INTERNATIONAL PARTNERSHIP *for* MICROBICIDES

IPM Evaluation Report
Management Response

October 2008

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Public and private donors to the International Partnership for Microbicides (IPM) initiated an evaluation of IPM at year five as part of their governance responsibilities. IPM is grateful to its donors and to the evaluation team for their careful and thoughtful review, which was completed in June 2008.

The evaluation found that IPM "has contributed significantly toward the goal of developing safe and effective microbicides." Furthermore, the evaluation found that "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." Dr. Diarmuid McClean, who chaired the evaluation on behalf of the broader donor community, stated that "After thoroughly examining IPM's work—from its strategic direction to its operating systems, and myriad aspects of its research in between—the evaluation concludes that IPM has recorded impressive accomplishments and has positioned itself well to reach its research goals of developing safe and effective microbicides to prevent HIV."

The evaluation contains recommendations to strengthen IPM and provide the highest probability for success in achieving its mission. IPM agrees with the evaluation findings overall and will make every effort to implement the recommendations meaningfully in support of its mission. Given the range of recommendations, IPM will prioritize these efforts in the most appropriate and effective way.

This document outlines specific steps IPM will take to address donor recommendations and build upon successes achieved since the organisation was founded in 2002.

Recommendations and Responses

- Module A: Portfolio and Product Development

Recommendation: Formalize Portfolio Management Processes
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.

Response: IPM established a new structure to formalize drug portfolio management and has implemented the decision-making process defined in the document Terms of Reference for IPM Product Development Management. This document establishes a Development Committee, which governs the process, and Product Teams, and it describes the relationship of the committee and the teams to IPM's departments that support their work. These departments include Research and Development, Clinical Affairs, Manufacturing and External Relations.

The Development Committee makes high-level strategic decisions and determines whether and how Product Teams are formed. Product Teams create and implement the product development plan; create and update the design control, the target product profile, and the development plans (annually or when major deviations occur); identify and communicate risks to the Development Committee; and recommend changes to the broader product development strategy, if necessary.

The Development Committee and the first Product Team, the Dapivirine Gel/Ring Product Team, were officially formed on 1 July 2008. The Development Committee will create additional Product Teams in 2009.

Recommendation: Increase Engagement with the Scientific Advisory Board
IPM should take steps to ensure that the SAB EC (Scientific Advisory Board Executive Committee) 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.

Response: IPM is developing plans to restructure and strengthen its SAB and the SAB executive committee. IPM's scientific leadership and its SAB chair hope to formalize recommendations regarding a new SAB structure in the coming months.

- Module B: Clinical Trials

Recommendation: Review Phase III Timeline
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 centres.

Response: IPM agrees, and expects to begin its initial Phase III study in 2011.

The timeline for the initial Phase III study has been affected by several factors:

- Increased attention and scrutiny from regulatory and ethics bodies, as well as other stakeholders. Because of disappointing results from HIV prevention research generally—and early generation microbicides and vaccines specifically—safety studies, acceptability studies, and even incidence studies are receiving increased scrutiny. As a result, significant delays in protocol review and approvals have occurred.
- Product development and manufacturing challenges. In addition to gel dosage forms, IPM has been focusing heavily on the development of a silicone vaginal ring containing dapivirine as a microbicide product. Initial clinical studies were successfully conducted with silicone rings fabricated via a specific silicone chemistry system that was not stable long term with dapivirine, nor would it lend itself well to scale-up manufacturing. Consequently, IPM had to reconfigure its dapivirine ring chemistry and manufacturing processes. The limited manufacturing options for rings at contract manufacturing organisations also dictated the need to set up ring production in-house at IPM's Clinical Trial Material facility. Investing in

infrastructure and modifying the ring production process have added to the ring development timeline.

- Development by IPM of an adaptive two-stage microbicide clinical trial design for Phase III. The first stage will start with multiple candidate products and use early review of the data to identify the single best candidate product whose safety and efficacy will be formally evaluated in the second stage. The second stage will also feature an adaptive component—monitoring through futility stopping rules based on conditional power. Rather than setting up separate Phase II and III studies, this adaptive approach allows IPM to seamlessly continue enrolment and follow-up between Phase II and Phase III. This continuity could offer several advantages, including a single regulatory and ethics approval process, and retention of experienced site staff.
- Efforts to monitor adherence to protocols. In addition to the adaptive trial design, IPM is currently piloting a directly monitored adherence strategy to address the critical issues of adherence identified in previous Phase III trials of early microbicide candidates.

Thus, for the reasons outlined here and to ensure sufficient preparation time both for IPM's clinical team and clinical research centres, IPM's Phase III timeline has been adjusted.

Recommendation: Strengthen the Clinical Team
IPM should engage additional experienced clinical trial managers, CRAs (Clinical Research Associates), and a senior clinical research physician to better support the CMO (Chief Medical Officer). IPM should also consider increasing QC (Quality Control) capacity, implementing mentoring between experienced, proven investigators and new research centres. IPM should explore leveraging its partnerships with pharmaceutical companies, who may be willing to consider loaning experienced staff or offering greater technical assistance.

Response: IPM agrees, and is engaged in attracting additional expertise to the clinical team. IPM has based its clinical program in South Africa near its trial sites, and this presents unique challenges for recruitment. IPM hired a dedicated in-house recruiter in the South Africa office and is recruiting for a Chief Human Resources Officer in Silver Spring to accelerate the process.

IPM plans to strengthen the Clinical Affairs team by:

- Recruiting an Executive Director of Clinical Affairs, a senior level clinical physician to serve as the deputy to the Chief Medical Officer. This search is being conducted broadly and is seeking to identify professionals from pharmaceutical, contract research organisations (CROs), and other medical research organisations.
- Filling key positions such as Director for Project Management, Clinical Project Manager, Director of Clinical Affairs Operations, Director of Social and Behaviour Science, Clinical Program Director, Phase I and II, and Clinical Program Director, Phase III.
- Recruiting for Project Managers for the Site Development, Community Engagement, and Operations and Safety teams.
- Recruiting CRAs. Three experienced CRAs have recently been appointed as Associate Project Managers. A Project Manager training program will be implemented under the mentorship of an experienced Project Manager.

In the area of quality control, IPM has standardized the internal quality control process and is building local quality assurance (QA) capacity to support IPM clinical efforts. In South Africa IPM hired a Clinical Quality Assurance Manager and a Clinical Quality Assurance Associate. IPM is also building QA capacity at the CTM facility in Bethlehem, Pennsylvania.

IPM agrees that it is appropriate to "explore leveraging its partnerships with pharmaceutical companies, who may be willing to consider loaning experienced staff or offering greater technical assistance" and is discussing various arrangements, including secondments of clinical experts with several of its pharmaceutical partners.

On a related note, IPM has a search under way for a Chief Scientific Officer. In addition to the Chief Medical Officer, this position will be available to offer expertise and leadership to the clinical team.

Recommendation: Establishing High-Quality New Clinical Research Centres
IPM should ensure that criteria and decision-making for identifying clinical research centres (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.

Response: By way of context, IPM had identified early on the need to expand and strengthen the infrastructure and capacity of clinical research centres in developing countries, especially those in high HIV incidence settings, to support its product development efforts. IPM's Site Development Team, based at the South Africa office, established an operational platform that identifies and standardizes vendor supply between research centres and countries, sets standard operating procedures and monitors progress. IPM's has formulated detailed criteria for identification of new or established clinical research centres.

The Site Development Team has identified at least 15 potential safety and/or efficacy research centres in Kenya, Malawi, Rwanda, South Africa, Tanzania, and Zimbabwe. It will continue to evaluate potential clinical research centres in Mozambique, Zambia and elsewhere through visits and on-site assessments. Other countries may also be added to the list of potential sites. The team expects to work with 25–30 research centres at any given time in order to ensure that approximately 15 research centres are qualified to support the proposed Phase II/III study. IPM collaborates with others in the microbicide field and other research areas to ensure the most cost-efficient utilization of research centres.

IPM is committed to the participation of local communities prior to, during, and after clinical trials. IPM has developed and is implementing a detailed community engagement plan, recognizing and taking into consideration the varying levels of development of the research centres. While some centres are experienced and have highly developed community engagement programs, IPM will focus on bringing the capacity of new research centres up to the level of the more experienced ones. This will be achieved through training in early formative research and

community mapping, community engagement and education, and participant recruitment and retention strategies.

Opportunities will also be created for information exchange and sharing lessons among the centres through regular multicentre workshops and a new website launched by IPM that includes information designed for and by the research centres. The website, which is password-protected, contains a wide range of essential information about site development, community engagement, clinical safety, external relations, key trainings and events, as well as specific study protocol materials.

Capacity building at the clinical research centres has recently been expanded to include communications support. A recent needs assessment by IPM revealed that most research centres require help with routine communications such as preparing presentations and documents for local ethics committees and other key stakeholders, as well as with risk and crisis communication strategies. Because of the complexities of communicating with multiple constituencies involved in clinical trials, from study participants to local and national leaders to media and advocates, IPM's communications support to the selected clinical research centres will be a key element of technical support.

Recommendation: Strengthen Clinical Partnerships
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.

Response: IPM recognizes the value of investing in sustained and deepening relationships with clinical research partners, policy-makers, community leaders, advocates, the media and other local stakeholders to create an enabling environment in the countries and communities hosting studies. IPM's Country & Trial Support Work Plan for 2008-09 outlines IPM's strategy for strengthening advocacy and encouraging supportive policies for microbicide development in Africa and elsewhere. The work plan highlights, among other activities, ongoing and planned efforts to strengthen IPM's relationships with clinical partners, governments, and communities. IPM recognizes that its clinical partnerships need to be flexible to respond to events that affect microbicide development. Illustrative ongoing and planned activities include:

- Recruitment of an External Relations Advisor to be based in Southern Africa: This advisor will support IPM's regional and country outreach, advocacy and stakeholder engagement. The ideal candidate will be a public health professional with political and advocacy skills.

- Greater involvement, consultation and training of IPM clinical partners through trainings and conferences, including IPM annual clinical meetings. IPM's second annual meeting was held in Cape Town in September 2008. All IPM research centres were represented, as well as other partners working in the field of HIV prevention research. A variety of technical workshops and trainings were conducted.

- Development of the password-protected website for clinical research centres (please see the response to the previous recommendation: Establishing High-Quality New Clinical Research Centres).

- Meetings and briefings with government officials and regulatory/ethics committees when appropriate and requested: IPM continues to conduct face-to-face meetings and briefings with government officials and stakeholders in countries hosting microbicide studies, particularly in Africa. Many of these meetings are conducted in connection and in consultation with IPM clinical investigators. IPM will continue to pursue these types of meetings.

- Increased support for community engagement efforts: IPM has created a Community Engagement Guidance Document and is assisting in the process of developing customized research centre plans for community engagement. These plans will be implemented and evaluated on a yearly basis, with special focus on communications in the community, and on general education of potential trial participants and the community at large.

- Continued involvement in the Microbicides Media and Communications Initiative (MMCI): IPM is an active member of the MMCI and is represented on the steering committee. This communications network seeks to unite both clinical and communications/advocacy partners working on microbicide and HIV prevention research.

As noted in the response to the previous recommendation, IPM has expanded capacity building at the clinical research centres to include communications support.

Recommendation: Strengthen Clinical Trial Processes
IPM should enhance clinical trial processes with clinical development plans and harmonise core and trial specific Standard Operating Procedures (SOPs) across research centres to ensure uniform application of ICH GCP procedures.

Response: IPM recognizes the need to continue to strengthen and harmonise clinical trial processes according to Good Clinical Practice (GCP) procedures established by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). Over the past several years, IPM has been working to improve the standardization of the processes for preparing and monitoring clinical trials. Protocol teams frequently share best practices and lessons learned to ensure standardization between different protocols, team members and research teams. Going forward, clinical development plans will be an important part of the work of the formal portfolio management process within the Development Committee and Product Teams (please see the response to the first recommendation, Formalize Portfolio Management Processes).

Recommendation: Strengthen Country-level Communications
IPM should continue to support advocacy and communication efforts at the country level for

Recommendation: Strengthen Country-level Communications
trial execution, and should continue conducting due diligence on the advocacy "funding window".

Response: IPM understands the need to strengthen its advocacy and communication capacity in Africa and elsewhere to ensure that trials are managed as efficiently and transparently as possible, and to mitigate potential risks related to clinical trials. IPM is in the process of expanding its network of key stakeholders and partners, and strengthening plans to generate information to develop appropriate strategies, including communication and media plans.

Plans described in responses to previous recommendations will also help to strengthen country-level communication, for example, strengthening clinical partnerships and engagement with local communities. Other activities include hiring a Clinical Communication Officer to produce posters, documents, brochures, and presentations that support the trial process; working with experts in South Africa and elsewhere to provide strategic guidance on communicating in the local political context; and strengthening IPM's ongoing efforts to build an enabling environment for effective advocacy.

IPM has not received formal clarification from advocates regarding the establishment of a "funding window" and is continuing to conduct due diligence on the issue.

- Module C: Access

Recommendation: Define Explicit Access Criteria
As part of developing a Target Product Profile (TPP), IPM should explicitly define the access criteria that feed into product prioritization and development decisions.

Response: IPM has previously defined five "access" criteria that can help address challenges to delivering microbicide products and supporting their use: *Availability*—Sufficient high-quality supply of a safe and effective microbicide to meet user demand, which cannot be assumed and needs to be generated; *Accessibility*—Reliable channels to distribute microbicides to service points that are close to intended target populations; *Acceptability*—Acceptable formulations and delivery systems for end users and gatekeepers (e.g., policy makers and health professionals) who control availability; *Affordability*—Products and delivery programs that are affordable, with sufficient available financing (public and/or private); and *Appropriate use*—Microbicides that can be used appropriately as part of personal and programmatic strategies to prevent HIV transmission.

To inform the development of a TPP, IPM is further defining, specifying and operationalizing these five criteria. The expanded criteria will also inform go/no-go decision-making and the prioritization of products competing for development and approval (see Annex 1). For example, the expanded "availability" criteria comprise four definitions: Define the minimal acceptable efficacy level when the product is used with a high level of adherence; define the minimal

acceptable average adherence levels under the assumption of direct consumer education; define the maximal acceptable level of safety issues and define specific unacceptable safety issues; and define the maximal acceptable level of regular clinical management needed in the care of women using the product.

IPM appreciates the need to explicitly define the access criteria that feed into product prioritization and development decisions as part of developing TPPs.

Recommendation: Begin Planning for Manufacture, Scale-up, and Distribution
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.

Response: IPM has recognized the need to grow manufacturing capacity. Prior to 2008, the Research and Development department managed manufacturing with a focus on supporting early product development. In 2008 IPM formed a separate Manufacturing Department and hired an experienced director from the pharmaceutical industry. IPM is early enough in its product development life cycle to incorporate the concepts of quality by design that the pharmaceutical industry is now embracing. This risk management approach will streamline the optimization and scale-up activities associated with the product development activities. Furthermore, the manufacturing group will implement a formal production forecasting process. Initially, however, it will incorporate several launch scenarios for which the initial manufacturing and distribution strategy will be written. Over the next 18 months as the group forms and hires additional staff and as the Phase III initiation approaches, the manufacturing plan will be refined to support registration and launch.

Recommendation: Clearly Communicate Plans for the Access Program
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.

Response: Ensuring access is a cornerstone of IPM's drug development process. Since 2004 IPM has obtained several non-exclusive royalty-free licenses from pharmaceutical companies to develop, manufacture and distribute antiretroviral compounds as microbicides in developing countries. Once an effective microbicide is developed, these licensing agreements give IPM the full rights to distribute that product at no or low cost in resource poor countries, as well as emerging market countries such as Brazil, China and India. IPM also integrates acceptability studies into its product development program.

In addition, from its inception, IPM has had a strong program of policy research related to access, including modelling and mapping studies and early planning and introduction scenarios. Going forward, and especially once "proof of concept" is established for ARV-based

microbicides to prevent HIV, IPM will need to establish not-for-profit commercialization and marketing strategies, capacities and expertise. Given current timelines, IPM could be contributing to the regulatory and early access strategy for the first ARV-based microbicide with proof of concept (tenofovir) at the same time that it is undertaking the initial efficacy study of dapivirine. This would be a welcome confluence of events. IPM is heeding lessons learned from the introduction of a variety of other health technologies, including other "first in class" product introduction efforts such as AIDS treatment therapies, and lessons learned in the reproductive health area regarding product introductions.

IPM collaborates and communicates with the field on access issues in a variety of ways. For example, IPM annually convenes a Microbicide Access Forum, having cosponsored the first microbicide access forum with WHO and the U.S. Agency for International Development (USAID) in 2007 in Nairobi, Kenya, and a second one in 2008 at the International AIDS Conference in Mexico City with WHO, the European Community, the Population Council, and USAID. The objectives of the fora are to share information and collaborate to facilitate access to microbicides; provide an update on microbicide development and introduction timelines to access stakeholders; review and adopt lessons from the introduction of other relevant health commodities; review acceptability studies of microbicides and other related products; provide a forum to discuss results and the role of microbicide introduction modelling; and share lessons on managing expectations at the community level.

IPM appreciates the need to clearly communicate its continued commitment to access issues going forward, especially as its access strategy and capacity evolve.

- Module D: Advocacy

Recommendation: 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.

Response: IPM is committed to continuing to identify opportunities to increase the visibility of microbicides as a promising new HIV prevention tool among donors, advocates, policymakers and the media globally. IPM recognizes that it is in a unique position to help draw attention to these issues. IPM will continue to participate in appropriate platforms, including plenary or large panel sessions at key health and international development conferences; continued advocacy through diplomatic and other channels; and increased focus on press coverage of microbicide development to help ensure that the microbicide development agenda is conveyed to relevant audiences.

Recommendation: 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.

Response: IPM's advocacy program is based on understanding the regional, national and local context in which its work is taking place, as well as regularly gauging the overall political and policy environment of donors, countries supporting clinical studies, and other key stakeholders. IPM agrees with the need to enhance efforts to strengthen its relationships with key decision makers, stakeholders and current and potential civil society partners. IPM's activities in this area will be strengthened and coordinated between its offices in South Africa, Belgium and the U.S., and in consultation with its governmental and civil society partners.

IPM's has established a significant number of formal partnerships with nongovernmental organisations. These organisations have cultivated strong allies for microbicide development in their respective regions, and IPM values these relationships enormously. IPM agrees that every effort should be made to strengthen these relationships and ensure meaningful support and engagement.

IPM has identified the need to develop a range of communication tools to meet the varying information needs of diverse stakeholders around issues of ARV-based "next generation" microbicides. In preparing training sessions, briefings, consultations and dialogue, and providing networking opportunities at international conferences/events, IPM will work with its partners and coordinate with existing organisations such as the MMCI, the AIDS Vaccine Advocacy Coalition, the Global Campaign for Microbicides and others.

Recommendation: 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.

Response: IPM recognizes its responsibility to advocate for microbicide development, and will seek opportunities to do so in balance with advocacy for IPM's own priorities and agenda. Because of its size, IPM also appreciates the risk that its messages may be presumed to be those of the entire field. IPM remains committed to distinguishing between the two.

- Module E: Organisational Effectiveness

Recommendation: Develop Updated Five-year Strategic Plan
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.

Response*:* IPM has begun a process of strategic planning through 2015. The plan will incorporate recommendations from the evaluation and additional priorities for IPM as the organisation prepares to initiate efficacy studies and plan for eventual product access of a

microbicide if proven effective. The plan will address product and portfolio management; capacity management and resourcing; and execution of product development, clinical studies, and manufacturing and distribution. In September 2008 IPM senior management attended a retreat facilitated by the Boston Consulting Group, which worked with the Rockefeller Foundation in 2002 to help write the first IPM business plan. A new strategic plan is expected by spring 2009.

Recommendation: 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.

Response: Unrestricted funding has been critical to supporting IPM's successes over the past five years. Unrestricted funding allows IPM to make timely, data-based decisions regarding product development, site development and clinical studies. Restricted funding limits IPM's ability to allocate resources to the most promising initiatives and increases operational, reporting and accounting requirements. As IPM intensifies its research and development efforts and clinical studies, and moves closer to its large-scale Phase III efficacy trial, IPM will perform best if donor contributions remain unrestricted and in support of the overall mission and core work plan of the organisation.

To this end, IPM will continue to prioritize accountability for donor funds through strong governance by the Board of Directors and further engagement of the Scientific Advisory Board. IPM will also continue to directly engage with donors through regular donor country visits for meetings with government officials and other key stakeholders; the Annual Donors Meeting; and comprehensive semi-annual donor reports on activities, progress and challenges. IPM is in a strong financial position based on its success in mobilizing over US$235 million (€175 million) in support of its mission from a diverse donor base of governments, multilateral organisations and foundations. Ensuring that IPM is a good steward of donor funds entrusted to the organisation and mission continues to be one of IPM's highest priorities.

Recommendation: Improve Communication with Partners
IPM should consider processes for better communication of plans and priorities with key partners.

Response: IPM builds on partnerships at every level—with governments, foundations, universities, researchers, industry, policymakers, advocates and, most especially, with women living in communities most affected by HIV. IPM highly values these partnerships and agrees that every effort should be made to ensure that strong communication channels are maintained so that the organisation's strategies, plans and priorities are regularly shared with key partners. Throughout the organisation, greater effort is being made to ensure appropriate communication

with IPM collaborators. For example, the expansion of the Research and Development team has allowed more face-to-face communication with key partners. New staff are now dedicated to external project management, alliance management, and business development with key partners. And, as noted earlier in this document, IPM is recruiting additional clinical staff, including a clinical communication specialist, to improve communication with key partners supporting clinical trials. IPM's efforts to strengthen community engagement will improve communication in areas where clinical trials are being conducted. IPM will continue working with advocacy partners through training sessions, briefings, and consultations.

In short, IPM recognizes that its partners commit significant time and resources to supporting microbicide development on multiple levels. Collaboration fuels IPM's work and advances the microbicide field. IPM will continue to strengthen efforts across the organisation and externally to ensure ongoing and appropriate communication and dialogue with its partners.

Annex 1

Expanded Access Criteria for Product Prioritization and Development Decisions

The five access criteria are availability, accessibility, acceptability, affordability, and appropriate use. The expanded definitions of these criteria are:

- Availability
    - Define minimal preventive efficacy level acceptable when the product is used with high level of adherence.
    - Define minimal average adherence levels acceptable under the assumption of direct consumer education.
    - Define maximal level of safety issues tolerable and define specific non-tolerable safety issues.
    - Define maximal level of regular clinical management acceptable, needed in the care of women using the product.
- Accessibility
    - Define maximal acceptable distribution barriers to use.
        - Under the assumption that an antiretroviral-based microbicide is both a medical device and a medicine, simple distribution pathways, like those used for condoms, might not be possible.
        - Need to define unacceptable access and control mechanisms for the successful implementation of microbicide use.
    - Define minimal acceptable distribution outreach level.
        - Under the assumption that a large part of the female population in need of a microbicide does not have regular access to medicines, mechanisms to overcome these barriers need to be described.
- Acceptability
    - Define minimal everyday user acceptability levels (e.g., percentage of women using the product regularly, when products provided and user is educated).
    - Define specific product characteristics that are associated with high user acceptability and high gatekeeper acceptability.
- Affordability
    - Define maximal acceptable price for consumer.
    - Define maximal acceptable third-party payer's subsidy per annual supply per woman.
    - Define maximal acceptable cost of goods per annual supply per woman.
- Appropriate use
    - Define maximal acceptable level of necessary user education.
        - For example, the level of training needed to safely self-administer insulin for diabetes would not be acceptable for microbicides.
    - Define maximal tolerable level of misuse when direct consumer education is available.