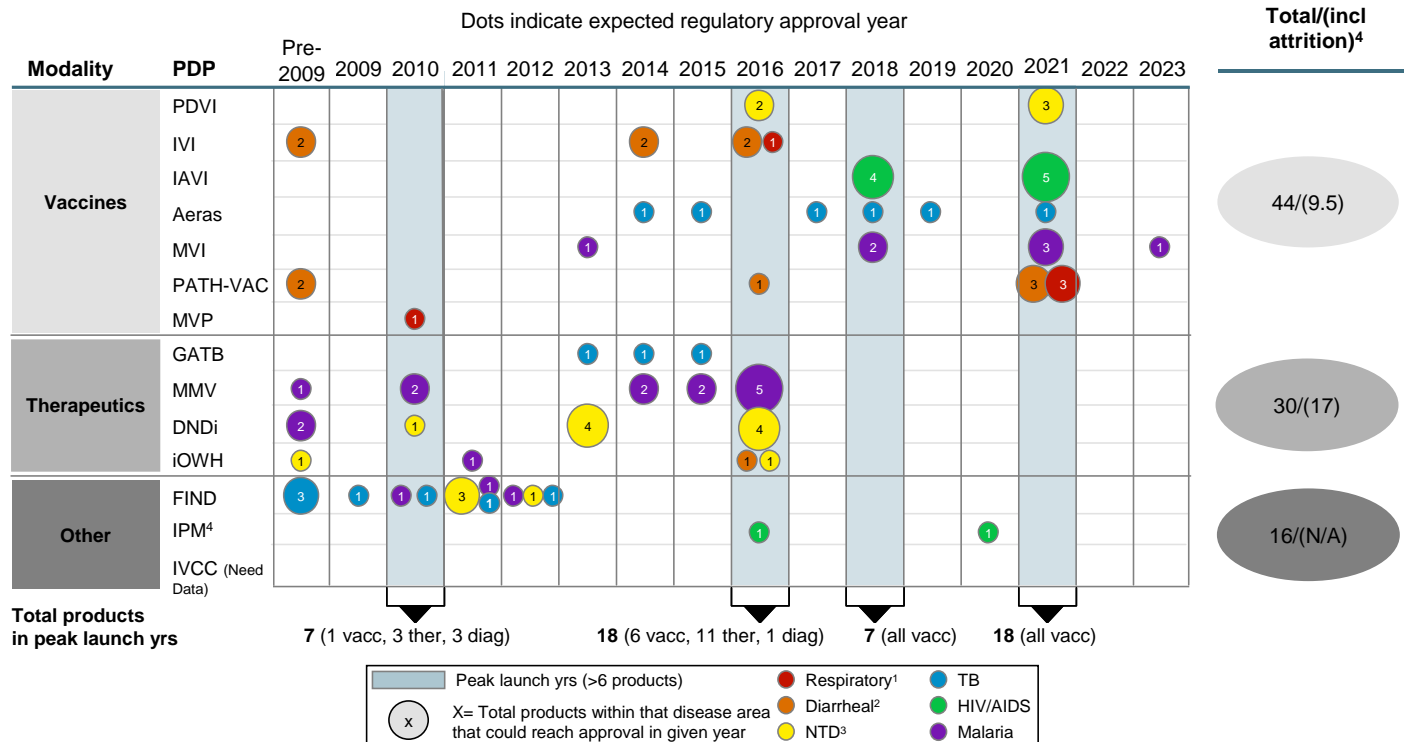
Florence Camus-Bablon, Senior Access Advisor, DNDi
 Alan Brooks, Director, Policy and Access, PATH MVI
 Antoinette Ba-Nguz, Senior Programme Officer, PATH MVI
 Alex Adjagba, Programme Associate, PATH MVI
 Rhonda Sarnoff, Director, Access, iOWH
 Raj Shankar Ghosh, Regional Director, South Asia, iOWH
 William Wells, Director, Market Access, TB Alliance
 Lois Privor-Dumm, Director, Alliances and Information, IVAC
 George Jagoe, Executive Vice President, Global Access, MMV
 Tom McLean, Senior Executive Officer, IVCC
 Evan Lee, Senior Medical Officer, FIND [no interview notes available]
 Emmanuel Mugisha, Country Manager, PATH HPV Vaccine Project, Uganda
 Francisco Songane, ex-MoH Mozambique
 Saul Walker, DfID

B: Draft list of PDP Endemic Country offices

- 1) DNDi (Kenya, Brazil, DRC, India, Malaysia), where it may be as small as a 1-person office
- 2) MVI (Kenya with dedicated project staff, plus PATH offices in Africa that can be called upon in Senegal, Ghana, Ethiopia, Uganda, Tanzania, Zambia, and South Africa)
- 3) MMV (Uganda, initially for pilot AmFm, now for regional interactions on guideline revisions)
- 4) iOWH (India)
- 5) TB Alliance (South Africa) – focused on clinical trial conduct, not access.
- 6) FIND (India)

- 7) IAVI (India, Kenya, South Africa)
- 8) Aeras (South Africa)
- 9) IPM (South Africa)

C: Snapshot of PDP Portfolios, June 2009^{4,5}



1. Includes pneumonia and meningitis 2. Includes cholera, typhoid, and rotavirus 3. Includes HAT, visceral leishmaniasis, chagas, hookworm, and dengue 4. IPM products listed are a subset of all candidates in development. This is due to IPM's novel approach to Phase III clinical trials, which includes forced product attrition
 Sources: To estimate time until launch, survey responses from the 2008 PDP Access meeting were used where available. Next, public sources were referenced including the STOP TB website and PDP websites. Where no launch dates were available, vaccine launch dates were estimated using industry averages published by BIO, the biotechnology industry association (Pre-clin=3yrs, PI=2yrs, PII=2 years, PIII=2 yrs, Reg=3yrs). Drug launch dates were estimated using the industry averages as reported in a 2007 IFPMA report (Pre-clin=1yr, PI=1yr, PII=1.5yrs, PIII=2.5yrs, Reg=1.5yrs). Microbicide launches were estimated using data from the IPM Strategic Plan 2009-15. For all estimates, it was assumed that candidates were starting the current phase 5. Drug attrition was estimated using industry averages of success by phase, published by IFPMA in 2007 (Pre-clin=0.01, PI=0.7, PII=0.5, PIII=0.5, Reg=0.9). Vaccine attrition was estimated using industry average success rates by phase, published by Andrew Farlow from the University of Oxford in the TB Vaccine Scoping Study, 2008 (Pre-clin=0.6, PI=0.8, PII=0.6, PIII=0.75, Reg=0.9). Microbicide attrition is assumed to be included in IPM's total expected products. IPM uses a novel approach to Phase III clinical trials, which includes forced product attrition. Diagnostic attrition was excluded because diagnostics follow a unique regulatory path

⁴ BCG/BMGF Design Team, "Snapshot of PDP Portfolios" 2009

⁵ Update: NECT combination for sleeping sickness was launched by DNDi and WHO in 2009