

The future of multipurpose prevention technology product strategies: understanding the market in parallel with product development

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The development of multipurpose prevention technology (MPT) products for combined protection against sexually transmitted infections (STIs), including HIV, and unintended pregnancy is a priority. MPTs have a number of potential benefits over single-indication products and could provide meaningful health benefits for individuals and at a public health population level. Co-formulated or co-administered products that address multiple unmet sexual and reproductive health needs for women in resource-constrained parts of the world could offer meaningful advantages over single-product/single-indication strategies. For example, women seeking contraception and HIV prevention would probably prefer a single product to address both indications. By leveraging the pre-existing acceptability and demand for specific contraceptive product dosage forms, co-formulated or co-administered products addressing two indications may be more readily introduced into appropriate target populations than products that only provide a single type of prevention. Women with a greater perceived risk of pregnancy could opt to use an MPT primarily for contraceptive purposes and receive the benefit of the STI prevention indication as well. Similarly, women concerned about potential stigma within their families or communities associated with using HIV prevention products could be more inclined to use an MPT contraceptive product that also provides discreet protection against HIV.

In addition to likely consumer acceptability and desirability advantages, there are also potential delivery and cost efficiencies with single-product entities that address multiple sexual and reproductive health needs. For example, a single vaginal ring that delivers anti-retroviral drugs to prevent HIV infection and hormonal contraceptives to prevent pregnancy could be more efficient and cost effective to

produce and deliver to the end user than separate products for each indication. Even with the risk of a higher cost of goods for an MPT relative to single-indication products, the cost benefit of an MPT could still be realised because most of the fully burdened costs are associated with delivery and access to products and such costs would be reduced with a single product addressing multiple indications.

At present, the possible benefits of MPT products are hypothetical and early-stage MPT product development is ongoing under these assumed advantages. Although these proposed benefits are plausible, data confirming the positive public health impact potential of MPT products from a commercial perspective are lacking. Proper development and clinical evaluation adequate for regulatory approval are necessary for successful MPT commercialisation; however, regulatory licensure alone will not be sufficient to achieve high public health impact. For example, the female condom has been approved by regulatory agencies, and this barrier method should be an effective MPT. However, this method has struggled to achieve high levels of uptake in target populations.¹ Therefore, understanding user preferences, acceptability and uptake of products early in development, along with well-funded efforts to develop product markets, are as important as regulatory licensure.

For new reproductive health products to have a meaningful public health impact, it is crucial that product development from the earliest stages be informed by the critical market factors that will ultimately determine their successful delivery, access, uptake and proper long-term use. For MPT products, the key market groups that need to be understood include the product end-users, the healthcare providers, local country health ministries and procurement

organisations, who each have a unique set of considerations in terms of product design, performance, cost, access and use.

Parallel product development and market assessment

The parallel application of product development and market assessment strategies is standard practice in the pharmaceutical industry and is just as relevant in the development of public health products. When product development is appropriately informed of market requirements, successful launch and commercialisation of the resulting licensed product is more readily achieved. Failure to adequately assess market issues and to incorporate market data into product development could have negative effects on commercialisation. A noteworthy instance of such an outcome is the case of Exubra[®], the inhalable insulin product developed by Pfizer (New York, NY, USA), and approved in 2006.^{2,3} Despite its approval and perceived advantages over injectable insulin, Pfizer withdrew the product from the market in 2007, citing a lack of acceptability by patients and providers.⁴ Although positive acceptability data were obtained for Exubra[®] in early clinical trials,⁵ other analyses suggested limitations in previous acceptability studies, as well as cost issues that made this a less attractive option.⁶ Ultimately, this resulted in the loss of US \$2.8 billion of development and marketing investments by the parent company for this product.⁴

The MPT field is similarly at risk from the consequences of product development that is not sufficiently informed by acceptability and other types of market data. For example, despite recent successes with oral Truvada[®] (Gilead Sciences Inc., Foster City, CA, USA) in HIV pre-exposure prophylaxis efficacy trials involving MSM⁷ and serodiscordant couples,⁸ the magnitude and duration of any positive public health impact of this product remains unknown and will be based largely on the willingness of people at risk for HIV to acknowledge their risk and adhere to the proper use of anti-retroviral drugs for prevention. The clinical successes resulting from these oral pre-exposure prophylaxis strategies may be limited to specific populations comprised of individuals who know and recognise their risk, such as people living within serodiscordant relationships. Studies testing the same products in broader populations of HIV-negative women who did not necessarily know the HIV status of their partners failed to demonstrate efficacy because of low adherence with the study products even though the women agreed to use the products and received monthly counselling.^{9,10} These results may suggest potential acceptability issues with this particular product (or generally with daily oral dosage forms) in these specific popula-

tions. Whether poor adherence to these drugs was the result of concerns about potential adverse effects of the product, stigma associated with the use of anti-retroviral drugs, low perceived risk of HIV infection, the potential randomisation to the placebo group, the benefits of being in a trial without regard for adherence, or social and cultural factors is unknown. While work continues to better understand the underlying causes of the nonadherence outcomes in these studies, these results emphasise the need to fully explore the desirability of such products for public health markets early in development.

It is important to avoid using assumptions regarding the target market in product development and the same applies to MPT development going forward. First, it must be recognised that medical *need* and population *demand* for a product are governed by different forces. Mortality and morbidity statistics and economic impact calculations can justify product need, but successful commercialisation is ultimately determined by more complex market factors. Modelling the cost per HIV infection or pregnancy averted by an MPT at a population level relative to public health and economic consequences could show impressive positive impact. However, this impact can only be achieved if the cost is acceptable to the procuring organisations, if the product is accessible through appropriate delivery channels, and is desired by users. Second, assuming that a product will be used simply because it is shown to be safe, efficacious and available is risky. For example, the adverse effect profile for an MPT product may be acceptable to regulatory bodies, but unacceptable to the target population. MPT products containing hormonal contraceptives that employ alternative dosing regimens could have different effects on bleeding patterns,¹¹ which may have varying degrees of acceptability in diverse populations of women. Although typically not a safety issue, this could be a marketing challenge for a product intended for global distribution among users with different lifestyle effects associated with menses. Hence, data-based understanding of the diverse market factors relevant to all aspects of potential MPT products and the avoidance of intuitively attractive assumptions will be critical to the successful development of MPT products.

How can the dual needs for high-quality technical or clinical development and accurate, comprehensive market data be satisfied for MPT products? Early development of a robust target product profile (TPP) that appropriately defines the necessary MPT label claims and the requisite data necessary to achieve those label claims would be an important first step. Guidance on format and content for an appropriate TPP is available from the United States Food and Drug Administration.¹² An appropriate TPP defines the quality (chemistry, manufacture, control, or 'CMC'), preclinical safety and pharmacokinetics or pharmacodynamics, and the necessary clinical data required

for licensure. It is important to assure that the product attributes addressed in the TPP are also acceptable to the intended users of the products. Failure to appropriately capture market forces in the details of the TPP could result in a licensed product that no one chooses to buy, provide or use.

Incorporating relevant market factors into a TPP represents an expansion in scope as proposed by Tebbey and Rink.³ Here, an overall 'Strategic Evaluation Framework', which partners a traditional TPP with the additional requirements to satisfy market needs, is described. This framework, if supported by robust data, can serve as the primary means of making go or no go decisions during product development, from both technical or clinical and market perspectives. Importantly, modifications to the TPP during the course of product development should be considered with caution. Revising a TPP to accommodate technical limitations that are identified during the course of development could lead to development of a final product that has deviated from the market requirements that were defined earlier. Hence, the TPP must be developed in the context of an overall strategy that is consistent with market needs.

Of course, successful partnering of technical and market assessments in MPT development requires effective means of achieving both. Regulatory and international guidelines are available to address technical and clinical development; however, there are no comparable formal mechanisms for assessing market drivers. Approaches that provide quantitative and reliable market data on user preferences such as cross over design clinical trials to determine acceptability of alternative dosage form options¹³ should be a part of MPT product development going forward. Conjoint analysis in the assessment of product attributes and user preferences has been used in the past to evaluate HIV prevention products,¹⁴ and along with discreet choice experiments¹⁵ represent other important options for market assessment of MPT products.¹⁶ Provider concerns, and local country and procurement organisation requirements are also crucial market drivers in product development and should be an area of focus by the broader MPT field through direct dialogue. Traditionally, product acceptability and other types of market assessments have been underfunded relative to technical and clinical development. Acknowledging the importance of robust market assessments will require greater funder commitment to the study of these key variables.

Conclusion

Realising the high potential of MPT products will require careful and comprehensive planning that is informed by technical, clinical and market data. In an era of limited resources for the development of public health products, investment and development decisions for MPT products

must be as comprehensively informed as possible. Product development in the absence of proper market assessment data is risky and could make specific MPT product investment difficult to justify. Hence, the challenges to obtaining and using accurate market data in MPT product development must be addressed.

Disclosure of interests

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