

# International Partnership for Microbicides EVALUATION REPORT

*Prepared for Review by  
the Evaluation Management  
Group of the IPM Donors*

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# IPM Evaluation Report

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## I. Executive Summary of IPM Evaluation

This summary includes a brief statement of the context of this evaluation, the conclusions based on the Organization for Economic Cooperation and Development, Development Assistance Committee (OECD DAC) General Evaluation Issues, and a list of recommendations for IPM's next five years. The supporting data and analyses can be found in the IPM Review section of this document.

### **Context**

IPM was founded in 2002 as a new Product Development Partnership (PDP) in response to a global effort to identify how to best move the field of microbicide research and development forward. While a number of PDPs now exist to develop drugs, vaccines or diagnostics for diseases of the developing world, the PDP model is still a relatively novel approach to develop new technologies for such diseases as malaria, TB and AIDS.

As a new organization operating within the emerging model of a PDP in 2002, it was envisaged that IPM would play a coordinating role among the researchers pursuing microbicides, prioritizing candidates from the global pipeline, incubating projects, fundraising, enhancing capacity for the field and addressing advocacy and access gaps. While many of these functions remain part of IPM's mandate, IPM has placed greater emphasis on its own projects and less emphasis on coordinating the efforts of other researchers in the field. This was a logical evolution of the organization's goals given the fact that at the time, few, if any researchers were focused on next-generation compounds. When IPM recognized that gap, it sought to address it and developed a robust portfolio of antiretroviral-based candidates in partnership with leading pharmaceutical firms.

As the evaluation team commenced its work of the first five-year assessment of IPM, the question about the organization's original mission and how IPM has interpreted its own role to bring value to the field of microbicides was a central feature of interviews and team reflection. It became clear as the evaluation team reviewed hundreds of documents and engaged in dozens of discussions that IPM made a deliberate decision to add value to the field by developing a pipeline of microbicide projects. IPM has not viewed its role as a coordinator or gate-keeper vis-à-vis the global pipeline of candidate compounds. The evaluation team concurs with this vital interpretation of IPM's role.

This evaluation, conducted by FSG-Social Impact Advisors (FSG) with significant contributions by two HSLP evaluators, was conducted to bring a third-party assessment to IPM's role and evaluate the organization's actions, achievements and processes supporting decision-making during the last five years. The evaluation team provides findings and conclusions about the organization's past work. In particular, the team focuses on the issues of risk and how the organization has identified risk points and the systems to effectively counter them. While IPM's past actions receive their due attention in this report, the evaluation team fundamentally believes that the organization and the field itself must move beyond the legacy discussions of the original mandate and focus squarely on the future. Developing a microbicide is one of global health's grandest

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challenges and, against the backdrop of recent HIV vaccine and other prevention failures and the sheer enormity of the scientific task, all effort and creativity needs to be directed at future actions.

Therefore, this evaluation has largely taken a forward-looking perspective. Because IPM's role has evolved significantly as it has grown both in purpose and in complexity of operations, the evaluation emphasizes critical improvements for IPM to consider in the next five years. We believe this is the most useful orientation, both because it recognizes the challenges that IPM will face in the future and because it will be most relevant for senior management as a tool for improvement. The evaluation team believes that the women who wait for a microbicide can be best served by a strong organization that is highly motivated to become even stronger.


To be such an organization, the evaluation team has identified two top-line themes that incorporate nearly all the content of this report. First, IPM can improve the way it manages risk in its scientific decision-making and operational implementation. Ultimately, IPM's long-term success will be measured by whether safe and effective microbicides are approved. We believe that if IPM progresses its portfolio and conducts clinical trials while controlling risk to the greatest extent, it will have performed admirably. Second, IPM can apply even greater emphasis on the partnership component of its work. As a virtual organization, dependent upon others to complete many of the key activities in its strategy, it is critical that IPM have strong, positive relationships that will withstand the inevitable ups and downs in clinical research. IPM depends upon a web of strong partners to work effectively together. This evaluation highlights how IPM can ensure that its partnerships are as strong as possible.

### Summary of DAC General Evaluation Issues

The DAC General Evaluation issues were refined during a six-week Inception Phase in order to better reflect the key questions for IPM. These questions were then used to bring together the high-level conclusions which are summarized in this section.

Figure 1: Cross-Cutting DAC Questions

Cross-Cutting DAC Questions	
Relevance	Has IPM's role been appropriate to the global effort towards microbicides?
Effectiveness	Did IPM choose the right strategies to achieve its goals, assessing and managing risk appropriately, and has it executed those strategies effectively?
Efficiency	Has IPM allocated resources appropriately and delivered value-for-money?
Sustainability	Has IPM's resource mobilization strategy been adequate, effective, and based on reasonable resource estimates?
Impact	What has been the impact of IPM on its goal of accelerated development of microbicides and how have its activities benefited the field?



Implications	What should IPM and its donors consider going forward?
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## A. Relevance

*Has IPM's role been appropriate to the global effort towards microbicides?*

### **Key Messages:**

- The original 2002 business plan envisioned IPM as a coordinating organization for the field that would also address critical gaps or rate limiting factors. IPM has evolved into a product developer, addressing the gap in the field at the time for greater focus on antiretroviral-based microbicides.
- This evolution was appropriate. The evaluation has found that no microbicide organization has the authority or the perceived neutrality to coordinate the field and that this role can only appropriately be filled by microbicide donors.

At the time of IPM's creation, the microbicides field was described as a relatively mature but fragmented field with a number of existing product developers comprised of small biotech, nonprofits, and academic institutions that had limited funding and capacity, and little coordination across their efforts. The original 2002-07 business plan envisioned IPM as a coordinating organization that would create greater focus among these players and form partnerships to address critical gaps or rate limiting factors. IPM's mission was and continues to be to accelerate the development of safe and effective microbicides. From its inception, IPM has maintained the option of conducting projects itself if deemed necessary.

Based on interviews with key stakeholders in the field, the evaluation team believes that IPM's role as a coordinator for the field was not feasible. IPM did not have the authority to coordinate multiple players, each with their own projects, and tasks such as prioritizing compounds, eliminating less promising leads, or coordinating Phase III trial capacity were beyond IPM's influence.

IPM plays a highly relevant role today as a product developer solely focused at this time on antiretroviral-based compounds and in its role as a partner to leading pharmaceutical firms. It is the only research organization in the field with an expressed mandate to develop new products. In addition, IPM has pursued formulation development for new delivery mechanisms (e.g., vaginal rings, tablets, films), built additional clinical trial capacity, and collaborated with established advocates to engage global leaders, representatives from European bilateral agencies, and multilateral organizations to raise the profile of microbicides globally.

IPM has also played a relevant role partnering with the field on various initiatives (e.g., Microbicide Development Strategy, Microbicides Media and Communications Initiative). IPM has further contributed to the field by establishing a pre-clinical compound screening service, co-hosting regulatory forums, and gathering key stakeholders for access and other forums.

## B. Effectiveness

*Did IPM choose the right strategies to achieve its goals, assessing and managing risk appropriately, and has it executed those strategies effectively?*

### Key Messages

- Based on the original 2002 business plan goals, IPM has performed effectively, achieving the 8 out of 10 of the original goals and addressing parts of the remaining two.
- Across IPM's key activities (Portfolio and Product Development, Clinical Trials, Access, and Advocacy), IPM has largely pursued the right strategies and appropriately assessed and managed risk. Summaries of key findings and recommendations are below; for greater detail, see module specific sections.

As a broad view of how IPM has performed against its goals, the evaluation team compared IPM's progress against the goals articulated in the original 2002 business plan. IPM has achieved the majority of these goals, which is an achievement few start-ups can boast. While IPM's activities have evolved over the past five years, it is notable that it has accomplished much of what it was originally purposed to do (See Table 1).

**Table 1: IPM Goals As Articulated in the 2002 Start-Up Business Plan<sup>1</sup>**

Activities	Status	Description
Evaluation of the microbicide pipeline	Complete	The SAB met twice in 2003 to conduct a thorough review of the microbicide pipeline and establish principles to guide IPM's research
Establish partnerships to fill product development gaps for 2-5 products	Complete	IPM has created partnerships with five major pharmaceutical companies and in-licensed six antiretrovirals
Assistance in brokering partnerships directly between microbicide sponsors and larger pharmaceutical and biotechnology companies	Complete	See above
Development of central manufacturing resources for microbicide developers	In process	IPM has built a ring and gel manufacturing facility which can be made available for other developers, and has also made available a pre-clinical screening mechanism

<sup>1</sup> International Partnership for Microbicides 2002 Start-up Business Plan

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Activities	Status	Description
Commission of a program of research to develop a range of drug delivery approaches for active agents	Complete	IPM has invested significantly in developing an effective ring formulation, including building a ring manufacturing facility; IPM has also begun research into other formulations such as vaginal tablets and films
Recruitment of new organizations to the field, specifically those with pharmaceutical and drug delivery expertise	Complete	IPM has created partnerships with five major pharmaceutical companies and has engaged with organizations that have expertise in drug delivery
Establishment of partnerships to develop 10-12 new clinical research centers	Complete	IPM has partnered to establish 15 clinical research centers with 14 in sub-Saharan Africa; 11 of those consist of new research centers
Conduct survey of regulatory requirements and processes for microbicide evaluation, approval, and introduction with in-depth pilot projects in 2-3 countries	In process	IPM has partnered with CONRAD and WHO to convene regulators to hold discussions on approval processes and criteria
Implement plans to raise the profile of microbicides within the political, scientific and NGO communities, with particular emphasis on Europe	Complete	IPM has effectively advocated to high-level government and multilateral officials to raise the profile of microbicides and demonstrated particular success in Europe

The evaluation also examined IPM’s effectiveness across its key activities which are covered in greater detail in the “IPM Review” section. Overall, IPM has pursued the most appropriate strategies and has appropriately assessed and managed risk. In summary:

- Portfolio and Product Development:** IPM has effectively expanded its portfolio and advanced one of its lead compounds, dapivirine. Looking forward, as IPM prepares to manage a more complex portfolio with numerous compounds, more formalized portfolio management processes will greatly reduce the operational risk. This would include a portfolio management committee with periodic benchmarking of the portfolio, establishing target product profiles<sup>2</sup> with explicit go/no-go criteria at key milestones in the development path, and operational implementation by multidisciplinary project teams. A target product profile would be supported by comprehensive product and clinical development plans, including risk analysis and contingency planning. IPM’s Scientific Advisory Board (SAB) is not currently configured to provide the level of input and guidance required to support its complex portfolio; changes to the composition of this body and modus operandi will strengthen effective decision-making going forward.

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<sup>2</sup> A target product profile (TPP) defines the desired product characteristics, target efficacy, and population served by the eventual product to increase the probability of success and ensure access for the target population. The TPP is periodically tested to assess whether changes are warranted. By making hypotheses explicit and transparent, the TPP provides a baseline to guide decisions and communicate priorities

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- **Clinical Trials:** Since its inception in 2002, IPM has conducted eight clinical trials and seven HIV incidence studies using a combination of experienced and newly established clinical research centers across Africa and in Europe. In addition, one market research study was conducted in seven different settings in Africa. Additional clinical, incidence, and market research studies are being planned at various locations in Europe, Africa, and the United States. The trials are designed to offer an increasing level of complexity to new research centers in preparation for the Phase III trial currently planned for Q4 2009/Q1 2010. Given the range of experience internally and among its current partners, as IPM prepares for complex Phase III trials, it should revisit its timeline for implementation. Delaying the start beyond Q1 2010 will provide greater opportunity for recruiting additional high-quality research centers, increasing the experience of new clinical research centers, strengthening clinical trial processes, and supporting country-level advocacy and communication efforts. IPM should also strengthen the in-house clinical team with additional expertise in clinical trial management and monitoring, also including a senior clinical research physician to support the Chief Medical Officer. Finally, IPM's track record with its research partners is mixed. IPM should continue to ensure robust, positive relations with in-country research partners. This will be critical to IPM's ability to successfully conduct its trials and will help ensure strong stakeholders that will be effective advocates on IPM's behalf in managing relationship with government officials.
- **Access:** IPM has been a leader in the field in advancing access issues and has demonstrated its commitment to access criteria in its product design. In order to ensure that momentum is maintained, IPM should make its access-related criteria explicit in its product prioritization and development decisions; begin planning for manufacture, scale-up, and distribution of an eventual microbicide; and communicate clearly with the field concerning its future access program.
- **Advocacy:** IPM has effectively championed microbicides at the global level and brought attention to high-level government officials and multilaterals in North America and Europe. Going forward, IPM should proactively engage with its advocacy peers to strengthen those relationships and continue to balance advocacy for the field with advocacy for its own work.

### C. Efficiency

*Has IPM allocated resources appropriately and delivered value-for-money?*

#### **Key Messages:**

- IPM's value-for-money proposition is difficult to evaluate due to the lack of available benchmarks. General product and clinical development costs were not relevant for comparison and peer microbicide trial costs were not available.
- IPM's expense allocations appear reasonable and in line with expectations with no distortions uncovered.

IPM's value-for-money proposition was difficult to evaluate due to the lack of benchmarks available. Data on product development costs related to microbicides are



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scarce and it is a challenge to find similar portfolios or organizations that can be compared to IPM. Further, while there are many players running microbicide clinical trials, finding trial cost data is difficult and has not resulted in useful data. Going forward, IPM could create tracking systems that better capture its own costs and allow it to benchmark against its own historical performance (e.g., how costs per patient per trial evolve over the years). IPM has recognized this need and is currently instituting accounting tools that will track costs by project.

An important contextual note is that IPM has often prioritized speed over resource efficiency by conducting activities in parallel rather than sequentially (e.g., building an intravaginal ring manufacturing facility and progressing toward Phase III efficacy trials before acceptability research on a ring is completed). The benefit of moving activities in parallel is potentially saved time while the risk is potentially wasted resources (e.g., if ring acceptability studies show very poor adherence and a ring formulation is decided to be untenable). However this is a reasonable approach to product development provided the potential risks have been first evaluated with contingency planning. As IPM's strategy and operations are evaluated for efficiency, this trade-off should be kept in mind.

Overall, the evaluation team has found IPM's expense allocations to be reasonable and in line with expectations with no distortions uncovered. The trend in resource allocation has followed IPM's evolution as an organization, with the proportion of costs associated with R&D being high as IPM focused on product development. As IPM has focused greater resources on developing clinical research centers and preparations for a Phase III trial, it has allocated an increasing amount of funding to site development and clinical trials.

Management and general costs were consistent with peer benchmarks that were available (10-15%). As noted, clinical trial cost benchmarks were not available, but stakeholders in the field cited IPM as rigorous in its cost controls and accounting standards. IPM's resource development operations (housed in external affairs) have been efficient, with wide recognition in the field of IPM's ability to raise significant new funding in support of its mission.

Finally, IPM's internal systems have served its needs to date (e.g., human resources, knowledge management, information technology) though there is room for improvement. Some concerns relating to knowledge management and standardization of documents and procedures exist, which is normal for many organizations at this stage of development. Improvements in this area will help IPM to better coordinate across multiple research centers for its clinical trials. Similarly, programs such as the Clinical Trial Management System (specialized software that helps track data during clinical trials) will need strengthening given the size and complexity of upcoming trials. IPM has recognized the overall need for increased coordination and standardization of internal documents and should ensure that the necessary investment in infrastructure and processes are made to support its future efforts.

## D. Sustainability<sup>3</sup>

*Has IPM's resource mobilization strategy been adequate, effective, and based on reasonable resource estimates?*

### **Key Messages:**

- IPM has effectively mobilized resources, raising both adequate funding and funding from diverse sources. IPM is financially well positioned to conduct an expensive Phase III trial based on its current cash reserve and its strong resource mobilization track record.
- IPM's long-term planning can be improved going forward. IPM is over-due for its next strategic plan (the original five-year plan was developed in 2002) which should articulate its strategies for managing its portfolio and launching additional Phase III trials. While IPM is currently refining its projections for a first Phase III, scale-up, manufacturing, and distribution costs need to be more fully developed.

IPM's resource mobilization to date has been both adequate and effective, and has positioned IPM well to address the substantial financial requirements for implementing its first Phase III trial. IPM's donor base is extremely diverse and includes numerous governments, and a few private foundations and multilaterals. Relative to other microbicide developers, IPM has very diverse funding. IPM has repeatedly under-spent against its budgets, which is consistent with other PDPs (e.g., DNDi operates at a 15% surplus). This strategy is appropriate and IPM has committed the funds to its clinical trials, given the difficulty of raising such a large sum of money at one time. IPM has been explicit that money not spent will go towards funding Phase III trials, consistent with donor expectations.

IPM's current strategic plan was developed in 2002 and the organization has re-set its priorities since then through the development of two to three year workplans. IPM annually updates its financial projections for donors. The estimates for the Phase III trial, which will constitute the largest single expense going forward, were originally modeled in 2006 and are being updated based on the new Phase III design. Access costs associated with country preparedness, scale-up, manufacturing, and distribution are currently not fully developed and will need to be refined as IPM's Phase III approaches.

A new strategic plan will be required to help set priorities for the next five years. This would articulate the organization's strategies in all key areas: product development, clinical trials, access and advocacy. With these strategies identified, IPM can model a new, 5-year financial projection. A new strategic plan will enhance IPM's sustainability by setting expectations with partners and funders regarding its top priorities and the associated costs of its work.

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<sup>3</sup> Sustainability is generally a reference to the permanence of impact to the target population. However, in the context of this evaluation, there is no approved microbicide for the target population. Based on the questions in the Terms of Reference (see Annex), sustainability therefore refers to the ability of IPM to support itself from a resource perspective until it can accomplish its mission.

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Finally, it is important to note that in interviews with donors there was generally strong support for IPM's mission and the expectation that IPM would enter Phase III trials in the next five years. Most donors understand the risks of product development and voice support for the PDP model as a risk-mitigating model that improves the chances of eventually developing a microbicide.

### E. Impact<sup>4</sup>

*What has been the impact of IPM on its goal of accelerated development of microbicides and how have its activities benefited the field?*

Neither IPM nor the field has thus far developed a safe and effective microbicide to the point of regulatory approval. While original expectations in the field were optimistic, there has been widespread recognition that microbicide development is a long and difficult process with substantial risk of failure.

IPM has nonetheless contributed significantly toward the goal of developing safe and effective microbicides, and peers recognize its accomplishments as ones which would not have otherwise been achieved. IPM's key successes in the past five years, many of which benefit the field overall, have included:

- **Expanding the Pipeline of Microbicides:** IPM has in-licensed a number of important antiretrovirals from pharmaceutical companies which has substantially expanded the pipeline of potential microbicides, both in number and potential mechanisms of action. Peers in the field also hold in high regard IPM's IP agreements with pharmaceutical partners.
- **Formulation Development:** IPM has emphasized exploring formulation options beyond gels and has done significant work on an intravaginal ring as a depot for antiretroviral drugs, as well as some research into vaginal tablets and films. This has addressed an important gap in thinking about product design and eventual acceptability of microbicide products. IPM is now seen as a leader in formulation development and beyond developing its own technologies, has shared information with the field at convenings and conferences concerning resources in formulation development and toxicology.
- **Building Clinical Trial Capacity:** IPM has established a number of clinical research centers including investing significantly in infrastructure and training in ICH GCP standards for new PIs and research center staff. This has expanded both the local research capacity and the specific capacity for microbicides research in preparation for IPM's Phase III.
- **Raising the Profile of Microbicides:** IPM has effectively engaged with high-profile individuals and organizations and played a key role, in collaboration with its advocacy partners, to put microbicides on the global health agenda.

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<sup>4</sup> Impact is generally a reference to the outcome in the target population. However, in the context of this evaluation, there is no approved microbicide for the target population, so health impacts can be assessed. Based on the questions in the Terms of Reference (see Annex), impact therefore refers to the achievements of IPM toward the development of a safe and effective microbicide.

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- **Pre-clinical Compound Screening Capabilities:** IPM has made this service available to other researchers and organizations in the field, which represents a significant investment in infrastructure and technical capacity.
- **Regulatory Pathways:** IPM has co-hosted a regulatory meeting with CONRAD and the WHO for regulators in developing countries to discuss regulatory pathways for microbicides and to clarify trial standards.
- **Access Convenings:** IPM has convened other key microbicide organizations to discuss the importance of planning for access, both from the perspective of 1) product and clinical development, and 2) scale-up, manufacturing, and distribution of an eventual product.

### Summary of Recommendations

As IPM prepares for the challenges ahead, the evaluation has identified five specific next steps that must be addressed to ensure the highest probability of success:

1. **Formalize Portfolio Management Processes:** IPM has rapidly expanded its portfolio to include a wide array of products and formulations. However, management processes and structures to match this complexity have not yet been implemented. IPM should adopt formal portfolio management processes with a portfolio management committee, and implement comprehensive product and clinical development plans, target product profiles, explicit go/no-go criteria, and multi-disciplinary project teams.
2. **Increase Engagement with the Scientific Advisory Board Executive Committee (SAB EC):** Donors rely heavily on the SAB EC to provide IPM with independent advice which brings wider expertise to IPM's scientific decisions. While the SAB EC should remain an advisory body and should not impede IPM's operational flexibility, it is important that the SAB EC is more actively involved in scientific planning and decision-making. IPM should take steps to ensure that the SAB EC is appropriately engaged and that this process is robustly implemented. The SAB EC could augment its annual meeting with an additional meeting, quarterly conference calls, and/or sub-committees intended for more direct engagement. This may require that IPM revisit the membership and expertise of the SAB EC.
3. **Review the Timeline for the Phase III Efficacy Trial:** IPM's timelines are challenging and the pressure upon IPM's staff and clinical research centers to be ready for a Phase III trial are considerable. IPM recognizes that the current timeline for IPM's Phase III efficacy trial is aggressive, and the evaluation team believes that IPM should revisit the planned initiation date for a first Phase III to ensure sufficient preparation time both for IPM's clinical team as well as for clinical research centers. While there has been significant pressure from donors to pursue ambitious and optimistic goals, a more realistic timeline and preparation plan is critical to ensure the highest probability of success.
4. **Strengthen the Clinical Team:** IPM has begun training its clinical team in preparation for Phase III trials, but currently does not yet have the number of experienced staff that will be required. IPM should engage additional experienced

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clinical trial managers and clinical research associates (CRAs). IPM should also recruit a senior clinical research physician to better support the Chief Medical Officer (CMO). This person should have considerable experience in designing, implementing, and managing clinical trials. IPM should also consider increasing quality control (QC) capacity, preferably based in South Africa, and implementing mentoring between experienced, proven investigators and new research centers. IPM should explore leveraging its partnerships with pharmaceutical companies, who may be willing to consider loaning experienced staff or offering greater technical assistance.

5. **Develop Updated Five-year Strategic Plan:** IPM requires a clear plan for managing the complex portfolio of compounds and wide range of activities that it is now responsible for. IPM has evolved significantly since its inception and should develop an updated five-year strategic plan that clearly communicates its positioning in the field, priorities, and key activities both internally and externally. As part of this process, IPM should also develop financial projections that take into account product and clinical development associated with its whole portfolio.

The full list of recommendations by “module” is below with greater detail on findings, evidence and conclusions in the following “IPM Review” section.

Module	Full List of Recommendations
<b>Portfolio and Product Development</b>	<b>Formalize Portfolio Management Processes:</b> IPM should adopt formal portfolio management processes with a portfolio management committee, and implement comprehensive product and clinical development plans, target product profiles, explicit go/no-go criteria, and multi-disciplinary project teams.
	<b>Increase Engagement with the Scientific Advisory Board:</b> IPM should take steps to ensure that the SAB EC is more engaged in its scientific planning and decision-making, and that this process is robustly implemented. The role of the broader SAB should be reconsidered and dissolved if the group is not currently providing value to IPM.
<b>Clinical Trials</b>	<b>Review Phase III Timeline:</b> IPM should revisit the planned initiation date for a first Phase III to ensure sufficient preparation time both for IPM's clinical team as well as for clinical research centers.
	<b>Strengthen the Clinical Team:</b> IPM should engage additional experienced clinical trial managers, CRAs, and a senior clinical research physician to better support the CMO. IPM should also consider increasing QC capacity implementing mentoring between experienced, proven investigators and new research centers. IPM should explore leveraging its partnerships with pharmaceutical companies, who may be willing to consider loaning experienced staff or offering greater technical assistance.
	<b>Establishing High-Quality New Clinical Research Centers:</b> IPM should ensure that criteria and decision-making for identifying clinical research centers (new and established) are objective, clearly communicated, and documented. IPM should continue to proactively explore where it might take advantage of existing capacity as it prepares for Phase III trials.
	<b>Strengthen Clinical Partnerships:</b> IPM should continue to work toward deeper partnerships that are critical to generating country-level support, communicating progress, and managing potential setbacks to communities and to governments.
	<b>Strengthen Clinical Trial Processes:</b> IPM should enhance clinical trial processes with clinical development plans and harmonize core and trial specific Standard Operating Procedures (SOPs) across research centers to ensure uniform application of ICH GCP procedures.

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Module	Full List of Recommendations
	<b>Strengthen Country-level Communications:</b> IPM should continue to support advocacy and communication efforts at the country level for trial execution, and should continue conducting due diligence on the advocacy “funding window”.
<b>Access</b>	<b>Define Explicit Access Criteria:</b> As part of developing a TPP, IPM should explicitly define the access criteria that feed into product prioritization and development decisions.
	<b>Begin Planning for Manufacture, Scale-up, and Distribution:</b> Within the next 18 months, IPM should begin planning explicit activities, identifying partners, and projecting costs that will be necessary to ensure rapid manufacture, scale-up, and distribution of an eventual microbicide.
	<b>Clearly Communicate Plans for Access Program:</b> As IPM evolves its access approach, it should clearly communicate its continued commitment to access issues and set expectations for how IPM is going to engage the field on access going forward.
<b>Advocacy</b>	<b>Continue High-level Global Advocacy:</b> IPM should continue to champion microbicides at the global level, speaking broadly about the need for increased attention and funding from international donors and policy makers.
	<b>More Fully Engage Advocacy Partners:</b> When IPM is advocating for microbicides broadly, it should proactively engage with its advocacy peers to ensure consistency in messaging and a deeper feeling of partnership.
	<b>Balance Advocacy for the Field with Advocacy for IPM:</b> IPM should continue to balance advocacy for the field with advocacy for its own work. IPM should also continue to distinguish between its messaging on behalf of the field and messaging associated with its own portfolio.
<b>Organizational Effectiveness</b>	<b>Develop Updated Five-year Strategic Plan:</b> IPM should develop an updated five-year strategic plan that clearly communicates its positioning in the field, priorities, and key activities both internally and externally. IPM should also develop financial projections that take into account product and clinical development associated with its whole portfolio.
	<b>Continue Advocating for Unrestricted Funding:</b> IPM should continue to advocate to donors for unrestricted funding and should position the strong governance mechanisms through its board and a more engaged SAB as sufficient accountability.
	<b>Improve Communication with Partners:</b> IPM should consider processes for better communication of plans and priorities with key partners.
	<b>Strengthen the Clinical Team:</b> (see above)
	<b>Formalize Portfolio Management Processes:</b> (see above)
	<b>Increase Engagement with the Scientific Advisory Board</b> (see above)

The evaluation also makes recommendations for the future of the field of microbicides and for the field of Product Development Partnerships (PDPs):

- **For Microbicides:** There continues to be a need for greater coordination of resources (e.g., advocacy, clinical research centers) and collaboration towards common goals (e.g., regulatory capacity) across the field. IPM cannot play this coordinating role as a product developer, and the evaluation believes that no microbicide organization has the authority or the perceived neutrality to coordinate the field. At this time, this role can only appropriately be filled by microbicide donors.
- **For PDPs:** The IPM review is only the third evaluation of a PDP to date. No standards for evaluation have yet emerged. The experience of this evaluation suggests that the field may be better served through prospective setting of performance metrics embedded in strategic plans. Ideally, these plans would be

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created with donor input, thereby setting the stage for known progress measures well before evaluations take place.

## II. Introduction

### Background

The five-year IPM Evaluation was commissioned by its donors<sup>5</sup> to gain a comprehensive view of IPM's strategy and activity over its first five years of existence. The evaluation was conducted to meet two goals:

- 1) Identify IPM's achievements, both independently and with partners, in its efforts to accelerate access to safe and effective microbicides for women living in the developing world
- 2) Identify lessons learned and opportunities for improvement to guide IPM's activities in the future

FSG Social Impact Advisors (FSG)<sup>6</sup> and HLSP<sup>7</sup> jointly conducted this evaluation which merged management consulting and technical expertise to provide a perspective on IPM's performance during the last five years. The evaluation spanned from January through June 2008 and has been conducted based on a Terms of Reference that highlighted major areas for investigation drawing on the OECD Development Assistance Committee's (DAC) evaluation framework.

### Methodology

The evaluation process included an Inception Phase that refined the Terms of Reference, identified the specific questions to be addressed, and detailed the evaluation approach and methods. The Inception Report, which is available in the Annex to the evaluation, was informed by internal IPM documents, secondary research, and interviews with IPM senior staff, select donors, and a limited number of stakeholders in the field. A total of 18 interviews were conducted during the Inception Phase.

In the evaluation itself, the evaluation team reviewed approximately 1,100 documents from IPM and the field, conducted 148 interviews with IPM staff and external stakeholders, and made in-person visits to seven locations including IPM offices in Cape Town (South Africa), Bethlehem (PA), Silver Spring (MD), and Brussels (Belgium), as well as IPM supported research centers in Rwanda and South Africa. The team also conducted a brief benchmarking study to compare IPM's processes to those of other

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<sup>5</sup> IPM's donors include Canadian International Development Agency\*, Danish Ministry of Foreign Affairs\*, UK Department for International Development\*, the Bill and Melinda Gates Foundation\*, Irish Aid\*, the Netherlands Ministry of Foreign Affairs\*, Norwegian Ministry of Foreign Affairs\*, the Rockefeller Foundation\*, and Swedish International Development Cooperation Agency\*, US Agency for International Development, the European Commission, Belgian Ministry of Development Cooperation, German Federal Ministry for Economic Cooperation & Development, French Ministry of Foreign Affairs, the World Bank, and UNFPA. \* Indicates donors who are funding this evaluation.

<sup>6</sup> FSG Social Impact Advisors is a nonprofit strategy consulting firm and has worked with leading private, corporate, and community foundations across a range of social issues.

<sup>7</sup> HLSP is a professional services firm specializing in the health sector both internationally and in the UK.



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PDPs, biotechnology firms and pharmaceutical firms. Finally, a survey of stakeholders was also completed, although the response rate was too low to allow for robust interpretation. The breakdown of interviewees follows (see Table 2) and the full list of external interviewees can be found in the Appendix.

**Table 2: Number of Interviews Conducted for IPM Evaluation**

<b>Internal and External Stakeholders Interviewed</b>	
<b>Internal IPM Staff</b>	47*
<b>Board</b>	11**
<b>SAB</b>	13^
<b>Funders</b>	11
<b>Advocacy and Access Partners</b>	14
<b>Industry Partners</b>	5
<b>Clinical Partners</b>	7
<b>Site Team</b>	6
<b>Community Group Members</b>	5
<b>Peers</b>	29
<b>Total</b>	<b>148</b>

Note: \* Includes 2 former IPM staff; \*\* Includes 2 former Board members; ^ Includes 10 Executive Committee members and 3 members of the broader SAB

### Report Structure

This report has been structured to first provide the “Summary of the DAC General Evaluation Issues,” which includes Relevance, Effectiveness, Efficiency, Sustainability, and Impact. These issues span across IPM’s activities and represent the high-level view of IPM’s performance. This section also covers the general context for the evaluation and the full set of recommendations for IPM, and can be read as a stand-alone “executive summary” for the evaluation report.

The “IPM Review” section includes the more in-depth examination of IPM in terms of: Portfolio and Product Development, Clinical Trials, Access, Advocacy, and Organizational Effectiveness. This section provides greater detail on the findings and evidence supporting the recommendations.

The report concludes with implications for IPM, for the field, and for donors in terms of other evaluations of PDPs. The appendices provide greater detail on the evaluation approach, evaluation team, workplans, external interviewees, lists of figures and tables, and abbreviations.

## Situation Assessment

The HIV epidemic remains among the highest priorities for global donors. Prevention is the key to breaking the cycle of infection, yet current tools are lacking, especially for women who often cannot negotiate the use of condoms and other prevention approaches. Support for the development of new protection tools against HIV is strong, with global bodies including the UN and the G8 endorsing investment in new and high-profile financing mechanisms to ensure markets for new products. Today UNAIDS reports 15.4M women living with HIV, and the increasing proportion of women affected by HIV has placed greater emphasis on woman-initiated technologies such as microbicides.

Microbicides have reached global prominence during the last five years. Funding to the field has expanded from \$65M in 2002 to \$212M in 2006<sup>8</sup>. The pipeline of potential microbicides has expanded beyond the early generation to include antiretroviral-based microbicides. New partners in the field, notably pharmaceutical companies, have begun to invest time and resources in working with the public sector to develop alternatives. IPM has played a central role in this expansion.

However, setbacks to the broader prevention field and challenges in developing microbicides have intensified pressure on microbicide developers. During the course of this four-month evaluation, the Phase III Carraguard trial ended without showing efficacy. Of the early generation microbicide candidates, only the 0.5% gel concentration of Pro 2000 and Buffergel remain in Phase III trials at the time of writing, following disappointments with Nonoxynol-9, cellulose sulfate, and Savvy. The difficulty facing the current generation of HIV vaccine trials in the last year surfaces questions about the technical and financial sustainability of the global effort to achieve an effective vaccine. Oral pre-exposure prophylaxis with antiretrovirals provides an alternative near term hope for HIV prevention and trials are underway. Male circumcision is considered to be beneficial in reducing HIV transmission for men (but not for women), and condoms (male and female) are available alternatives. However, use of condoms has not brought a halt to the epidemic. Finally, access to female condoms has been challenging to scale up, due to factors such as cost and concerns about appropriate targeting and programme integration strategies (issues also acknowledged as relevant to eventual microbicide access).

In addition to the contextual challenge of setbacks in HIV prevention technologies more generally, there are significant challenges to developing a microbicide. First, the target characteristics are not clear. Short of an ideal, over-the-counter, 100% safe and effective product, there is no agreed-upon threshold for a product's efficacy. Second, the field has yet to define a target product profile for a microbicide product. Whereas the field of HIV therapeutics can measure viral load or CD4 lymphocyte counts early on in clinical trials to infer potential efficacy, benchmarking microbicide products is more difficult in the absence of surrogate markers predictive of prophylactic efficacy. HIV-infection is the only endpoint and requires large efficacy trials to acquire adequate data. The

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<sup>8</sup> Building a Comprehensive Response, HIV Vaccines and Microbicides Resource Tracking Working Group, November 2007

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programmatic challenges of microbicide introduction and scale up are also likely to be significant, and will in part depend on product cost and effectiveness. Finally, the field as a whole, in the absence of compelling scientific data, has not reached consensus on the right approach to microbicide development. Debate continues over the value of animal models, method and periodicity of dosing, drug induced viral resistance, adherence, and clinical trials methodology. As the field moves forward, there is a need to answer some of these critical questions and create greater collaboration and consensus.

IPM was founded as a Product Development Partnership (PDP) in 2002 to respond to this call for increased coordination in the development of microbicides. In its first five years of existence, IPM has engaged pharmaceutical companies, developed a strong product portfolio, set up clinical research centers, and advocated on behalf of microbicides. IPM has successfully in-licensed a set of antiretroviral agents and brought them through phases of pre-clinical and clinical development. To date IPM's activities have focused upon dapivirine. IPM has engaged a wide set of donors, expanding interest in the field of microbicides. As IPM has grown, the field of microbicides has expanded dramatically with microbicide efficacy trials driving an increased need for funding in the field. Today, IPM is one of a number of organizations working with extraordinary diligence and urgency to find a solution to HIV prophylaxis in women.

### III. IPM Review

The detailed review of IPM's work is guided by "modules" focusing on the major areas of IPM's work: Portfolio and Product Development, Clinical Trials, Access, Advocacy and Organizational Effectiveness. For each module, the recommendations for future work are summarized, followed by the evaluation findings and conclusions. Recommendations across all modules are summarized at the conclusion of this section of the document.

#### A. Portfolio and Product Development

##### *Summary*

Portfolio and Product Development represent a major focus of IPM's work to date, and IPM has rapidly expanded its operations to include a large portfolio of potential microbicides. In the next five years IPM will need to evolve its processes to proactively manage this portfolio. It should be noted that many of our recommendations relate to what is now needed to manage a complex portfolio going forward rather than what was required in the past when IPM's activities were more limited to dapivirine. As a product development organization, IPM has set a high bar for itself which is more relevant to pharmaceutical and biotechnology companies.

##### *Recommendations*

The evaluation findings and conclusions suggest several recommendations for IPM moving forward and the overall theme is to further strengthen decision making at all levels within the organization and reduce project risk:

- 1) **Formalize Portfolio Management:** IPM should adopt a formal portfolio management process, and consider the following:
  - Implement a portfolio management function, a role which IAVI has incorporated into its structure. This would take the form of a portfolio development committee and would include members of IPM's senior management.
  - Develop target product profiles for each product and associated formulations.
  - Commit to benchmarking IPM's portfolio of products to facilitate internal prioritization of projects, enable rational resource allocation, and provide structured comparisons with products being championed by other groups in the field.
  - Establish formal, multi-disciplinary project teams which would include the diverse operational functions required to manage a project(s).
  - Develop explicit criteria and go/no-go decision points in the development process for review against the target product profile, facilitating decision-making and investment. This would be linked to comprehensive product and clinical development plans and risk management, and would be implemented

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and managed by project teams. The Product Development Committee would then focus on oversight and mentoring project teams and not the operational implementation of projects.

- Clearly communicate the prioritization of projects to pharmaceutical partners and the field.

The above approach to portfolio management should lead into more formal product and clinical development plans linked to target product profiles.

2) **Increase Engagement with the Scientific Advisory Board:** There is an expectation from IPM's Board of Directors and donors that the SAB Executive Committee provide a level of scientific input that is currently not being exercised. IPM should consider the following:

- **Increase engagement with the SAB EC:** Donors rely heavily on the SAB EC to provide IPM with independent advice which brings wider expertise to IPM's scientific decisions. While the SAB EC should remain an advisory body and should not impede IPM's operational flexibility, it is important that the SAB EC is more actively involved in scientific planning and decision-making. IPM should take steps to ensure that the SAB EC is appropriately engaged and that this process is robustly implemented. The SAB EC could augment its annual meeting with an additional meeting, quarterly conference calls, and/or sub-committees intended for more direct engagement. This may require that IPM revisit the membership and expertise of the SAB EC. It is worth noting the difficulty of convening the SAB EC, as well as the importance of not impeding IPM's operational flexibility.
- **Revisit the use of the broader SAB:** The role of the broader SAB should be reconsidered and dissolved if the group is not currently providing value to IPM.

### *Context*

Since its inception in 2002 IPM has established itself as a highly professional organization dedicated to developing a microbicide for preventing HIV transmission to women in the developing world. When IPM was created, the majority of efforts in the field were focused primarily on microbicide candidates that were large molecules with non-specific activity against HIV. In collaboration with the pharmaceutical industry, IPM has assembled a varied portfolio of HIV-specific antiretroviral drugs for development as potential microbicides.

The microbicide field has not come to firm conclusions regarding fundamental questions on the appropriate profile of a successful microbicide such as how antiretroviral agents should be delivered, whether drug induced viral resistance will be problematic, the level of effectiveness a microbicide must demonstrate in a Phase III trial to be useful, the ideal mechanism of action, the frequency and mode of application, and the intended target population. These are clearly issues that need resolution, and a product developer should

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have developed a position on each of these issues before a microbicide enters a costly late stage efficacy trial.

Much of the confusion in the field stems from uncertainty in the science behind microbicides. The underlying process of how HIV gains entry into the host is still being elucidated. There are no alternative surrogate markers to proven HIV infection and therefore, efficacy trials cannot be preceded by smaller studies using surrogate end points predictive of efficacy. Technical difficulties have further compounded the difficulty of developing microbicides, and inadequate site preparedness, poor adherence to the investigational agent, and lower than expected HIV incidence rates in communities have all contributed to difficulties in many of the early and recent Phase III trials.

### *Findings*

#### **IPM's Portfolio**

IPM has chosen to focus on antiretroviral-based vaginal microbicides and has been remarkably successful in attracting pharmaceutical partners and building a robust portfolio (Table 3). The guiding idea behind IPM's portfolio has been that if an antiretroviral agent could be locally administered in the vagina at high drug concentrations, it would interrupt HIV transmission. This hypothesis has been supported by many experts in the field who further recognize IPM for its expertise in formulating antiretroviral agents for microbicides and developing delayed release formulations via intra-vaginal rings.

**Table 3: IPM Portfolio Expansion**

<b>Year</b>	<b>Company</b>	<b>Compound</b>	<b>Type</b>
2004	Tibotec (J&J)	Dapivirine (TMC120)	NNRTI
2005	Merck	M167, M872, M882	CCR5 blockers
2005	Bristol-Myers Squibb	BMS793	gp120 binder
2006	Gilead	Tenofovir (PMPA gel)	NRTI
2008	Pfizer	Maraviroc	CCR5 blocker
2008	Merck	L644	gp41 fusion inhibitors

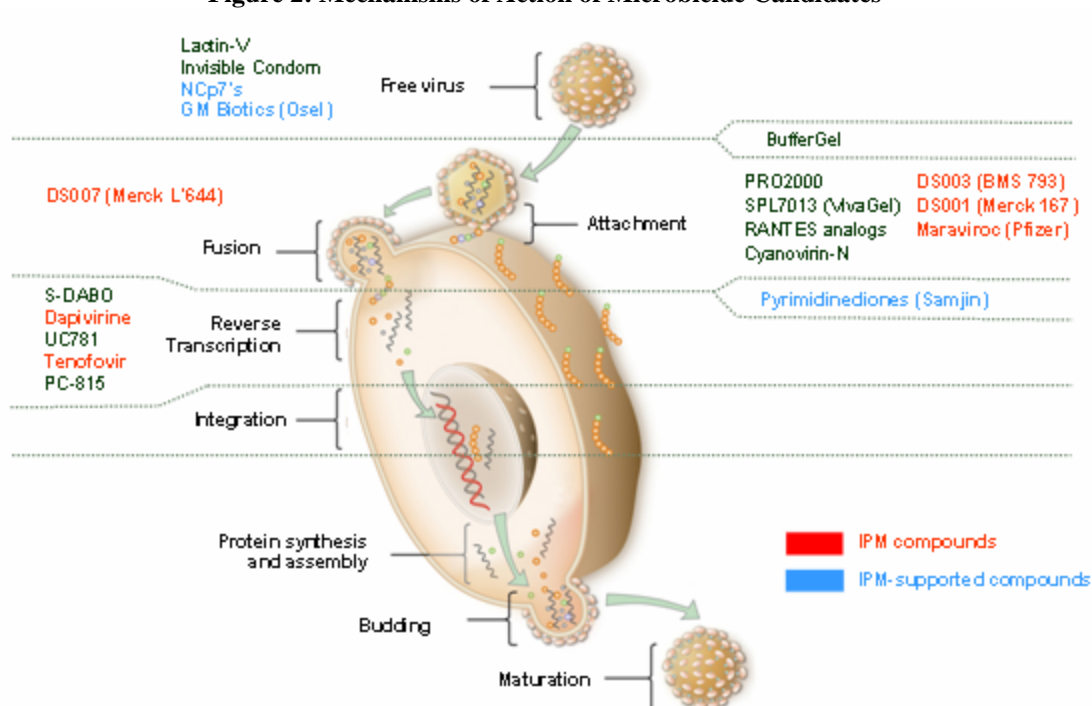
IPM's most advanced project in clinical development is dapivirine. IPM has demonstrated that very high antiviral concentrations of dapivirine are achievable and are well-tolerated in the female genital tract, and is currently focused on bringing dapivirine

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through a Phase III trial. While this is the immediate goal, IPM has recognized the high risks associated with drug development and its portfolio reflects antiretrovirals with a number of different mechanisms of action (Figure 2).

A portfolio approach therefore increases the overall probability that IPM will be successful even if one antiretroviral does not show high efficacy. IPM has successfully negotiated to obtain important intellectual property from several pharmaceutical companies. IPM is credited as having been highly successful in developing productive partnerships with pharmaceutical companies. In discussion with IPM's pharmaceutical partners, IPM is viewed as a highly respected partner, and this has been a significant motivation for industry to engage in licensing opportunities with IPM.

**Figure 2: Mechanisms of Action of Microbicide Candidates<sup>9</sup>**



IPM also recognizes the likelihood that the first approved microbicide may show only partial efficacy. Some members of IPM's SAB have noted that combinations of different antiretroviral agents may be more effective than a monotherapy microbicide. It has also been noted that the CCR5 HIV-entry inhibitors may eventually prove to be a better choice over the reverse transcriptase inhibitors, but this remains an unknown. Finally, some researchers believe that HIV cell entry inhibitors are less likely to be widely used and hence the risk of widespread drug resistance in the community may be less. These are largely questions currently without answers that will need to be addressed after proof of principle has been established for a microbicide containing an antiretroviral agent, but IPM has appropriately recognized the need to plan ahead beyond a single product.

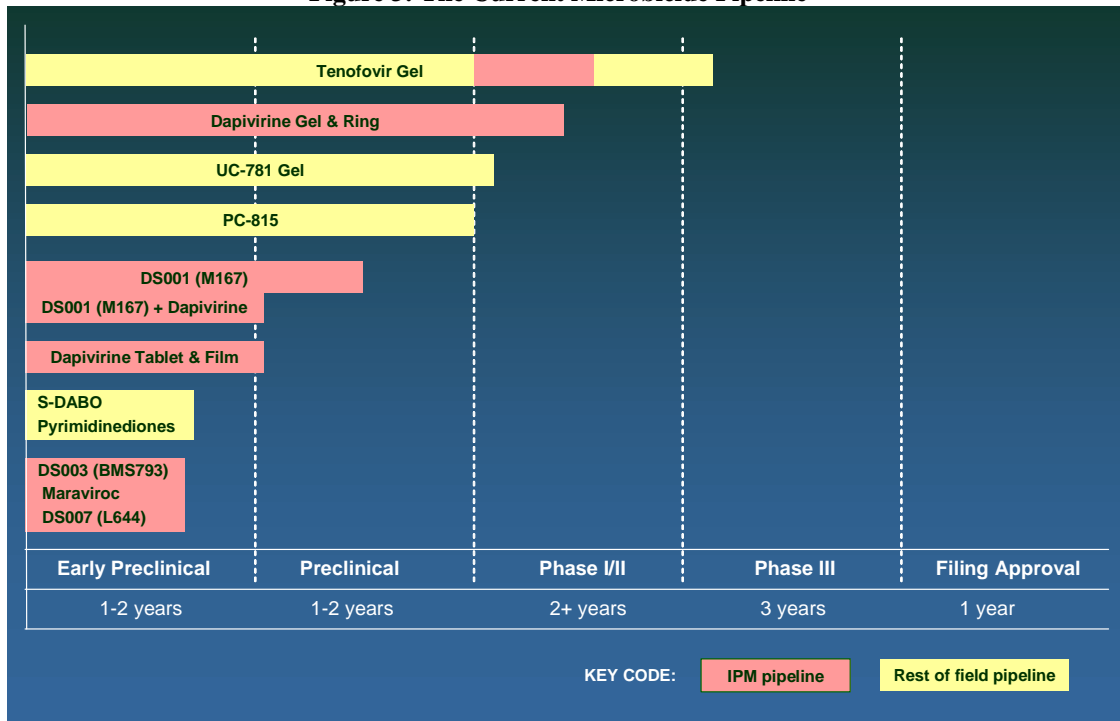
<sup>9</sup> Figure to be reproduced pending IPM review

**Portfolio Management**

IPM has rapidly expanded its portfolio to include a wide array of products and formulations. However, management processes and structures to match this complexity have not yet been implemented. With the exception of maraviroc which has only recently entered IPM’s portfolio, IPM’s microbicides are shown in Figure 3 (courtesy of IPM) by stage of development with non-IPM programs to illustrate the diverse approaches currently under evaluation by the field.

As stated previously, IPM has focused its efforts on developing dapivirine ring and gel formulations to date. In the past five years, however, the complexity of the portfolio has increased as additional compounds were added. The portfolio complexity is further increased by the number of formulations that may enter development and the potential to eventually combine antiretroviral agents of different classes.

**Figure 3: The Current Microbicide Pipeline<sup>10</sup>**



*Project Teams and Portfolio Management Committees*

In order to manage these projects, IPM has established steering committees with some of its pharmaceutical partners, but largely makes decisions through discussions among senior leadership including varied levels of participation in meetings. Decision-making processes appear informal and IPM has not yet adopted formal portfolio management processes that include a portfolio management committee and project teams. A portfolio management committee would include members of IPM’s senior management that currently functions as the Product Development Committee. Project teams are usually

<sup>10</sup> Figure to be reproduced pending IPM review



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multidisciplinary by function and are responsible for developing comprehensive development plans that support the target product profile. This would include the criteria for passing key Go/No Go decision points, risk analysis and contingency plans. These plans would be approved by IPM's senior management, the product development committee, who would have oversight of the operational implementation by the project teams. This should allow the product development committee to extricate itself from day to day operational activities, focusing on strategy and supporting the project teams. These structures provide a formal process for decision-making that ensures input from a range of expertise including quality control and overall should reduce operational risk.

### *Target Product Profiles*

IPM has not yet established target product profiles (TPP) that would guide the product and clinical development process. A TPP would define the desired product characteristics, target efficacy, and population served by the eventual product to increase the probability of success and ensure access for the target population. The TPP would be periodically tested at key development mile-stones to assess whether changes are warranted, and by making hypotheses explicit and clearly communicated, a TPP provides a baseline to guide decisions and communicate priorities. Both industry and non-industry experts commented that a TPP would be of great help not only internally, but also to the field and would assist in communicating IPM's priorities and thinking, and help build consensus around microbicides in development.

### *Financial Projections*

When IPM was created, expectations were optimistic on the timeline to a safe and effective microbicide and therefore IPM was seen as a short-term organization which would facilitate the development of a successful product without creating a large staff and a long-term presence. Since then, IPM has continued to receive some pressure from both the field and from donors to set ambitious timelines and not create a permanent institution.

However, the complexities and challenges of IPM's mission have revealed themselves, and IPM has recognized the longer-term nature of its activities. For example, IPM's pharmaceutical partners have contributed significant intellectual property that is in early-stage development with the expectation that IPM will follow through with the product and clinical development. A longer-term outlook is also clearly reflected in IPM's recognition of the importance of its portfolio, improved efficacy microbicides, and microbicides containing multiple antiretrovirals.

However, IPM's financial projections also do not yet reflect the funding requirements for the portfolio beyond the forthcoming Phase III efficacy trial and the development associated with dapivirine. For example, the future cost of developing maraviroc in Phase III is not currently shown in IPM's budgets. As IPM enters its next five years, it will be important to establish more comprehensive financial projections to better communicate expectations both internally and to donors.

### *Relationships with Pharmaceutical Partners*

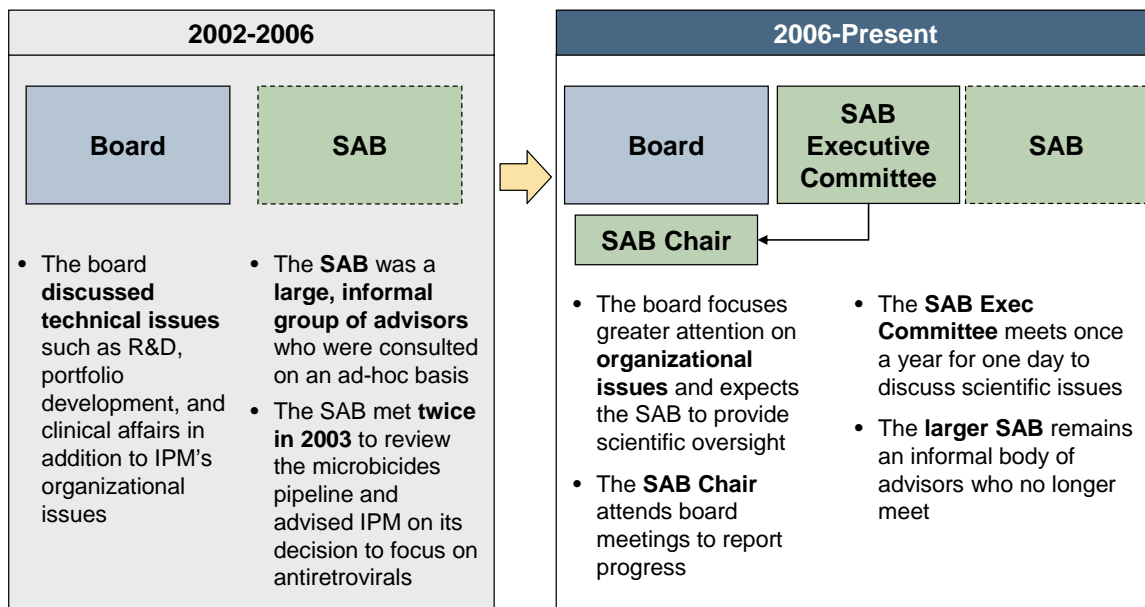
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IPM's pharmaceutical partners expressed high confidence in IPM and praise IPM for its professional approach, capabilities, and passion. However, partners also noted some concern over IPM's ability to manage multiple projects and felt that IPM's portfolio prioritization process was not clearly communicated (i.e., which products were being focused on and the rationale behind prioritization decisions). This has the potential to be sensitive for pharmaceutical partners who entered into agreements with IPM under the expectation that their products would be actively pursued. As IPM moves forward with a diverse portfolio that will need to be prioritized, it is important that it proactively and clearly communicates with pharmaceutical partners to maintain strong relationships and shared intellectual property.

### Scientific Advisory Board (SAB)

Originally, the SAB was intended to consist of small formal groups. The SAB quickly evolved into a larger, more informally convened group of advisors who met twice in 2003 to review the microbicides pipeline and advised IPM on its decision to focus on antiretrovirals. In 2006, the SAB further evolved with a smaller subset forming the SAB Executive Committee (SAB EC) which meets annually for one day to discuss IPM's progress to date and planned activities (Figure 4).

Figure 4: The Structure of the IPM Scientific Advisory Board



The SAB EC currently includes eleven experts with interests ranging from basic and applied laboratory research in HIV, clinical research, women's health and advocacy. The Chair of the SAB EC also advises the IPM board, sits in on one of the two board meetings each year, and provides a formal report at IPM's annual donors meeting. Since the 2006 restructuring, the SAB EC has had the primary responsibility to advise IPM on its scientific decision-making. The broader SAB currently does not meet and functions as an informal body of advisors.

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### *SAB Executive Committee*

SAB EC members felt IPM has generally been responsive to recommendations, for instance on the importance of pharmacokinetic drug disposition studies and the need to pilot the Directly Monitored Adherence (DMA) design intended for the Phase III. However, a majority of SAB EC members saw the current arrangement as not very robust or timely and did not feel engaged with IPM's scientific decision-making. The following concerns were highlighted:

- **Lack of Engagement:** The SAB EC felt that the limited meeting schedule meant that decisions presented were often already implemented, and that communication between meetings was *ad hoc* and limited. Further, meetings were not directed to specific questions and were perceived to be progress reports rather than scientific or strategic discussions.
- **Phase III Trial Strategy:** IPM has not yet finalized the Phase III trial design and has discussed the preliminary strategy with the SAB EC during both the 2006 and 2007 annual meetings. However, a number of SAB EC members felt that the risks associated with the Phase III had not been sufficiently discussed and desire greater engagement on the Phase III strategy. There were also questions concerning IPM's site development program and whether research centers would be prepared in time for the Phase III by Q4 2009/Q1 2010. The desire for greater engagement among SAB EC members despite opportunities for discussion during annual meetings points to the need for clearer expectations for the role of the SAB EC and the level of involvement in IPM's decision-making.
- **Greater Experience:** While the SAB EC represents a range of expertise, additional industry experience in product development and late-stage clinical methodology would be of significant benefit, especially as these will be greatest challenges for IPM going forward.

Our benchmarking analysis concluded that several PDPs have greater engagement than IPM with their equivalent scientific advisory bodies, meeting either more regularly or for longer periods of time. Medicines for Malaria Venture (MMV) spends eight days each year with its scientific body and the International AIDS Vaccine Initiative (IAVI) spends two days every six months. In addition IAVI has external expert project management and clinical trials sub-committees to provide additional expertise and guidance, as well as formal project teams and portfolio management committees internally to review decision-making.

### *Broader SAB*

Interviews with a limited set of the broader SAB suggest that these stakeholders are not in contact with IPM. Several of those interviewed have not received any formal communication from IPM since joining the broader SAB and are not part of any formal convening as part of the IPM advisory function. The broader SAB has not met formally since 2003 and members were not clear on IPM's expectations for their input going forward.

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### *Conclusions*

- 1) IPM has effectively engaged pharmaceutical companies to develop the first robust portfolio of antiretroviral-based vaginal microbicide candidates. These relationships are strong and will be essential for IPM's future success as products come to market.
- 2) IPM does not have formal portfolio management processes in place today. The structures and processes that exist are not sufficient to manage the growing portfolio to prioritize resource allocation against each project in a way that consistently drives toward the goal of minimizing risk.
- 3) Currently the Product Development Committee is responsible for both managing the portfolio and implementing projects. IPM does not have formal project teams or a portfolio management committee.
- 4) The SAB EC is not significantly engaged in IPM's scientific decision-making and a majority of members feel the current structure and process does not provide the maximum value to IPM. Peer PDPs are structured to have greater engagement with their scientific advisory bodies. It is recognized that greater engagement as it is being considered should be balanced against IPM's priority of moving quickly and should not delay operational decisions. The broader SAB is not engaged with IPM, has not had a formal convening, and many members have had little to no contact with IPM.

## B. Clinical Trials

### *Summary*

IPM has built clinical trial capacity as its portfolio has entered and progressed through the different stages of clinical development. Having assessed global clinical trial capacity, IPM made the decision to emphasize establishing its own clinical research centers. IPM has established ethical procedures to guide clinical development and to lay down a framework for engaging with country level partners. The challenges of building clinical research centers *de novo* have been substantial. Moving forward IPM has an opportunity to complement its team with increased experience, ensure consistently strong relationships with clinical principal investigators, and articulate comprehensive clinical development plans. IPM's timeline for the upcoming Phase III trial very likely needs to be revisited in light of this work ahead.

### *Recommendations*

- 1) **Review Phase III Timeline:** IPM's timelines are challenging and the pressure upon IPM's staff and clinical research centers to be ready for a Phase III trial are considerable. IPM recognizes that the current timeline for IPM's Phase III efficacy trial is aggressive, and the evaluation team believes that IPM should revisit the planned initiation date for a first Phase III to ensure sufficient preparation time both for IPM's clinical team as well as for clinical research centers. While there has been significant pressure from donors to pursue ambitious and optimistic goals, a more realistic timeline and preparation plan is critical to ensure the highest probability of success.
- 2) **Strengthen the Clinical Team:** IPM has begun training its clinical team in preparation for Phase III trials, but currently does not yet have the number of experienced staff that will be required. IPM should consider the following:
  - Engage additional experienced clinical trial managers and clinical research associates (CRAs)
  - Recruit a senior clinical research physician to better support the Chief Medical Officer (CMO). This person should have considerable experience in designing, implementing, and managing clinical trials
  - Increase quality control (QC) capacity, preferably based in South Africa
  - Implement mentoring between experienced, proven investigators and new research centers
  - Explore leveraging its partnerships with pharmaceutical companies, who may be willing to consider loaning experienced staff or offering greater technical assistance
- 3) **Establishing High-Quality New Clinical Research Centers:** IPM will need additional research centers for Phase III trials, and the decision to leverage

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existing clinical research centers vs. new research centers is complicated and depends on many factors including investigator experience, site environment, government pressures, and availability of infrastructure. IPM should ensure that criteria and decision-making for identifying clinical research centers (new and established) are objective, clearly communicated, and documented. IPM should continue to proactively explore where it might take advantage of existing capacity as it prepares for Phase III trials. The review of research center capacity that was recently conducted in the field should be leveraged.

- 4) **Strengthen Clinical Partnerships:** IPM has built a strong clinical program but interviews suggest that its relationships with clinical partners are mixed and could be strengthened. IPM should clearly communicate its long-term commitment, emphasizing recent bridge funding as well as clearly laying out its long-term strategy. IPM should also continue to involve clinical partners in joint workshops and international conferences, and lay out the need and rationale for stringent ICH GCP requirements. IPM constantly balances speed and the interests of clinical partners with available resources and quality standards, and should continue to work toward deeper partnerships that are critical to generating country-level support, communicating progress, and managing potential setbacks at the community level and to host-country government.
- 5) **Strengthen Clinical Trial Processes:** IPM should enhance clinical trial processes going forward, including:
  - Creating robust clinical development plans with critical path analysis and contingency planning
  - Standardizing clinical trial processes and procedures at research centers, based on a core set of SOPs and trial-specific guidelines
- 6) **Strengthen Country-Level Communications:** IPM recognizes that significant advocacy and communications efforts will be required to build a supportive environment at the country level for trial execution and eventual access to any successful product. A communications working group at the country level could facilitate early consultation with partners to ensure messages are developed jointly and activities are complementary.
  - We also recommend that donors assess the value of contributing to the advocacy funding window (proposed by the MDS Civil Society Working Group) to support organizations in trial countries. This could be a means to strengthen the policy and social environment needed for both successful trial conduct and microbicide access preparedness. However, details concerning this mechanism have not been made available yet and due diligence will need to be conducted on the eventual proposal.

### *Context*

Across the field there is a lack of consensus regarding how efficacy trials should be designed and implemented following recent microbicide trial failures. Some advocate the

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use of Phase IIb trials not primarily intended for licensure, such as the CAPRISA 004 trial. There is interest in the use of adaptive trial design to eliminate non-efficacious or unsafe products early on in comparative trials. Some investigators are uncertain that stopping rules can be easily implemented in a trial where the end-point, the number of new HIV-infections, is also the primary end-point that defines success or failure at the end of a trial. Finally, the more complicated the trial, the more difficult it will be to execute successfully, especially in an environment where many of the researchers and clinical research centers have limited experience conducting clinical trials to ICH GCP standards.

### *Findings*

IPM has made impressive progress over the last five years implementing a complex clinical development program in a region of the world where there is limited experience in the conduct of clinical trials to ICH GCP standards. IPM has engaged partners in existing research centers and has invested heavily in expanding clinical trial capacity in Africa by supporting the development of 11 new research centers. IPM has conducted or is planning to conduct more than 15 clinical, incidence, and behavioral studies before initiating a Phase III efficacy trial in Q4 2009/Q1 2010 (see Table 4). IPM is appropriately implementing ICH GCP standards across the clinical program.

The clinical program includes pharmacokinetic studies designed to evaluate the release and disposition of antiretroviral agents contained in gel and intravaginal ring products, and tolerability and acceptability studies for both gel and ring formulations. These studies also serve to inform formulation choices and the eventual design of the Phase III trial. The gel and ring formulations are designed to be used daily or monthly, respectively. Both are envisioned to be administered independent of coitus giving women greater freedom of use, and IPM has not decided which to bring forward into Phase III trials – both may ultimately be tested.

IPM has been building its organization and acquiring expertise in clinical development in parallel with implementing the clinical program. IPM is rapidly advancing the clinical program with significant pressure to meet timelines.

**Table 4: Clinical Research Centers and Clinical, Incidence & Behavioral Studies**

Clinical Trial Research Centers*			Clinical, Incidence & Behavioral Studies*					
Country	# of Research Centers	# New^	Type	# of Studies				
				Completed	Data Analysis	Ongoing	Total	Planned
<b>South Africa</b>	<b>9</b>	<b>7</b>	<b>Clinical</b>	<b>6</b>	<b>1</b>	<b>1</b>	<b>8</b>	<b>10</b>
<b>Kenya</b>	<b>3</b>	<b>1</b>	<b>Incidence</b>	<b>2</b>	<b>2</b>	<b>3</b>	<b>7</b>	<b>2</b>
<b>Rwanda</b>	<b>1</b>	<b>1</b>	<b>Behavioral</b>	<b>1</b>	<b>-</b>	<b>-</b>	<b>1</b>	<b>1</b>
<b>Malawi</b>	<b>1</b>	<b>1</b>						
<b>Tanzania</b>	<b>1</b>	<b>1</b>						
<b>Belgium</b>	<b>3</b>	<b>-</b>						
<b>Total</b>	<b>18**</b>	<b>11</b>	<b>Total</b>	<b>9</b>	<b>3</b>	<b>4</b>	<b>16</b>	<b>13</b>

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\*Data from IPM STAR database, updated 5/23/08; \*\* 2 research centers (Malawi, Suba – Kenya) do not have active studies but are planning for studies this year; IPM is also in discussions with additional potential clinical research centers ^ New research centers are sites that did not have an existing research team and/or facility in existence before IPM. 3 new research centers are new expansions with new teams but within organizations that do have clinical experience (Yeoville-Johannesburg under RHRU, Blantyre under University of Malawi, and Suba under KEMRI, Kenya)

### **Clinical Trial Network**

IPM has largely emphasized establishing its own network of clinical research centers rather than rely on existing research centers in Africa. This was an appropriate decision because at the time, most of existing trial capacity was fully engaged with other microbicide or vaccine development programs. IPM has also listened to the stakeholders where it is conducting its clinical trials work. For example, IPM has been encouraged to establish new clinical research centers by some government officials who desire new infrastructure and research capacity to be built rather than risk saturating certain communities with too many studies.

Building new research centers poses challenges for both IPM and its partners. New site development is complicated and requires substantial investment in infrastructure, training, monitoring, and actual trial experience. These challenges must be measured against the approach of leveraging existing trial capacity and the potential benefits of lower risk and greater cost-effectiveness.

The decision to leverage existing capacity or build new research centers is not straightforward. IPM has formed a number of relationships with existing research centers and experienced significant challenges. First, the site environment may be inappropriate with either an HIV incidence rate that is too low or a previous target population that does not match. Second, despite having clinical experience, the research center may not be experienced in relevant operational processes and the investigators may not be able to achieve ICH GCP standards. Finally, an existing research center may not have retained the original infrastructure on completion of the previous research or may demand new infrastructure for the new trial.

IPM has faced many of these specific issues and has found that the challenges of a new and inexperienced research center may be more attractive if the team is enthusiastic, willing to learn, and able to achieve quality standards. New research centers, once developed, also provide IPM a stronger guarantee of long-term capacity. Therefore, the decision on research center selection is not simple and requires flexibility and careful consideration. IPM has recognized many of these challenges and must continue to make its decision-making processes clear.

### **Site Development**



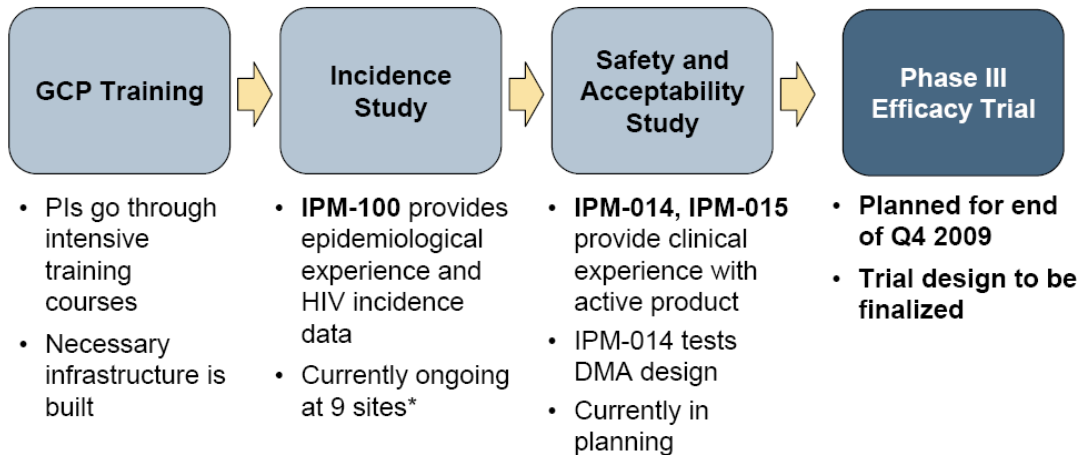
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IPM's site development plan for research centers is to progress them through increasingly complicated trials in preparation for a Phase III trial (Figure 5). It is difficult to estimate or benchmark how long it takes to prepare a new research center for Phase III clinical research. A number of interviewees commented that it would not be unusual to take three to five years of training in clinical research, although site development could take more or in special circumstances, less time. In addition it was suggested that very experienced clinical researchers could support a new research center and help in training. Research center preparation and training requires a strong collaborative commitment by both the research center and the sponsor, including regular monitoring visits and prolonged on-site training. IPM has made such a commitment and examples include regular training workshops on ICH GCP and CRA engagement. IPM has also recently taken steps to evaluate research center opportunities in a more systematic manner.

As part of its site development effort, IPM has developed a tool with Tibotec which maps the experience and facilities of a research center against ICH GCP needs. This approach further confirms IPM's commitment to implement and standardize ICH GCP across all of its research centers.

IPM is also developing core standard operating procedures (SOPs). Currently there is a lack of uniformity as individual research centers are developing their own SOPs and sharing across research centers is limited. Partly this is due to a feeling among some research centers that their SOPs are intellectual property and should not be shared. IPM has recognized the danger of SOPs that are not standardized, and IPM's Quality Control (QC) group is actively identifying gaps and is promoting the writing of core SOPs.

**Figure 5: IPM Research Center Preparation Strategy**



- **IPM-100:** Cross-sectional study of HIV incidence with 800 participants; of these, 300 volunteers found to be HIV-negative are enrolled in a cohort study for 12 months
- **IPM-014:** Double-blind, randomized, placebo-controlled study of the safety & acceptability of gel-003 using daily monitored adherence over 6 weeks with 30-50 HIV- women per research center

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- **IPM-015:** Double-blind, randomized, placebo-controlled study to evaluate safety of a dapivirine vaginal matrix ring over 12 weeks with 70 HIV- women per research center

Although IPM’s clinical development pathway begins with ICH GCP training, GCP training continues to be reinforced by attendance at workshops and monitoring visits throughout the life of the program. Research centers gain initial experience in HIV incidence studies which are less challenging than safety studies (see Table 5). Research centers are constantly evaluated to determine their eventual ability to participate in the Phase III efficacy trial.

**Table 5: Summary of Late Stage Study Details**

Study Detail	IPM-014 (gel)	IPM-015 (ring)	Phase III Trial*
<b># of Women / Site</b>	30-50	70	150-350
<b># of Sites</b>	8	4	20-30
<b>Length of Follow-up</b>	6 weeks	12 weeks	52 weeks
<b># of Arms</b>	2	2	6 / 2*
<b>Double-Blind, Placebo Controlled, Randomized</b>	✓	✓	✓
<b>Directly Monitored Adherence</b>	✓		✓
<b>Regular HIV Testing</b>			✓
<b>Resistance Monitoring</b>			✓
<b>Statistically Powered to Show Efficacy</b>			✓

\*IPM’s preliminary Phase III design calls for two-stages. Stage one will include 6 arms (3 active, 3 placebo) and the single-best product with two arms (1 active, 1 placebo) will be selected and advanced to the second stage.

Although the Phase III efficacy trial will be its largest and potentially most complex trial to date, IPM believes the trial may actually be less challenging for the research centers compared to the ongoing safety studies. However, some stakeholders have questioned whether the incidence and safety trials are adequate preparation before a research center engages in a Phase III trial. Furthermore, if IPM requires 20-30 research centers for Phase III, it is unclear what level of experience all of the research centers will have had at the time of initiating Phase III, as IPM only has approximately half the required number of research centers today.

Finally, it is important to note that IPM has pursued a Phase III trial design that responds to the lessons learned from past Phase III trials for microbicides. While the design is still being finalized and represents a considerable increase in complexity, IPM has correctly sought to address many of the challenges that other microbicide organizations have previously faced (see Table 6)

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**Table 6: IPM Lessons Learned from Previous Microbicide Trials**

<b>Lessons Learned</b>	<b>What IPM hopes to do differently</b>
<b>Prioritization</b>	<ul style="list-style-type: none"> <li>• Utilize adaptive design, multiple arms</li> <li>• Advance best product only</li> </ul>
<b>Safety</b>	<ul style="list-style-type: none"> <li>• Conduct early analysis for harm and ability to halt trial</li> <li>• Conduct multiple data reviews during the trial</li> </ul>
<b>Adherence</b>	<ul style="list-style-type: none"> <li>• Utilize longer acting formulations</li> <li>• Conduct product acceptability studies</li> <li>• Maintain daily contact with participants</li> <li>• Develop smart applicator</li> </ul>
<b>Incidence</b>	<ul style="list-style-type: none"> <li>• Conduct epidemiology studies in advance</li> </ul>
<b>Futility</b>	<ul style="list-style-type: none"> <li>• Emphasize early stop if efficacy is unlikely to be shown</li> </ul>
<b>Pregnancy</b>	<ul style="list-style-type: none"> <li>• Establish rigorous contraceptive requirements</li> <li>• Provide family planning, including female condoms</li> </ul>
<b>Trial Locations</b>	<ul style="list-style-type: none"> <li>• Diversify the number of countries &amp; sites</li> <li>• Address “co-enrollment” concerns</li> </ul>

### **Relationship with Clinical Partners**

Interviews with clinical partners showed that they view IPM in mixed terms. Clinical partners recognize that IPM has made a considerable investment, including building new clinical infrastructure, training staff in ICH GCP standards, and creating opportunities for important research. IPM has also convened its investigators to help encourage cross-site learning including ICH GCP workshops and beginning to facilitate standardization of SOPs. Finally, IPM has sent a limited number of investigators to international meetings in recognition of their commitment to the microbicide program. IPM is planning to send more clinical research center representatives to Microbicides 2010 and other relevant conferences when investigators will have more data to present.

However, several of IPM’s clinical partners have also expressed feeling that IPM is contracting with them on a transactional basis rather than showing a deeper, long-term commitment to partnership. New clinical partners felt this most keenly, noting that as IPM is testing out the relationship, it feels like investigators are taking on more of the risk, liability, and responsibility for setting up a research center. The burden was especially significant with regards to creating budgets and other operational skills that investigators often struggle with. Clinical partners also expressed concern that IPM usually did not communicate clearly about plans for future studies, leaving investigators unsure of whether they would be able to keep their research centers running. Clinical

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partners also desired greater opportunities to publish and saw this as a strong way to build the relationship.

IPM has moved to address some of these concerns by instituting bridge funding for clinical partners that would provide full operating support between trials and help to ensure that research centers are able to maintain local employment contracts with staff. This plan should be clearly communicated to investigators.

Some more experienced investigators have also expressed concern regarding IPM's extensive monitoring and research center requirements, as well as a desire for greater flexibility in training requirements based on their existing clinical skills and research experience. IPM needs to uphold stringent ICH GCP requirements to comply with regulatory standards linked to eventual product approval, and clearly communicating the rationale for requirements will continue to be important. There is general eagerness for more frequent communication and a better understanding of IPM's long term strategy, and this could be easily achieved by IPM.

Clinical research in HIV prevention is associated with significant political sensitivity which has been amplified in the last year by the failure of several prevention approaches. IPM will need to rely heavily on local clinical partners for generating country-level support, communicating progress, and managing potential setbacks at the community level and to host-country governments. The current relationships between IPM and its clinical partners are mixed, and it will be important as IPM moves forward to strengthen these relationships. In this area, IPM faces the challenge common to all organizations running clinical trials: balancing speed and the interests of clinical partners with available resources and quality standards.

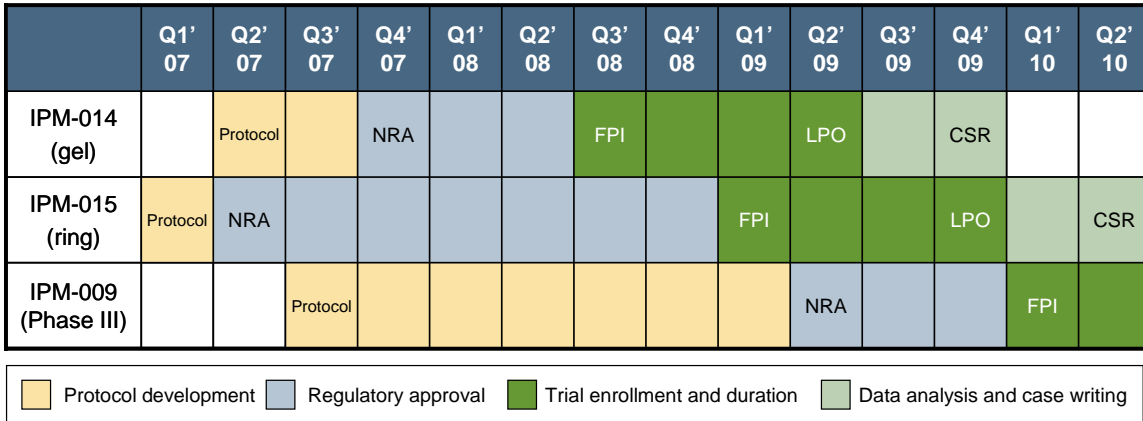
### **IPM Clinical Timelines**

IPM's timelines are challenging and the pressure upon IPM's staff and clinical research centers to be ready for a Phase III trial are considerable. Not all research centers will be initiated at the same time and there will be the opportunity to bring research centers on line as they are deemed ready to participate in a Phase III trial. IPM's current timelines are illustrated in Figure 6 with site initiation beginning at the end of 2009.

IPM's first Phase III efficacy trial is scheduled to start in Q4 2009/Q1 2010. For the moment the Phase III trial design has not yet been finalized. Early concerns have been voiced regarding IPM's strategy and ability to conduct this scale of research within the proposed timeline. IPM's anticipated adaptive trial design is regarded as the most complex trial yet attempted in the field. Several experts who attended consultations on trial design with IPM, expressed concerns regarding the use of an adaptive trial design and the very ambitious timelines.

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**Figure 6: Dapivirine Clinical Program Timeline**



IPM recognizes that the timelines for Phase III are aggressive relative to the completion of the gel (IPM 014) and ring (IPM 015) safety trials. IPM is planning to use an interim analysis from the IPM 015 study to gain time in preparing for the launch of the Phase III trial. In consideration of the need to submit trial results to local ethics and regulatory authorities, the timelines for beginning Phase III are almost certainly overly optimistic. The logistics and costs are further complicated by the fact that research centers that have already completed earlier studies cannot be left unemployed for extended periods of time. All of the above further contribute to the considerable pressure that IPM is now under to begin Phase III efficacy trials.

### IPM Clinical Human Resources

IPM’s clinical program is complex and clinical research associates (CRAs) are required to work closely with investigators who are often new to clinical research in order to ensure that necessary infrastructure and ICH GCP standards are in place. IPM initially used clinical research organizations (CROs) in South Africa but had mixed success with quality and felt that the expertise of a CRO did not necessarily extend to the type of work IPM required. IPM has had similarly mixed results recruiting experienced CRAs and has since emphasized training its own in-house clinical research team.

IPM has recruited a number of CRAs with limited experience and is planning on training them in-house as they monitor and prepare the research centers for a Phase III trial. The current plan is for new research centers to be exposed to progressively more complicated trials both to facilitate greater experience for clinical researchers and for CRAs. However, this strategy presents significant challenges going forward. Excluding clinical trial assistants, IPM currently has only eight CRAs in South Africa with between 10 and 20 months of in-house experience. IPM anticipates needing as many as 20 trained CRAs to monitor 20-30 research centers for the Phase III trial. This represents a significant shortfall in experienced clinical trial monitoring capacity that IPM intends to address. While recognizing that recruiting in Africa is difficult, bringing in new CRAs with greater industry experience could significantly improve IPM’s clinical operations both

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through quicker uptake of the necessary skills and the ability to mentor and help train other CRAs.

IPM has recognized a need for greater clinical experience at higher levels, including additional experienced clinical project managers in Africa and greater support for the Chief Medical Officer (CMO), who has taken on all tasks related to clinical trials, including site development, clinical projects, safety, and community engagement. IPM is considering the appointment of a Deputy Chief Medical Officer who would reduce the current burden of work on the CMO. This would be a new position and a senior clinical research physician with considerable experience in designing, implementing, and managing clinical trials should be of great help. IPM is also recruiting for a Chief Scientific Officer whose level of expertise in late stage pharmaceutical development should be very complementary to IPM's leadership. As IPM seeks to add greater clinical experience among both higher level management and at the CRA level, it could explore leveraging its partnerships with pharmaceutical companies, who may be willing to consider loan experienced staff or offering greater technical assistance.

The current quality control (QC) group is based in the US and frequently travels to research centers in Africa. IPM is currently recruiting for additional QC staff to add to its South Africa-based team and overall the QC group recognizes the need to prioritize the recruitment of additional experience going forward. IPM is also recruiting for a social-scientist to support its research in product acceptability and other areas across different contexts in Africa.

### **Clinical Development Plans**

IPM does not yet use clinical development plans which cover the overall clinical strategy leading from the very first HIV incidence studies, pharmacokinetic, tolerability and acceptability, safety and eventually Phase III efficacy trials through to regulatory approval. Clinical development plans flow from the TPP (see discussion above) and should explain the overall logic of the program, how the different pieces of the program relate and support the regulatory strategy, and include critical path analysis and contingency planning. At each major milestone, agreed criteria will determine whether the characteristics of the product still adequately support the TPP and whether the program should progress or be discontinued. IPM's organization is diverse and spans the USA, Europe and South Africa and the TPP and clinical development plan should unite the different functions in the project team, ensuring a common understanding of the project and clear communication of progress to senior management.

### **Country Level Advocacy**

Effective advocacy and communication are recognized by IPM and others in the field as essential to building a supportive environment for HIV prevention efforts leading to timely product access, as set out in IPM's Country and Trial Support Strategy. The strategy highlights the need to collaborate with other advocacy groups (e.g., AMAG,

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GCM). IPM has also contributed to the MMCI concept paper, as an Executive Committee member, which includes a recommendation for country level communications activities.

IPM funds some advocacy activities at regional levels, with an intended focus on trial countries. At a country level, there is a need for continued advocacy for microbicides in general, tied to HIV prevention and gender equality. Peers such as GCM recognize that it is early for dialogue and seek joint strategy development with national advocates and trial implementers. IPM also recognizes local advocacy as important. However, there is a conflict of interest risk if IPM provides direct funding to these groups as they must remain independent.

The MDS Civil Society Working Group (2008) has proposed the creation of a grant-making window dedicated to issuing small grants to the nongovernmental and community-based organizations that advocate for HIV prevention research in Africa. The early proposal is that this be administered by an independent group, but advised by the HIV prevention research community. While the details are not yet clear, funding this type of facility could contribute to a more positive local environment for clinical trials.

### **Standards of Care and Ethical Practice**

IPM has established robust guidelines and processes to ensure that its clinical trials are conducted to high ethical standards. These are in line with ICH GCP standards and WHO UNAIDS recommended good ethical practice for HIV prevention trials and IPM continues to update its protocols based on best practices in the field.

For instance, study participants all receive ongoing risk reduction counseling, male and female condoms or other contraceptives, treatment for those who seroconvert during the course of the trial, and treatment and compensation in the unlikely event that physical harm results from trial participation. IPM has also noted in updated standards of care that all participants must be on a stable form of contraception at the time of enrollment and for the duration of their participation in the clinical trial. Finally, IPM has committed to pay for antiretroviral treatment for study participants during and after the clinical trial until national HIV programs are able to provide this care.

One additional concern that was raised in interviews with research center teams is that as IPM sets up clinical research centers and begins screening women for HIV, the number of women seeking local health services for treatment of STIs, prevention services, etc. will drastically increase. This may strain the capacity of the local healthcare system and result in women not being able to access the services they need. While IPM has already set high ethical standards and is not purposed to invest more broadly in health infrastructure or services beyond clinical trials, consideration for what happens to women after they are tested will be important to IPM's relationship with the community.

### ***Conclusions***

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- 1) The assumptions supporting the Phase III trial that is currently planned for Q4 2009/Q1 2010 are aggressive and optimistic. The complexity of the current trial design would be difficult for the most experienced clinical researchers, and given the mix of experience internally and across the range of IPM's partners, IPM should consider revising the timeline to ensure adequate preparedness. This would greatly reduce the operational risk for IPM and should be communicated clearly to donors and other stakeholders.
- 2) IPM has recruited a number of CRAs and is planning on training them in-house, but has not yet built a sufficiently large or experienced clinical team at this point to run a Phase III trial.
- 3) IPM may be able to reduce the risk in its clinical program by leveraging more experienced research centers to supplement the new research centers, not all of which are likely to be ready for the launch of the trial. However, an established research center should not automatically be given precedence over a newer research center. An established research center should demonstrate ability to participate in ICH GCP driven clinical research, an appropriate local HIV incidence rate, and necessary infrastructure. This is a difficult decision-making process which IPM has managed well and one which IPM should continue to proceed with carefully.
- 4) Given the sensitivities in the field and the anticipated challenges associated with IPM's Phase III trial, it is critical that IPM has strong local advocates and that its clinical partners will stand by IPM's work and communicate constructively with national and local stakeholders. Strong relationships with its clinical partners are therefore critical to IPM's success.
- 5) IPM does not yet use formal clinical development plans to guide its clinical activities. Research centers are also currently developing their own SOPs and IPM also has not yet implemented standardized clinical trial processes and procedures at research centers that would establish a core set of SOPs and trial-specific guidelines.
- 6) IPM's plans recognize the critical importance of creating an enabling political and social environment for the trials and for longer term access. Community engagement plans are proceeding well, but there has been limited systematic engagement of relevant health authorities, except at the highest (often individual) level.
- 7) IPM's clinical trials are conducted to high ethical standards and IPM has worked to refine those to keep up with developments and best practices in the field. However, limitations in local healthcare capacity need to be accounted for as IPM refines its policies and practices.



## C. Access

### *Summary*

Access represents one pillar of the original IPM mandate, and IPM has woven access issues into the fabric of its work around portfolio and product development, clinical trials and advocacy. IPM has also contributed effectively to the broader field by establishing useful frameworks and convening stakeholders to build consensus on how to ensure access to an eventual microbicide. Moving forward IPM will be expected to provide leadership as the field progresses towards product scale-up and introduction.

### *Recommendations*

- 1) **Define Explicit Access Criteria:** As IPM formalizes its portfolio processes and creates a target product profile, it should explicitly define the access criteria that feed into product prioritization and development decisions. This will both ensure that internal decision-making adheres to access issues going forward and can be used to clearly communicate with the field on important access criteria for products in the pipeline.
- 2) **Begin Planning for Manufacture, Scale-up, and Distribution:** While it is premature to complete detailed manufacture and scale-up planning before a product has signs of success, it will take a tremendous effort to determine how a new product can be rapidly distributed to women who need it. Within the next 18 months, IPM should begin planning explicit activities, identifying partners, and projecting costs that will be necessary.
- 3) **Clearly Communicate Plans for Access Program:** IPM leadership on access issues has been effective and as IPM evolves its approach, it should clearly communicate its continued commitment to access issues as well as set expectations for how IPM is going to engage the field on access going forward.

### *Context*

The approach to access in the microbicide field was broadly defined by the Access Working Group (of the Rockefeller Foundation's Microbicides Initiative) in 2000. Its report, *Preparing for Microbicide Access and Use*, highlighted that "systematic and sustained attention to access is important because new health technologies rarely become available in developing countries until more than a decade after their approval." Access has continued to be a high priority for donors who want to ensure that if a product is successfully approved, it will have the appropriate product characteristics to serve the target population and can be rapidly manufactured and distributed in developing countries to the people who need it.

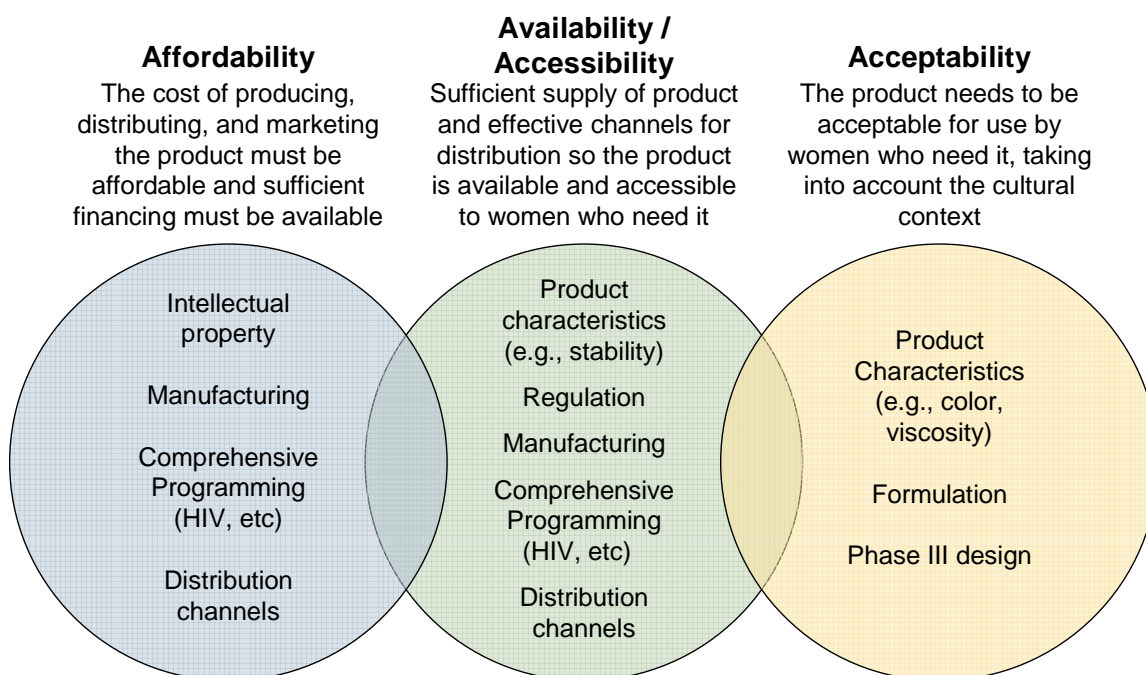
*Findings*

**Access Framework**

The original vision for access in the first IPM Business Plan 2002 is reflective of the Microbicide Initiative’s Access Working Group and is carried through in IPM’s workplans. This early vision emphasized the twin pillars of R&D and access, but was perceived by some in the field to be premature given the length of time to product approval and risking an artificial split between R&D efforts and access efforts. The strategy and workplan has since evolved to define and address access concerns through an integrated and cross-cutting framework which informs all of IPM’s activities.

In developing its access framework, IPM has drawn on work by the Access Working Group and other agencies addressing commodity access issues, such as WHO and John Snow, Inc. The framework aims “to guide, coordinate and sequence activities contributing to future access” and “emphasizes that supporting developing country access will require contributions from a wide range of stakeholders including researchers, product developers, manufacturers, distributors, policy makers, NGOs, donors and communities”<sup>11</sup>. IPM’s access framework addresses the key dimensions illustrated below (see Figure 7):

**Figure 7: IPM Access Framework**



<sup>11</sup> A framework for future microbicide access in developing countries, Walker S et al, WEPE0896, Toronto AIDS conference 2006

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IPM's access efforts have been evaluated both on its own and as a cross-cutting theme which is relevant for IPM's activities within Portfolio and Product Development, Clinical Trials, and Advocacy.

### **Portfolio and Product Development**

#### *Intellectual Property*

IPM has appropriately applied access concerns to its portfolio development efforts. Peers in the field widely recognize IPM as having skillfully negotiated the intellectual property rights for many antiretrovirals and ensured that to the extent possible, eventual pricing remains affordable. These innovative agreements aim to ensure low cost manufacturing and distribution in public and private sectors in developing countries, including some large middle income countries with high need. For reasons of confidentiality, this review cannot provide greater detail regarding the agreements reached with pharmaceutical partners.

#### *Product Selection*

IPM has applied access criteria to determine product selection and development, which include the mechanism of action, cost of active pharmaceutical ingredient, feasibility and cost of manufacturing, stability, user preferences (color, viscosity), safety for users and partners, etc. IPM has demonstrated its commitment to access principles and did not take dapivirine forward until it proved stable at 40°C, even though this resulted in a delay in the development process. However, while it is clear that these criteria are being taken into account, they have not yet been made explicit or publicly articulated.

#### *Formulation Development*

IPM is leading innovative formulation development and acceptability research through its own research and trial programs and in partnership with other organizations, including research into vaginal tablets, gels, films, and significant work on developing an intravaginal ring. There is broad consensus that this research would not have been undertaken without IPM's strategic focus and financing, and it is widely viewed as progressing the field in thinking about broader options for product acceptability.

#### *Regulatory Pathways and Capacity Building*

IPM has also succeeded in gaining regulatory approvals with the US FDA that have the potential to benefit the field, such as the ring IND. IPM is viewed by some as "smoothing the path" for other microbicide developers in this respect.

IPM has further played an important collaborative role in investing in local regulatory capacity building in the developing world. Regulatory capacity is a critical issue because IPM and other product developers will depend on local regulators to approve products and support product roll-out. If these structures are not in place and functioning efficiently, it could create a significant bottleneck to ensuring access to an eventual microbicide.

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IPM contributes to an informal PDP group (including peers such as MMV, MVI, DNDi and IAVI) which share experiences in issues such as regulatory approval processes, market development, and demand forecasting. IPM further collaborates with WHO and CONRAD and others to convene regulators to hold discussions about appropriate standards for differing risk-benefit profiles between developed and developing countries and move toward establishing a framework for approval. Greater efforts have been made with the FDA and the South African MCC. IPM is now developing an approach to working with the EMEA on an Article 58 licensure.

There is a recognized sensitivity and potential conflict of interest in this area as IPM is itself a product developer and attempts to invest in local regulatory bodies could be seen as co-opting their independence. This is a potential area for donor support and engagement. Since IPM is constrained by its position as a product developer, donors could invest in regulatory capacity building to support IPM's greater mission.

### **Clinical Trials**

#### *Country Preparedness*

IPM recognizes the need for a supportive policy environment at the country level for both its trials and longer-term access and has further committed to ensuring that trial participants will have access to an eventual microbicide. The new 2008 Country and Trial Support Strategy addresses stakeholder advocacy at multiple levels and IPM's community engagement plan further lays out a strong plan for building local support. Based on interviews with research centers, there has so far been limited outreach to national and regional authorities, not withstanding high level contacts with senior officials and IPM staff. While early planning is important, it is also recognized that IPM is still far from product approval and that there is a risk to raising expectations too early among key stakeholders. IPM is also aware that its capacity to implement this strategy at country level will be stretched.

#### *Socio-behavioral Research*

Socio-behavioral research is critical for IPM's success in ensuring eventual access and essential for generating knowledge on product acceptability among women who are the target users of a microbicide. IPM is pursuing greater socio-behavioral research but currently does not have significant socio-behavioral expertise in-house. This is a recognized gap and IPM is currently seeking a senior research officer to complement its current efforts.

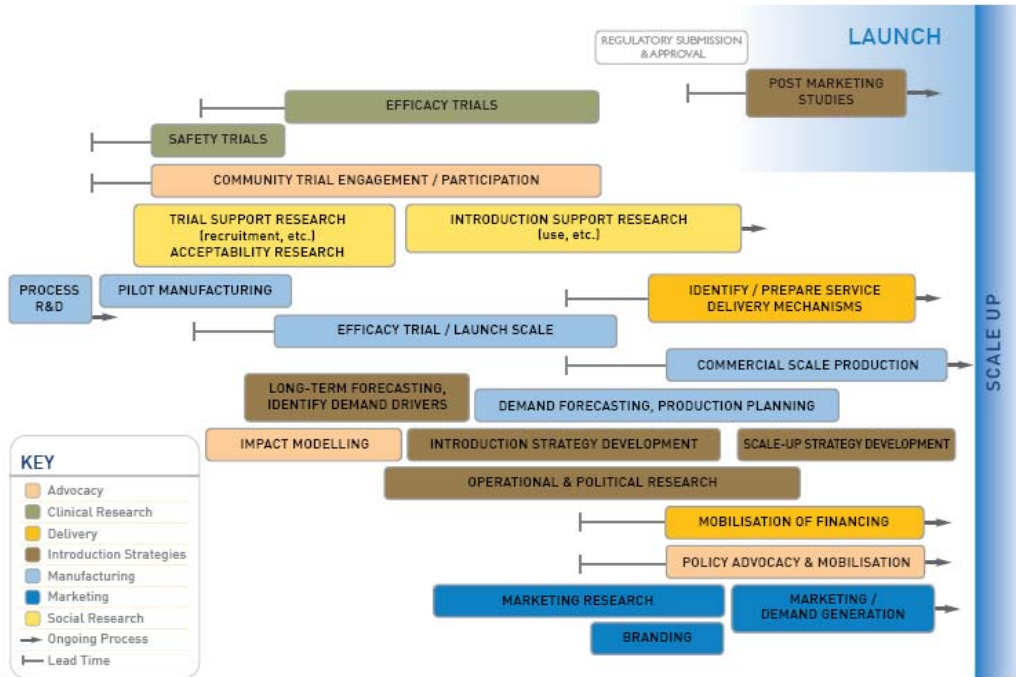
### **Scale-up, Manufacturing, and Distribution**

#### *Early Planning*

Once a product is approved, IPM recognizes that the challenge of scale-up, manufacturing, and distribution is substantial. The IPM 2007-2010 workplan places emphasis on filling in key gaps in planning for success and IPM has begun engaging relevant partners to discuss country preparedness and a product introduction strategy, as well as developing a preliminary access timeline for scale-up activities (Figure 8).

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**Figure 8: IPM Access Timeline for Scale-up**



IPM is now working with the London School of Tropical Medicine and Hygiene to complete a modeling of the uptake of a microbicide in three countries, which will help build a more detailed projection of the time and cost associated with introducing a new product. This modeling exercise is the second effort by IPM to model the uptake of a microbicide and has been well received in consultations with the field. IPM has also recently conducted a worldwide manufacturing survey to gather information on global options for larger-scale production of drug substance and formulations for a potential microbicide. The survey concluded that although viable manufacturing resources are present in the developing world, they are relatively small in scale and would need to be expanded.

While IPM has conducted some preliminary thinking (see Figure 8 above), it does not yet have a more detailed plan developed which defines the specific preparatory activities needed over the next five years, which partners might be approached, and what the potential cost is estimated at. An explicit timeline and strategy has not been documented, and current financial projections for access following a Phase III are placeholders rather than built on strong assumptions.

It is noted that IPM is currently far from an approved product and that it is difficult to plan for access without a more specific idea of eventual product characteristics. However, it will be important for IPM to move forward on defining its likely activities, partners, and costs associated with scaling up manufacturing and distribution.

## *Convening the Field*

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IPM has collaborated with other players in HIV and reproductive and sexual health fields to convene forums on access, and to contribute to the field's efforts to ensure that barriers and opportunities to access are comprehensively analyzed and developed in a timely fashion<sup>12</sup>. IPM has further funded several country preparedness studies, including in trial countries and has financed and co-hosted stakeholder meetings including the Microbicides Access Forum (MAF) with the WHO and USAID in Kenya in July 2007. The MAF brought together more than 45 key stakeholders (e.g., government representatives, advocates and clinicians) to discuss approaches to microbicide introduction, delivery, and scale-up. Building on lessons learned in the introduction of other reproductive health technologies, such as female condoms and emergency contraception, the forum emphasized factors such early investment in country preparedness, local stakeholder relationships, integration as part of comprehensive programming, and collaborations with WHO and other international bodies. IPM is convening a second MAF in Mexico City in August 2008, cosponsored by the WHO, USAID, and the Population Council.

IPM recognizes the importance of continuing to learn from experience and to work with experts in product introduction, including female condoms and other HIV and reproductive health technologies.

### **Leadership and Coordination**

Strong leadership has spearheaded efforts at IPM to develop the access program as a cross-cutting strategy and has delivered relevant and well-regarded outputs across this framework in line with its workplans. The Executive Director of Global Public Policy left in late 2007 and currently IPM is evolving how access should be structured internally and how it should adapt its access approach. The preliminary vision is that what has been an “access program” at IPM will eventually mature into a full “access department.” While leadership in this area is not being recruited at present, IPM continues to reflect upon what is best needed to suit its longer-term needs. In the meantime, IPM believes that the current team can appropriately maintain its access initiative. Furthermore, interviews with the IPM board revealed that access continues to be considered at a governance level.

### **Conclusions**

- 1) IPM's strategy to deliver an affordable, accessible, and acceptable product has evolved appropriately given IPM's emerging role and current stage of product development. IPM has addressed access issues across its relevant activities and has collaborated effectively with the field to think about access approaches.
- 2) While IPM has effectively addressed access issues in its product development, it has not made these criteria explicit or documented.

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<sup>12</sup> See for example, *Planning for Microbicide Access in Developing Countries: Lessons from the Introduction of Contraceptive Technologies*, Brown G et al, IPM 2007

## IPM Evaluation Report

- 3) Scale-up, manufacturing, and distribution plans are critical to ensuring timely access to an eventual product. While IPM has done some preliminary thinking concerning access issues, more comprehensive plans and documentation around expected activities, partners, and costs have not yet been developed.
- 4) IPM leadership on access issues has been effective. The Executive Director of Global Public Policy left in late-2007 and currently IPM is evolving how access should be structured internally and how it should adapt its access approach. The preliminary vision is that what has been an “access program” at IPM will eventually mature into a full “access department.”

## D. Advocacy

### *Summary*

IPM has contributed significantly to the growth of the global position of the microbicide field. IPM is widely recognized as having strong access to global leaders and building the reputation of the field as a whole. Going forward IPM will continue to need to balance its role as a global advocate with its need to ensure the success of its own portfolio.

### *Recommendations*

- 1) **Continue High-level Global Advocacy:** IPM should continue to champion microbicides at the global level, speaking broadly about the need for increased attention and funding from international donors and policy makers. This appears to be a comparative advantage compared with other advocacy groups. Keeping microbicides on the global agenda is going to be critically important given the long road associated with bringing a new product through licensure and distribution as well as IPM's upcoming Phase III trials.
- 2) **More Fully Engage Advocacy Partners:** When IPM is advocating for microbicides broadly it should proactively engage with its advocacy peers to ensure consistency in messaging and a deeper feeling of partnership. This is an important area for strong collaboration in order to ensure strong support for the field overall.
- 3) **Balance Advocacy for the Field with Advocacy for IPM:** IPM should continue to balance advocacy for the field with advocacy for its own work. IPM should also continue to distinguish between its messaging on behalf of the field and messaging associated with its own portfolio.

### *Context*

The review of IPM's advocacy activities will be limited to advocacy focused at the global level, and IPM's efforts to increase the global profile of microbicides, and in terms of resource mobilization and bringing new donors to support microbicide research. IPM's advocacy work at the country level as it relates to its clinical research program is discussed in the Clinical Trials section above.

The creation of IPM was the culmination of years of advocacy for a stronger global microbicide effort. IPM has added its voice to the voices of other advocacy groups as it has pursued its mission. When IPM was created, two dedicated advocacy organizations existed to serve both the global and in-country requirements for microbicides advocacy. The Global Campaign for Microbicides and the Alliance for Microbicide Development (among others) are partners with IPM and represent the organizations with a dedicated mandate to advocate for microbicides support. IPM's advocacy mandate has remained



relatively consistent and focused at the global level. The 2002 business plan defined the mandate as “helping to raise the visibility of microbicides on the global stage<sup>13</sup>” and the 2007-2010 workplan likewise states as the sixth goal for IPM, “to increase the global political commitment to microbicides”.<sup>14</sup>

### *Findings*

#### **Raising the Global Profile of Microbicides**

##### *Raising the Global Profile*

When asked about IPM’s key successes to date, stakeholders consistently point to IPM’s work in raising the global profile of microbicides. In 2005, “increased and sustained political commitment to microbicides in developed and developing countries” was added to IPM’s workplan goals, with objectives that suggested advocacy that would have field-wide benefits. The 2007-2010 workplan continues to reference IPM’s work in global advocacy as a key area of focus.

IPM has partnered with other HIV prevention organizations (e.g., IAVI) for advocacy at the global level in international fora such as the G8. IPM has also partnered with other microbicides advocates (e.g., the Global Campaign, and the Alliance for Microbicide Development, AVAC) to communicate to a broader audience of policymakers and donors about the importance of microbicides research. Finally, IPM’s strategy of partnering with NGOs in Europe was introduced both to achieve the organization’s goal of diversifying the funding base and as a mechanism to educate and earn the support of key stakeholders in both funding and policy positions in European donor countries.

Peers and advocacy partners widely cite IPM’s access to global leaders as unique to IPM in the microbicide field and as an important influence on increasing the profile of microbicides among key global stakeholders. IPM has gained access to national and international political leadership and institutions (e.g., UNGASS, G8, European Union Presidencies, U.S. Congress, European Parliamentarians) to help build support for microbicide research and has also reached out to influential figures to spread its message (e.g., Bill and Melinda Gates, Bill and Hillary Clinton, Stephen Lewis, Graca Michel, Barack Obama, etc.). With these audiences, IPM has appropriately sought to build momentum for microbicide research and to set expectations that a new product is still many years away.

IPM has also adapted its advocacy message well to the changing environment. Peers note that IPM has appropriately shifted from initially advocating strongly for greater attention and funding to microbicides early on, to managing expectation in the field as initial Phase III microbicide trials have failed. IPM has also collaborated with other key microbicide players around the Microbicides Media and Communications Initiative to ensure consistent and appropriate messaging from the field in response to any developments.

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<sup>13</sup> International Partnership for Microbicides, Start-Up Business Plan, 2002

<sup>14</sup> IPM Workplan, 2007-2010, July 2006

## IPM Evaluation Report

### *Relationship with Advocacy Partners*

IPM's advocacy partners noted that IPM values the contributions of its partners and engages and supports them in their work. However, while advocacy partners also voiced concerns in interviews that IPM does not necessarily engage with advocacy organizations in order to include broader perspectives in key messages. Where IPM has unique access to influential actors on the global stage, advocacy peers would like greater collaboration with IPM to ensure that any field-wide messaging is consistent with what others are saying. IPM recognizes the value in consistent messaging and balances its engagement with peers with its fast-moving approach and its messaging about its own work and scientific perspectives.

A further concern of advocacy partners is that IPM's mission is narrowly focused on developing a vaginal, antiretroviral-based microbicide that will be non-coitally dependent and that this approach is not representative of the whole field. This reflects IPM's changing role and its decision to pursue a specific set of products, which should continue to be clearly communicated.

### **Increased Funding for the Field**

#### *Global Funding*

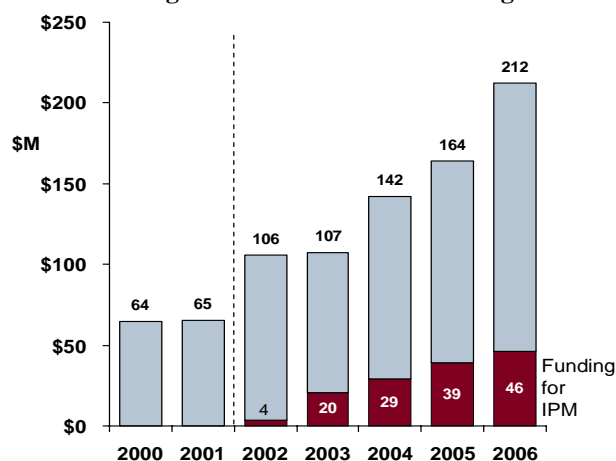
Funding for microbicides R&D has grown tremendously over the past seven years from \$64M in 2000 to \$212M in 2006. This growth is attributable to the general growth in interest in microbicides which led to the creation and subsequent funding of IPM, and many organizations in the field deserve credit for laying the groundwork for the level of financial support available today.

Peers and advocacy partners have consistently recognized IPM's role as an important catalyst and unique advocate for microbicides funding. As mentioned above, IPM has filled an important advocacy gap by targeting high-profile individuals and organizations.

Over the past five years, IPM's funding has grown quickly and the growth in IPM's financial resources generally mirrors the growth in funds available to the field overall, with approximately 20% of the field's funding supporting IPM. While IPM is the largest product developer in the field, significant funding continues to flow to many other players with \$166M in 2006 going to other efforts.

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**Figure 9: Total Funding for Microbicides vs. Funding for IPM (2000-2006)**



It is difficult to attribute the increase in funds for the field to any one player and as mentioned above, the advocacy efforts that led to IPM's creation, ongoing advocacy by existing organizations, and IPM's efforts all have been important factors. An additional dynamic at play recently has been the large number of Phase III microbicide clinical trials going on which has led to a significant increase in demand for funding. This is not an insignificant factor as clinical trial costs accounted for an estimated 43% of donor contributions in 2006<sup>15</sup>.

### *New Donors*

In addition to the increase in funding for microbicides, stakeholders have emphasized IPM's success in raising funds from new donors, especially from European bilateral donors. While the increase in global funding for microbicides is largely attributable to increased commitments from three large players (the United States government, the United Kingdom government, and the Bill and Melinda Gates Foundation), in 2006 these new European bilaterals represented approximated 15% of the global funds available. This funding can be significantly attributed to IPM's efforts and the efforts of its advocacy partners in those countries. Of the top European microbicide donors, five of seven began contributing in 2002 with the founding of IPM and have overwhelmingly contributed money only to IPM. To note, some of these new donors have also commented that few other microbicide organizations have approached them for funding, and IPM continues to be seen as the most involved microbicide developer in the European landscape.

<sup>15</sup> Building a Comprehensive Response, HIV Vaccines and Microbicides Resource Tracking Working Group, November 2007

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**Figure 10: Top European Donors to Microbicides**

Donor	Years Contributing	Total Contribution	Total to IPM	% to IPM
United Kingdom	2000-06	\$46.6M	\$6.4M	14%
European Commission*	2000-06	\$21.1M	\$0.2M	1%
Ireland	2002-06	\$17.3M	\$17.1M	99%
Netherlands	2002-06	\$15.7M	\$15.7M	100%
Norway	2002-06	\$10.2M	\$10.1M	99%
Sweden	2002-06	\$8.7M	\$4.1M	48%
Denmark	2002-06	\$4.5M	\$4.5M	100%
<b>Total</b>		<b>\$31.9M</b>	<b>\$23.4M</b>	<b>73%</b>

Note: \* The EC did not fund IPM in 2006 but has committed \$7M to IPM over 2007-10

Source: IPM internal documents; HIV Vaccines and Microbicides Resource Tracking Working Group, Building a Comprehensive Response: Funding for HIV Vaccine, Microbicide and New Prevention Tools Research and Development 2000 to 2006, November 2007

Some peers and advocacy partners have the perception that IPM’s advocacy efforts are more directed toward raising funds for itself rather than for the field in general. This perception is likely tied to IPM’s general success in raising significant funding, as well as IPM’s ability to bring in new donors who are supporting IPM almost exclusively. It should be recognized that IPM provides funding for various field-wide events, such as conferences, sponsorships, and grants for scientific and non-scientific inquiry.

### ***Conclusions***

- 1) IPM is recognized as a strong advocate that has contributed to the global chorus of voices that seeks to increase the profile of microbicide research among donors and policymakers. IPM has been successful at raising the global profile of microbicides and seems to have better access to global influentials than others in the field. Despite the fact that IPM has its own portfolio to champion, IPM is well positioned to continue to play a role on the global stage championing the field of microbicides research.
  
- 2) Global funding for microbicide research has grown over the last five years, in part due to IPM’s advocacy efforts. IPM has successfully targeted many new donors, especially European bilateral agencies. However, the benefits of this expanded “pie” from new donors are largely being received by IPM as a result of its willingness and ability to reach out more broadly. Donors interviewed noted that

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other microbicide players have not significantly reached out to many of these new microbicides funders.

- 3) IPM balances a number of pressures in its global communications. IPM is frequently speaking for the field, but needs to balance field-wide messaging with communications that relate to its own work. This tension will continue as IPM faces increased pressure to fundraise for its upcoming Phase III trials.

## E. Organizational Effectiveness

### *Summary*

IPM has grown quickly from a start-up to a mature organization prominent in its field. IPM's growth requires that the organization develop robust and formal processes to ensure continued success. Its prominence in the field demands that IPM develop regular communications and clear processes to maintain strong relationships with its many partners.

### *Recommendations*

- 1) **Develop Updated Five-Year Strategic Plan:** IPM requires a clear plan for managing the complex portfolio of compounds and wide range of activities that it is now responsible for. IPM has evolved significantly since its inception and should develop an updated five-year strategic plan that clearly communicates its positioning in the field, priorities, and key activities both internally and externally. As part of this process, IPM should also develop financial projections that take into account product and clinical development associated with its whole portfolio.
- 2) **Continue Advocating for Unrestricted Funding:** IPM should continue to advocate to donors for unrestricted funding and should position the strong governance mechanisms through its board and a more engaged SAB as sufficient accountability.
- 3) **Improve Communication with Partners:** IPM should consider processes for better communication of plans and priorities with its key partners. *Greater details for partnerships are covered in the Clinical Affairs and Advocacy sections.*
  - **Long-term Strategy:** Sharing IPM's long term strategy with clinical partners will help improve relationships and align expectations of IPM as a long-term partner in microbicide research.
  - **Better Communication on Prioritization:** Better communication of decision-making and proactive outreach to pharmaceutical partners will ensure understanding around IPM's decision-making. IPM can likewise use proactive communication with industry to solicit greater contributions of key expertise.
- 4) **Strengthen the Clinical Team:** *Greater details on strengthening the clinical team are covered in the Clinical Trials section.* IPM has begun training its clinical team in preparation for Phase III trials, but currently does not yet have the number of experienced staff that will be required. IPM should engage additional experienced clinical trial managers and clinical research associates (CRAs). IPM should also recruit a senior clinical research physician to better support the Chief Medical Officer (CMO). This person should have considerable experience in designing, implementing, and managing clinical trials. IPM should also consider

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increasing quality control (QC) capacity, preferably based in South Africa, and implementing mentoring between experienced, proven investigators and new research centers. IPM should explore leveraging its partnerships with pharmaceutical companies, who may be willing to consider loaning experienced staff or offering greater technical assistance

- 5) **Formalize Portfolio Management Processes:** *Greater details on formalizing portfolio management processes are covered in the Portfolio and Product Development section.* IPM has rapidly expanded its portfolio to include a wide array of products and formulations. However, management processes and structures to match this complexity have not yet been implemented. IPM should adopt formal portfolio management processes with a portfolio management committee, and implement comprehensive product and clinical development plans, target product profiles, explicit go/no-go criteria, and multi-disciplinary project teams.
- 6) **Increase SAB EC Engagement:** *Greater details on the SAB are covered in the Portfolio and Product Development section.* Donors rely heavily on the SAB EC to provide IPM with independent advice which brings wider expertise to IPM's scientific decisions. While the SAB EC should remain an advisory body and should not impede IPM's operational flexibility, it is important that the SAB EC is more actively involved in scientific planning and decision-making. IPM should take steps to ensure that the SAB EC is appropriately engaged and that this process is robustly implemented. The SAB EC could augment its annual meeting with an additional meeting, quarterly conference calls, and/or sub-committees intended for more direct engagement. This may require that IPM revisit the membership and expertise of the SAB EC.

### *Context*

IPM's workplans have identified the importance of building a strong organizational foundation. Framed as "Supporting Goals," IPM has articulated targets associated with building its team, its administrative support, its network of partners, and its governance processes to support its work appropriately.

This five-year evaluation follows a period of incredible organizational growth, both in terms of human and financial resources. IPM has grown its team to 113 people as of May 2008, established operations in four cities on three continents, and formed a board of directors and a scientific advisory board. While building this organizational infrastructure the organization has carried out its strategies in the areas described above and raised commitments of USD \$223M to support its mission. This evaluation also falls at a time where IPM is shifting from the activities associated with in-licensing products to more active management of a portfolio of candidates and a near-term focus on preparing for a complex Phase III trial.

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The Organizational Effectiveness analysis will examine the specific areas of governance, reputation and partnering, financial sustainability and the overall quality of the organization in the context of the factors described above.

### *Findings*

#### **Governance**

##### *Board of Directors*

IPM's board has primary responsibility for overseeing IPM's management performance and appears to be playing a robust and important role in IPM's decision-making and governance.

IPM's board is currently comprised of 12 people with a range of expertise who convene for two-day meetings twice a year. The board membership has evolved as IPM has moved away from the original mandate as a coordinator for the field (see the Portfolio and Product Development section above). As IPM became a product developer, the board composition included fewer stakeholders from the field and more people with industry experience in product development (e.g., Drs. Al Profy and Peter Corr).

Nine current board members and two former board members were interviewed and the majority of them (nine out of eleven) felt that the board played a sufficient governance role. Board members reported sufficient research and analysis had been presented to support key IPM decisions (e.g., the decision to build a ring manufacturing facility). However, much of the detail behind this research was not available to the evaluation team and may not have been documented.

IPM also reports progress against its workplan to the board and to the donors, providing a progress report against its goals every six months. Clear and robust accountability is a high priority for donors, and board members generally felt that the structure and meeting schedule of the board matched their expectations and needs. Benchmarking analysis suggests that IPM's board structure is similar to that of other PDPs.

##### *Funder Engagement*

There are currently no donors who sit on the board. General feedback from board members and donors was that this arrangement was appropriate and that donor engagement was satisfactory. However, donors with greater technical expertise desired a greater understanding of scientific decision-making and they do not currently have a mechanism for learning at a detailed level how decisions were made. Potential challenges with including donors on the board include greater sensitivity around what can be discussed as well as logistical difficulties of fairly including all donors.

##### *Scientific Advisory Board*

As noted previously, the SAB has evolved in its role and currently the SAB EC has primary responsibility for advising IPM on scientific issues across product and clinical development. The Chair of the SAB attends one board meeting per year as well as the



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annual IPM donor meeting, and plays an important role in ensuring that IPM is making the best decisions concerning its scientific program.

### **Reputation and Partnering**

IPM relies heavily on partners to achieve its goals and IPM's relationships will be critical to its future success. Three types of partnerships have been examined: pharmaceutical partnerships, clinical partnerships, and advocacy partnerships.

#### *Pharmaceutical Partners*

*IPM's relationship with pharmaceutical partners has been covered in previous sections.*

IPM's pharmaceutical partners expressed high confidence in IPM and praise IPM for its professional approach, capabilities, and passion. However, partners also noted some concern over IPM's ability to manage multiple projects and felt that IPM's portfolio prioritization process was not clearly communicated (i.e., which products were being focused on and the rationale behind prioritization decisions). This has the potential to be sensitive for pharmaceutical partners who entered into agreements with IPM under the expectation that their products would be actively pursued. As IPM moves forward with a diverse portfolio that will need to be prioritized, it is important that it proactively and clearly communicates with pharmaceutical partners to maintain strong relationships and shared intellectual property.

#### *Clinical Partners*

*IPM's relationship with clinical partners has been covered in-depth in previous sections.*

Interviews with clinical partners showed that they view IPM in mixed terms. Clinical partners recognize that IPM has made a considerable investment, including building new clinical infrastructure, training staff in ICH GCP standards, and creating opportunities for important research. IPM has also convened its investigators to help encourage cross-site learning and sent a limited number of investigators to international meetings with plans to send more going forward.

However, several of IPM's clinical partners have also expressed feeling that IPM is contracting with them on a transactional basis rather than showing a deeper, long-term commitment to partnership. In addition, some more experienced investigators have also expressed concern regarding IPM's extensive monitoring and research center requirements, as well as a desire for greater flexibility in training requirements based on their existing clinical skills and research experience.

IPM has moved to address some of these concerns. Most importantly, IPM has decided to institute bridge funding for clinical partners and this plan should be clearly communicated to investigators. IPM should also clearly communicate the rationale for stringent ICH GCP requirements to partners.

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Clinical research in HIV prevention is associated with significant political sensitivity and IPM will need to rely heavily on local clinical partners for generating country-level support, communicating progress, and managing potential setbacks at the community level and to host-country governments. The current relationships between IPM and its clinical partners are mixed, and it will be important as IPM moves forward to strengthen these relationships. In this area, IPM faces the challenge common to all organizations running clinical trials: balancing speed and the interests of clinical partners with available resources and quality standards.

### *Advocacy Partners*

*IPM's relationship with advocacy partners has been covered in previous sections.*

IPM's advocacy partners noted that IPM values the contributions of its partners and engages and supports them in their work. However, while advocacy partners also voiced concerns in interviews that IPM does not necessarily engage with advocacy organizations in order to include broader perspectives in key messages. Where IPM has unique access to influential actors on the global stage, advocacy peers would like greater collaboration with IPM to ensure that any field-wide messaging is consistent with what others are saying. IPM recognizes the value in consistent messaging and balances its engagement with peers with its fast-moving approach and its messaging about its own work and scientific perspectives.

A further concern of advocacy partners is that IPM's mission is narrowly focused on developing a vaginal, antiretroviral-based microbicide that will be non-coitally dependent and that this approach is not representative of the whole field. This reflects IPM's changing role and its decision to pursue a specific set of products, which should continue to be clearly communicated.

### *Overall*

Across its different partners, IPM was often described as not being very clear in its communication of decision-making. IPM's partners consistently mentioned that a greater understanding of the organization's decision-making processes, priorities, and longer-term plans would help ensure that appropriate expectations are set in order to best move towards the shared goal of a safe and effective microbicide for women.

### **Strategy**

The strategic plan governing IPM's first five years of operation was developed in 2002 with the support of the Boston Consulting Group. This start-up business plan has provided some high level guidance for IPM over the years but IPM's approach to microbicide development has evolved significantly from this original vision. The original document emphasizes IPM's role as a coordinator rather than a product developer and this has been the source of a great deal of confusion and friction for IPM in the field.

IPM has not developed a strategic plan since the 2002-2007 original business plan was released. However, IPM has developed high-level workplans that outline its priorities in

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two to three year timeframes. These workplans include the organization’s goals, supporting objectives, and in the most recent workplan, indicators of success. As part of this process, IPM will have an opportunity to systematically assess the financial requirements associated with its next five years of activity.

### Financial Sustainability

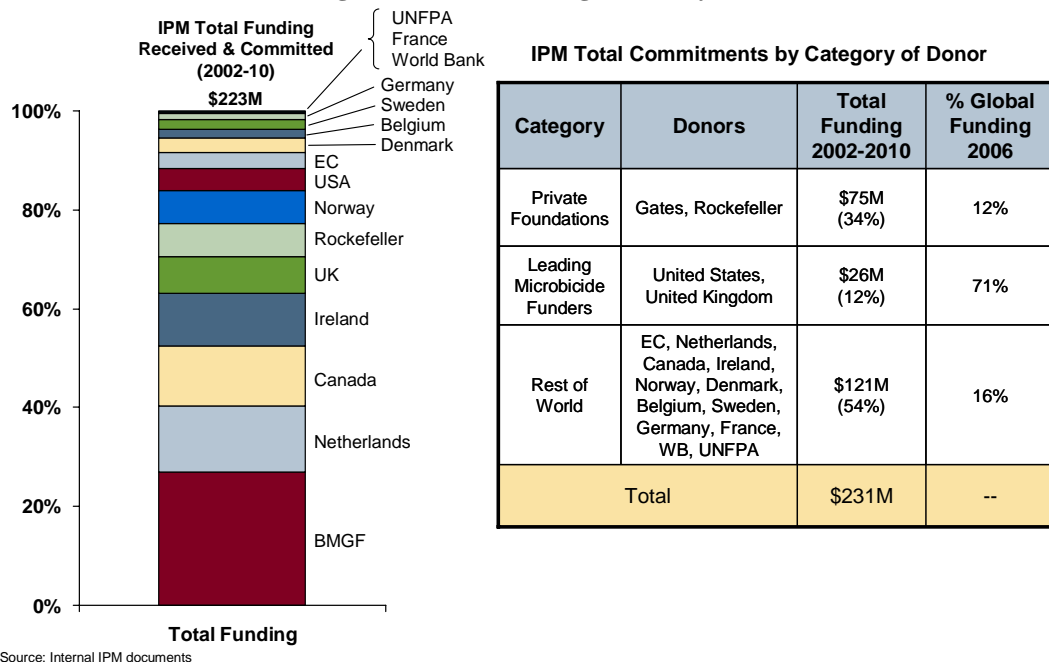
Financial sustainability was evaluated looking at the overall track record in raising funds, the presence of a reserve fund, the diversification of the funding base, any recurring revenue (earned), the impact of restricted funds and the future plans for resource mobilization. In addition, we examined the level of rigor behind financial projections.

#### Resource Mobilization

IPM has raised USD \$223M in commitments for its work to accelerate the development of microbicides and at the end of 2007 had almost \$100M in a cash reserve. IPM is well-resourced and well-positioned to address the substantial financial requirements of entering Phase III clinical trials. IPM’s historical under-budgeting is also seen as appropriate given the difficulty of raising the necessary funds for a Phase III all at once.

IPM has garnered financial support from a diverse collection of donors including private foundations, bilateral development agencies, and some small support from multilateral agencies. The largest donor is the Bill and Melinda Gates Foundation, which has provided approximately 27% of funds to date. IPM’s diverse set of donors is impressive especially in the microbicide field where over 80% of funding in 2006 came from just three donors: the US, the UK, and the Bill and Melinda Gates Foundation. IPM does not currently project any recurring earned revenue from its operations.

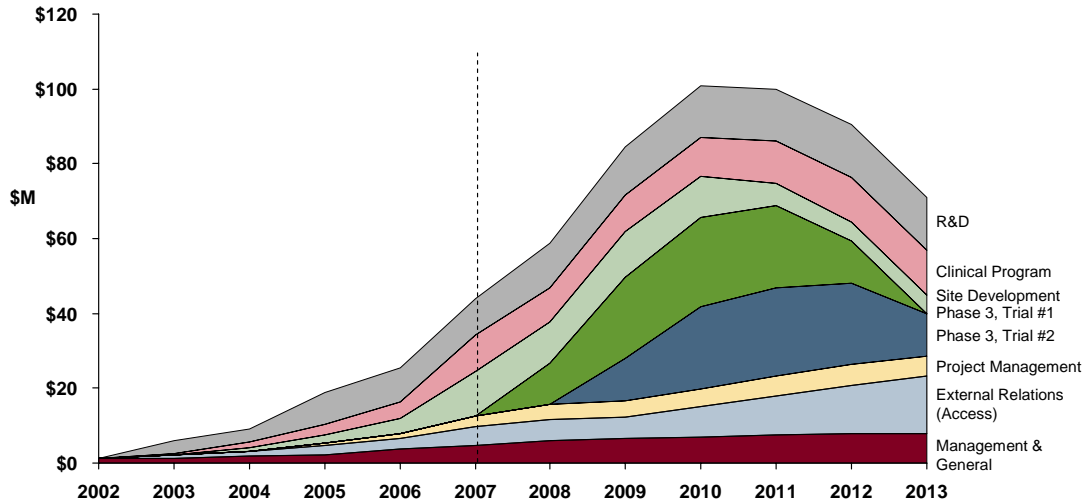
**Figure 11: IPM Funding Summary**



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IPM's strategy for raising the funds required for Phase III trials depends on renewing multi-year grants, securing annual contributions from its current donors as current grants expire and broadening the pool of government donors through continuing support to a network of HIV/AIDS organizations, reproductive health NGOs, and advocacy groups.

**Figure 12: IPM Financial Projections by Department (2002-13)**



IPM has recently experienced a growing number of restricted grants from donors, limiting its flexibility in how funding is utilized and potentially decreasing the efficiency of the organization due to special reporting and accounting requirements. Interviews with donors suggest that this is not expected to be an increasing trend. However, restricted funding, as well as funding which is tied to particular years, decreases IPM's flexibility, and hinders its ability to make swift decisions about a portfolio based on objective, rational, and scientific criteria. Restricted funding also creates the potential for poor trade-offs as IPM moves forward and makes prioritization decisions that may require killing a project based on the science but would risk losing funding attached to that project.

### *Quality of the Organization*

The quality of IPM as an organization is assessed based on an analysis of the IPM's overall skills, organizational structure, and operational processes.

### **Skills**

IPM's staff draws expertise from the fields of HIV research, the pharmaceutical industry and academia. The evaluation teams believes that strengthening the clinical expertise at IPM is the most critical from a skills perspective given upcoming Phase III trials. The findings and recommendations have been covered in-depth in the Clinical Trials section and are summarized below:

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- Engage additional experienced clinical trial managers and clinical research associates (CRAs)
- Recruit a senior clinical research physician to better support the Chief Medical Officer (CMO). This person should have considerable experience in designing, implementing, and managing clinical trials
- Increase quality control (QC) capacity, preferably based in South Africa
- Implement mentoring between experienced, proven investigators and new research centers
- Explore leveraging its partnerships with pharmaceutical companies, who may be willing to consider loaning experienced staff or offering greater technical assistance

### **Structure**

IPM's structure has evolved considerably with the significant growth in staff over the first five years. As of May 2008, there were 113 staff members reporting to the CEO across four departments: Finance and Administration, External Relations, Clinical Affairs, and Research and Development. This overall organizational structure appears appropriate and fits IPM's priorities going forward (the quality of IPM's internal systems was covered in Efficiency). However, there are some specific structural areas for improvement:

#### *Formal Portfolio Management Structures*

The Product Development committee is made up of senior staff and functions as both the operational project team and the review committee for projects. This has allowed IPM to make decisions quickly and to serve their needs given the small number of clinical projects in the past. However, a formal portfolio management function has not yet been implemented and as IPM moves forward, it would greatly benefit from formal project teams and a portfolio management committee. Project teams would manage and implement the product and clinical development plans for a set of compounds. A portfolio management committee would oversee the project teams and ensure that decision-making is sound and timelines are being managed appropriately. This formalization would improve the quality of decision-making.

#### *CMO Support*

The African operations are led by the Chief Medical Officer, who has taken on all tasks related to clinical trials, including site development, clinical projects, safety, and community engagement. Interviews with internal staff indicate that her workload is substantial and not easily delegated among the current staff. IPM is considering the appointment of a Deputy Chief Medical Officer who would reduce the current burden of work on the CMO, and should recruit a senior clinical research physician with considerable experience in designing, implementing, and managing clinical trials.

### **Processes**

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IPM has adequate processes in place to guide many of its administrative activities. Decision-making processes, especially related to the portfolio and product development, are less formal. For example, IPM has worked with some pharmaceutical partners to develop specific plans for certain candidates, but there is no current portfolio management process in place. Prioritization within the portfolio is described as *ad hoc*. Processes with respect to clinical trials are evolving, and the SOPs that govern all clinical trial activities have not yet been adopted by clinical research centers or have not yet been finalized. In addition, site selection criteria have not been clearly communicated such that potential partners can understand the requirements for inclusion in IPM's clinical trial network.

Interviews suggested that IPM has not yet fully formalized its communications processes for internal audiences and external stakeholders. Funders receive formal communications twice per year in addition to grant specific reporting and board members receive quarterly updates covering IPM's general activities, but many of the decisions associated with the portfolio prioritization and specific projects need to be shared more consistently. Interviewees recognize this as an easy area to improve that will have a positive impact across IPM's stakeholders enabling others to understand IPM's choices in a timely and clear manner.

### ***Conclusions***

- 1) IPM's Board of Directors has played an adequate role in overseeing IPM's management and has evolved to pass primary responsibility for scientific engagement to the SAB EC. The SAB EC however is not significantly engaged in IPM's scientific decision-making given the challenges ahead. Funder engagement is generally appropriate and the challenges of putting a funder on the board likely outweigh the benefits. Funder who desire greater involvement should be engaged with to a greater extent, but this should occur outside of the governance structures.
- 2) IPM has not updated its strategic plan since the original 2002-2007 five-year plan. IPM has evolved significantly since its inception and the original plan does not appropriately capture IPM's current positioning in the field.
- 3) IPM's relationships with clinical partners are mixed, with recognition of IPM's contributions and support but some concerns about IPM's partnering approach.
- 4) IPM has raised significant funds in the first five years and has a reserve that will help cover the costs of the planned Phase III trial. However, financial projections for access have not been fully developed. Further, current projections do not capture product and clinical development activities for advancing antiretrovirals beyond dapivirine, or combination antiretrovirals. IPM recognizes the need for more comprehensive projections.

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- 5) To address the challenges of IPM's future work in R&D and Clinical, the organization needs additional experienced staff and greater executive-level support for clinical trials. This is recognized by IPM, which is actively recruiting for these positions.
- 6) IPM's processes have been sufficient for its operations to date but lack the formalization, documentation of decision-making, and clear communication processes that will be important for managing the risks associated with a more complicated portfolio and large-scale efficacy trials.
- 7) Restricted funding is currently not a significant portion of IPM's portfolio, but a trend toward greater restrictions could be detrimental to IPM's flexibility, speed, and ability to make sound decisions based on the objective science.

## IV. Implications for the Future

### A. Implications for IPM

IPM is a highly successful start-up and should continue to operate at the same level of accomplishment in the coming years. IPM has engaged pharmaceutical companies in partnerships to establish and build the antiretroviral-based vaginal microbicide pipeline. These partnerships should continue to be nurtured. IPM has built a strong portfolio, the first in its field, and this portfolio represents an important de-risking mechanism for the field- it should continue to be IPM's focus. IPM also plays an important role in raising the global awareness of microbicides and should continue to play this role.

As mentioned earlier, this report has been written in a forward-looking manner with an emphasis on recommendations to improve IPM's performance going forward. IPM should obviously review the list of recommendations featured in this report. The most critical issues that IPM should take action on include the following:

#### **Launch Strategic Planning**

Having achieved notable success in its first five years, it is time for IPM and its donors to begin a strategic planning process in order to prepare for the next five years, and its next major evaluation. As IPM proves itself a competent product developer it may have an important role to play in the ongoing need to develop microbicides. Planning for success will require explicit plans for manufacturing scale-up, ongoing portfolio management, and a commitment to long term relationships with partners, including pharmaceutical companies, clinical research centers, advocates and governments.

#### **Formalize Management Processes to Reduce Risk**

IPM has successfully passed the hurdle of a start-up organization and begun to put processes in place that will be required for success in the future. IPM can benefit from formalizing decision-making in the organization, leading to a number of benefits:

- Decreased risk through explicit portfolio and project management
- Improved communication to partners concerned with IPM's ability to progress multiple candidates
- Internal alignment around agreed-upon priorities

#### **Improve Communication with Partners**

IPM is not a biotech firm, nor a traditional NGO, and operates against a blend of private and public sector demands. IPM has also needed to work quickly and make decisions in a dynamic environment. However, internal interviews and discussions with partners in the public and private sector indicated that now that IPM has established itself as a major force in the field, it needs to strengthen internal and external communication. Formal decision-making processes around the portfolio, publicly available target product profiles, explicit rationales for strategic decisions, and increased communication about shared priorities with global, national, and local stakeholders will help IPM manifest its promise as a partnership.



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### B. Implications for the Field of Microbicides and Donors

Though the scope of this evaluation was not to assess the field as a whole, the evaluation team developed a perspective and can share some high level observations regarding the broader needs within the microbicides field, especially as it relates to the role of donors.

#### **For the Field:**

As IPM enters the next five years, it is important for the field to accept IPM's role as a product developer focused primarily on developing its own portfolio of compounds. While IPM has worked to benefit the broader microbicide field and will continue to support important field-wide activities, it should not be expected to play the role of a coordinator for the field or a significant funder of activities outside of its strategy. The primary benefits to the microbicide field from IPM's work are likely to continue to be through accomplishing its mission, such as raising the global profile for microbicides and investing in formulations development.

This evaluation recognizes the important role that IPM's peers and complementary organizations play in the pursuit of microbicide development. The activities of others are key to IPM's success and it is critical that they continue. It is also critical that partnerships continue to evolve and reflect on the successes and challenges associated with close collaboration.

The field of research will benefit from continued pursuit of three areas of common concern. These lead to important implications for donors.

- Strengthened regulatory processes
- Strengthened advocacy at the country level to ensure support for microbicide research
- Ongoing efforts to strengthen the health systems that will ultimately provide women with access to a microbicide

#### **For Donors:**

The complexity of microbicide research will continue to require patient capital. Patience is also required as IPM and other organizations assess the timelines associated with complex activities, particularly Phase III trials. IPM will benefit from decreased donor pressure to accelerate towards its first Phase III, especially given the level of complexity that is expected for this trial based on the design to date.

Donors to microbicide development should also recognize that IPM's current role in the field is that of a product developer focused on antiretroviral-based, non-coitally dependent, vaginally applied microbicides. IPM currently represents the largest microbicide product developer, but is not a "one-stop shop" for the microbicide effort and is not a vehicle for funding general initiatives outside of its strategy. If donors view such other efforts as priorities, they should fund them separately from IPM. As IPM continues to evolve its strategy, these approaches may one day be within the organization's scope.

## IPM Evaluation Report

As noted in this report, the evaluation team believes that it was not feasible for IPM or any other organization to play a coordinating role for the microbicide field. At this point we do not recognize any group with the neutrality required to make global funding decisions that will be seen as credible by the field. There is likewise no central coordinator to rationalize the use of clinical research centers in developing countries. If donors seek greater coordination among researchers, it is the responsibility of the donors to coordinate their funding around agreed-upon priorities. Some progress has been made on this front as relates to the Microbicide Donors Committee, but further coordination is needed.

The under-resourced regulatory infrastructure in many African nations is a hurdle that faces all microbicide developers, and indeed all product development partnerships seeking licensure for their products. Resources need to be invested from a wide set of stakeholders to support oversight bodies and regulatory agencies, and to build capacity in basic processes and concepts in the field. There is an opportunity going forward for donors to play a role in terms of funding capacity building for regulatory bodies, as well as a role for industry to lend expertise to address this hurdle.

Another area which requires coordination is in advocacy, as articulated recently by the MDS Civil Society Working Group<sup>16</sup>. The Global Campaign for Microbicides, the AIDS Vaccine Advocacy Coalition, and other NGOs have proposed a “funding window” to coordinate funds to grassroots advocacy organizations. This approach could serve to strengthen support for clinical research at the country level and help maintain understanding and enthusiasm for microbicide development. It is essential for continued product development in multiple products across HIV prevention technologies.

Ensuring that women have access to microbicides once developed will depend in significant part on the strength of the health systems in Africa to make these products available to the women most in need. Donors have an important role to play in building the capacity of health systems as a component of ensuring access to eventual products.

Finally, this study found that the majority of funds provided to IPM are not restricted to a specific purpose. This provides appropriate flexibility for IPM as it shifts activities based on its thinking and results from its work. However, there is a concern that donors are moving toward greater restrictions as part of increasing accountability. This dramatically increases the burden on IPM from a financial management and operational standpoint, and could create inappropriate incentives for prioritization of projects. The evaluation team believes that proper governance rather than restricted funding creates real accountability, and donors will be best served in achieving their goals with the least risk if they provide unrestricted funding and demand strong governance and reporting from grantees.

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<sup>16</sup> *The first 55 steps: a report of MDS Civil Society Working Group*, Global Campaign for Microbicides 2008

## **B. Implications for PDP Funding and Evaluation**

### **Context**

This evaluation represents only the third evaluation of a PDP and few best practices for conducting PDP evaluations have emerged, especially in light of the unique contexts each PDP operates within. Currently, the PDP Funders Group, a coalition of donors who meet on a regular basis to share lessons on how best to support existing and future PDP grantees, is currently reflecting upon the issue of PDP performance measurement. FSG Social Impact Advisors wrote a white paper on this issue and the PDP Funders Group is taking the recommendations from that work to consider new tools and processes to improve the state of PDP performance measurement.<sup>17</sup> We hope that this evaluation and the lessons mentioned below can inform on-going discussions about PDP performance measurement. Perhaps this evaluation can serve as a new touchstone upon which other PDP assessments can learn and perhaps adopt some of its approaches.

Key lessons from this evaluation that may benefit other, future PDP evaluations include the following:

### **Evaluation Team Composition**

The evaluation team benefited from a mix of technical experts and management consultants, compared to past PDP evaluations which were staffed entirely by experts. The management skills allowed our team to bring a strong perspective on organizational strategy and forward-looking opportunities for impact while the technical experts provided deep knowledge and experience in international evaluation and the pharmaceutical industry. As is the practice in management consulting, a high priority was also placed on working together as a team, and the evaluation team was in constant communication as we gathered information and developed our thinking. The team also met in-person multiple times during the process for full-day meetings to collaboratively think through the findings to date, test hypotheses, and discuss next steps. This process was critical to developing a strong and balanced final perspective on IPM.

### **Value of Benchmarking**

A large part of the complexity of the task is that PDPs are largely still developing, and not yet delivering products to market. This means that one cannot benchmark standard outputs such as manufacturing and delivery, and must instead focus on processes and risk management. Quantitative data, such as costs for R&D are difficult to benchmark given the variability and unique nature of these expenses. However we found that benchmarking similar organizations through interviews with PDPs, biotech and

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<sup>17</sup> *Toward a New Approach to Product Development Partnership Performance Measurement*; FSG Whitepaper, June 2007; Sponsored by the Bill and Melinda Gates Foundation with support from the Rockefeller Foundation on behalf of the PDP Funders Group

## IPM Evaluation Report

pharmaceutical companies allowed us to identify areas where processes and risk management strategies could be compared. Particularly helpful was the data we gathered on oversight processes like the use of scientific advisory boards or portfolio management functions. In the ideal state, PDPs would be provided with the necessary support and feedback and across-industry benchmarks to optimize operations as they, and the environment that they work in, continues to evolve.

### **Stakeholder Involvement, Including Involvement of the Organization Being Evaluated**

Supporting and involving all stakeholders, including the donors and the grantees in evaluation processes only helps to make the process more productive. In this case, IPM was involved in drafting the Terms of Reference to ensure that the output would be valuable to them, and IPM was engaged with the project team throughout the process. IPM was present at the first presentation of findings in order to ensure that the findings were shared openly and presented in a way that could help them better achieve their goals. Donors for the evaluation have also been included in iterations of preliminary findings and feedback has been helpful toward producing a strong final product. As we believe that this evaluation is primarily targeted to the donors and to IPM, we believe that the high level of involvement of all parties has been invaluable.

### **Structure of Evaluation Approach**

The structure of the IPM evaluation was informed by the Terms of Reference which were based on the DAC General Evaluation Issues, as well as the general categories that members of our team had developed in the FSG whitepaper on PDP performance measurement. The generic framework from that paper was the basis for the modules presented in this report (Portfolio and Product Development, Clinical Trials, Access, Advocacy, and Organizational Effectiveness). We believe that this comprehensive list of evaluation areas, rather than a more narrow focus on the R&D, is important to carry forward as the categories for future PDP evaluations.

The evaluation team found that the module categories were the most straightforward to evaluate as well as the most useful to IPM as they clearly divided IPM's main activities. The evaluation was therefore conducted focusing on the modules and then treated the General Evaluation Issues as cross-cutting, pulling findings from the modules to inform the conclusions for Relevance, Effectiveness, Efficiency, Sustainability, and Impact. The evaluation team felt this was an efficient and comprehensive approach that ensured value for both donors and for IPM.

### **The Future of PDP Performance Measurement**

This evaluation also allowed the team to think about the future of PDP performance measurement as a whole. Most importantly, this evaluation pointed to the importance of thinking prospectively about performance measurement. We understand that the design of the Terms of Reference was a significant task in itself. In reflecting upon this process,

## IPM Evaluation Report

we question whether evaluation terms of reference should ever be designed in a retrospective manner. Ideally, an evaluation design should be guided by a strong strategic plan that incorporates specific measures of success mutually agreed upon by the PDP and donor. Thus, evaluations are the end point of a longer process that starts with a strategic plan. The advantages of prospectively developing evaluation metrics within a strategic plan are significant:

- Reduced ambiguity/uncertainty in what will be evaluated
- Increased collaboration between the donor and PDP throughout the performance measurement lifecycle
- Fit-for-purpose team of evaluators: the strategic plan should provide the best guidance for the skills and capabilities needed for the evaluation team
- Greater enthusiasm by the PDP and higher probability that the recommendations in the evaluation will be highly relevant and acted upon by the PDP management team

At present, PDPs create their strategic plans with varying degrees of involvement by donors. We do not view donor review of strategic plans and consideration of those as foundations for future evaluations requires any changes to existing governance expectations. Ultimately, the strategic plans are the responsibility of the PDP but they also reflect the “value for money” plans that the PDP will undertake using donor funds.

Our hope is that this evaluation will encourage the development of an updated five-year strategy for IPM. While IPM has continually updated 3-year workplans, these do not contain specific timelines or strategic plans for the organization to evaluate itself against. A prospective evaluation design built into an updated strategic plan can lead to a more focused future evaluation. Furthermore, if IPM can articulate specific metrics in its next plan, then it could be possible to engage in more frequent, topic-specific assessment activities that help it improve as part of more consistent self-improvement efforts rather than infrequent, more resource intensive evaluations every five years.<sup>18</sup>

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<sup>18</sup> *From Insight to Action: New Directions in Foundation Evaluation*; FSG Whitepaper, 2007

## V. Appendices

### A. Evaluation Process

Following the issuance of the Terms of Reference, FSG Social Impact Advisors (FSG) and HLSP jointly proposed to conduct an evaluation. The evaluation took place between January, 2008 and May, 2008, with phases of work as follows:

- I. Inception Phase
- II. Internal Perspectives and Analysis
- III. External Perspectives and Analysis
- IV. Develop Draft Report
- V. Present Final Report

It was the goal of the Inception Phase to build on the original proposal to prioritize issues for investigation, articulate limitations and concerns, refine the workplan and include additional expertise to the team. In the course of the Inception Phase, the evaluation team met with the IPM Evaluation Management Group in Dublin to kick off the process, paid a visit to Silver Spring, Maryland to meet with and interview IPM management, reviewed key documents gathered from IPM and referenced in the Terms of Reference<sup>19</sup>, and conducted a set of 18 interviews with donors, IPM leadership, partners, and peer organizations (see below: Evaluation Interview List for detail).

The Evaluation Phase relied heavily upon the generosity of IPM as a whole, which shared numerous documents and engaged in multiple discussions. Overall the evaluation included 148 interviews and a review of over 1,100 documents. The evaluation team conducted site visits to IPM facilities and field sites in Silver Spring, MD, Bethlehem, PA, throughout South Africa and in Kigali, Rwanda. The Evaluation Team also benchmarked a set of PDPs and peer biotechnology firms along key dimensions relevant to IPM<sup>20</sup>.

Evaluation findings were shared with donors and IPM in a series of consultative meetings, and in this final report.

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<sup>20</sup> An external survey was also completed as part of the evaluation, but did not yield enough responses to yield robust results

## **B. Evaluation Team**

The IPM evaluation team included the following members:

- Kyle Peterson, Managing Director, FSG
- Laura Herman, Director, FSG
- Nel Druce, Institute Deputy Director, HLSP
- Keith Bragman, Independent Consultant
- David Zapol, Senior Consultant, FSG
- Yi-An Huang, Associate, FSG

The team was also fortunate to have the support of the attorneys Karin Rivard and Steven Snyder at Goulston + Storrs, who joined the team to conduct a targeted review of three IP agreements between IPM and pharmaceutical partners.

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## C. External Interviewees

Row	Type	Name	Organization
1	Advocacy and Access	Manju Chatani	AMAG
2	Advocacy and Access	Polly Harrison	AMD
3	Advocacy and Access	Serge Rabier	Equilibres & Populations
4	Advocacy and Access	Joerg Maas	Former DSW, now Gates Foundation
5	Advocacy and Access	Stephen Lewis	Former UN, AIDS Free World
6	Advocacy and Access	Lori Heise	GCM
7	Advocacy and Access	Rebekah Webb	GCM Europe
8	Advocacy and Access	Marc-Andre LeBlanc	GCM, IRMA
9	Advocacy and Access	David Gold	Global Health Strategies
10	Advocacy and Access	Carol Bradford	Independent Consultant
11	Advocacy and Access	Sue Perl	Independent Consultant
12	Advocacy and Access	Marion Zibelli	Planeta Salud
13	Advocacy and Access	Barb Friedland	Pop Council
14	Advocacy and Access	Marth Brady	Pop Council
15	Board	Alex Coutinho	Infectious Disease Institute at Makerere, Univ of Kampala
16	Board	Seth Harrison	Apple Tree Partners
17	Board	Peter Corr	Celtic Therapeutics
18	Board	Helene Rossert-Blavier	Former director, AIDES
19	Board	Els Borst	Former Minister of Health, Welfare and Sport of the Netherlands
20	Board	Anjali Nayyar	PATH India
21	Board	Al Profy	Indevus Pharmaceuticals
22	Board	Rajat Gupta	McKinsey & Co.
23	Board	Anandi Yuvaraj	PATH India
24	Board (former)	Jerry Karabelas	Care Capital
25	Board (former)	Mahmoud Fathalla	Former chair of board
26	Clinical Partner	Marleen Temmerman	Ghent, PI
27	Clinical Partner	Evelyne Kestelyn	Kigali
28	Clinical Partner	Ken Ford	Kigali
29	Clinical Partner	Janneke van de Wijgert	Kigali, PI
30	Clinical Partner	Joseph Vyankandondera	Kigali, PI
31	Clinical Partner	Josh Matambo	Ladysmith, PI
32	Clinical Partner	Philip Kotze	Ladysmith, PI
33	Clinical Partner	Colleen Herman	Massephumehle
34	Clinical Partner	Jennifer Pitt	Massephumehle
35	Clinical Partner	Ntando Yola	Massephumehle
36	Clinical Partner	Linda Gail Bekker	Massephumehle, PI
37	Clinical Partner	Melanie Marais	Mbekweni
38	Clinical Partner	Lize Hellstrom	Mbekweni, PI
39	Community Groups	Ansunet Botha	Ladysmith
40	Community Groups	Jean Blott	Ladysmith
41	Community Groups	Lawrence Schoeman	Ladysmith
42	Community Groups	Mbume Zwane	Ladysmith
43	Community Groups	David Gumenge	Mbekweni
44	Funders	Paul Avontroodt	Belgium
45	Funders	Anne Philpot	DFID
46	Funders	Sue Kinn	DFID
47	Funders	Renee Rizdon	Gates Foundation
48	Funders	Diarmuid McClean	Irish Aid
49	Funders	Marijke Wijnroks	Netherlands
50	Funders	George Brown	Rockefeller
51	Funders	Jeff Spieler	USAID
52	Funders	Lee Claypool	USAID
53	Funders	Robert Oelrichs	World Bank
54	Funders	Sadie Chowdhury	World Bank
55	Industry Partner	Jim Rooney	Gilead
56	Industry Partner	Daria Hazuda	Merck
57	Industry Partner	Mark Feinberg	Merck
58	Industry Partner	Mike Clark	Pfizer
59	Industry Partner	Paul Stoffels	Tibotec
60	Peers	Andy Gray	CAPRISA
61	Peers	Quarraisha Abdul Karim	CAPRISA
62	Peers	Henry Gabelnick	CONRAD
63	Peers	Marianne Callahan	CONRAD
64	Peers	Michael Makanga	EDCTP
65	Peers	Thomas Nyirenda	EDCTP
66	Peers	Jessica Price	FHI Rwanda
67	Peers	Abboud	IAVI
68	Peers	Jean-Louis Excler	IAVI
69	Peers	Paul Wilson	IAVI
70	Peers	Seth Berkeley	IAVI



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### External Interviewees Con't

Row	Type	Name	Organization
71	Peers	Alan Stone	International Working Group on Microbicides
72	Peers	Sheena McCormack	MDP
73	Peers	Anna Wang	MMV
74	Peers	Renia Coghlan	MMV
75	Peers	Andrew Nunn	MRC
76	Peers	Ben Masse	MTN
77	Peers	Jim Turpin	NIAID
78	Peers	Chris Elias	PATH
79	Peers	Scott Jackson	PATH
80	Peers	Etienne Karita	Projet SF
81	Peers	Kayitesi Kayitenkore	Projet SF
82	Peers	Kevin Whaley	ReProtect
83	Peers	Ian Sanne	Right for Care
84	Peers	Michelle Galloway	SAAVI
85	Peers	Michael Kramer	TRAC Plus
86	Peers	Mugabo Jules	TRAC Plus
87	Peers	Janet Darbyshire	UK MRC
88	Peers	Tim Farley	WHO
89	SAB	Mark Wainberg	AIDS Centre
90	SAB	Joep Lange	University of Amsterdam
91	SAB	John Mellors	University of Pittsburgh, MTN
92	SAB Exec	Lynn Paxton	CDC
93	SAB Exec	Gustavo Doncel	CONRAD
94	SAB Exec	Ben Chang	George Washington University
95	SAB Exec	Martin Springer	Merck (former)
96	SAB Exec	Gita Ramjee	MRC
97	SAB Exec	Ruth Merkatz	Pop Council
98	SAB Exec	Tom Moench	ReProtect
99	SAB Exec	Robin Shattock	St. George's, University of London
100	SAB Exec	Sharon Hillier	University of Pittsburgh, MTN
101	SAB Exec	Richard Bax	ViroPharma

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## E. Abbreviations

AMAG	African Microbicides Advocacy Group
AMD	Alliance for Microbicide Development
CAPRISA	Centre for the AIDS Programme of Research of South Africa
CDC	Centers for Disease Control
CEO	Chief executive officer
CMO	Chief medical officer
CRA	Clinical research associate
CRO	Clinical research organization
CSO	Chief scientific officer
DMA	Directly Monitored Adherence
DNDi	Drugs of Neglected Diseases initiative
EMA	European Medicines Agency
FDA	United States Food and Drug Administration
FSG	FSG Social Impact Advisors
GCM	Global Campaign for Microbicides
GCP	Good clinical practice
GMP	Global Microbicide Project
HIV	Human immunodeficiency virus
IAVI	International AIDS Vaccine Initiative
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
IND	Investigational New Drug Application
IPM	International Partnership for Microbicides
MAF	Microbicides Access Forum
MCC	Medicines Control Council of South Africa
MDS	Microbicide Development Strategy
MMCI	Microbicides Media and Communication Initiative
MMV	Medicines for Malaria Venture
MRC	Medical Research Council, UK
MVI	Malaria Vaccine Initiative
NDA	New Drug Application
NGO	Non-governmental organization
NIH	National Institutes of Health
PDP	Product Development Partnership
R&D	Research and development
SAB	Scientific Advisory Board
SAB EC	Executive Committee of the Scientific Advisory Board
SOP	Standard operating procedure
STI	Sexually transmitted Diseases
TPP	Target product profile
UNGASS	United Nations General Assembly
WHO	World Health Organization