BioOne COMPLETE

Bridging the gap: advancing multipurpose prevention technologies from the lab into the hands of women†

Authors: Holt, Bethany Young, Kiarie, James, Kopf, Gregory S., Nanda, Kavita, Hemmerling, Anke, et al.

Source: Biology of Reproduction, 103(2) : 286-288

Published By: Society for the Study of Reproduction

URL: https://doi.org/10.1093/biolre/ioaa085

BioOne Complete (complete.BioOne.org) is a full-text database of 200 subscribed and open-access titles in the biological, ecological, and environmental sciences published by nonprofit societies, associations, museums, institutions, and presses.

Your use of this PDF, the BioOne Complete website, and all posted and associated content indicates your acceptance of BioOne's Terms of Use, available at www.bioone.org/terms-of-use.

Usage of BioOne Complete content is strictly limited to personal, educational, and non - commercial use. Commercial inquiries or rights and permissions requests should be directed to the individual publisher as copyright holder.

BioOne sees sustainable scholarly publishing as an inherently collaborative enterprise connecting authors, nonprofit publishers, academic institutions, research libraries, and research funders in the common goal of maximizing access to critical research.

Downloaded From: https://bioone.org/journals/Biology-of-Reproduction on 11 Oct 2024
Terms of Use: https://bioone.org/terms-of-use

Biology of Reproduction, 2020, 103(2), 286–288
doi:10.1093/biolre/ioaa085
Contraceptive Special Issue
Advance Access Publication Date: 27 May 2020

OXFORD

Contraceptive Special Issue

Bridging the gap: advancing multipurpose prevention technologies from the lab into the hands of women†

Bethany Young Holt[1,*], James Kiarie[2], Gregory S. Kopf[3], Kavita Nanda[3], Anke Hemmerling[1,4] and Sharon L. Achilles[5,6]

[1]Initiative for Multipurpose Prevention Technologies, CAMI Health, Public Health Institute, Sacramento, California, USA, [2]UNDP-UNFPA-UNICEF-WHO-World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP), World Health Organization, Geneva, Switzerland, [3]Reproductive Health Product Innovation & Introduction, FHI 360, Durham, North Carolina, USA, [4]Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, California, USA, [5]Department of Obstetrics, Gynecology, and Reproductive Sciences, University of Pittsburgh, Pittsburgh, Pennsylvania, USA and [6] Magee-Womens Research Institute, Pittsburgh, Pennsylvania, USA

***Correspondence:** Initiative for Multipurpose Prevention Technologies, CAMI Health, Public Health Institute, 1750 Howe Avenue #550, Sacramento, CA 95825, USA. Tel: +9163370967; E-mail: byh@cami-health.org

†**Grant Support:** Support for this work was provided by the American people and the United States Agency for International Development under the terms of Cooperative Agreement no. AID-OAA-A-16-00045 and funding through an Inter-Agency Agreement with the National Institutes of Health.

Received 10 March 2020; Revised 19 May 2020; Accepted 25 May 2020

Multipurpose prevention technologies (MPTs) are being designed to deliver multifaceted reproductive health prevention, largely focused on contraception and prevention of human immunodeficiency virus (HIV) and/or other sexually transmitted infections (STIs). They could revolutionize sexual and reproductive health by reducing stigma associated with the need to prevent of HIV and other STIs by incorporating these features into contraceptives, which are less stigmatized [1]. MPTs may also help address increasing concerns about social inequalities and the environment by providing more varied contraceptive choices to help ensure that all children are planned, wanted, and born into healthy families [2]. Support for MPTs has increased over the past decade and their development is endorsed and informed by women, men, civil society, healthcare providers, and policymakers [3–5]. While MPT development is scientifically and logistically complex, financial and technical resources critical for transitioning promising preclinical product candidates/formulations into clinical evaluation remain limited. We contend that this transition requires not only funding, but also technical expertise to inform necessary rigorous criteria and benchmarks to evaluate and advance promising preclinical products into clinical formulations, approved for human testing and poised for clinical trial evaluation. This commentary presents a strategy for bridging MPT funding and development gaps and to advance these products to reach the hands of women.

Most preclinical MPT candidates have been developed by academic research centers and small biotechnology companies, largely supported by the US government and predominantly by the United States Agency for International Development (USAID) and the National Institutes of Health (NIH). These academic investigators and small company developers require significant capitalization to complete the translational preclinical research and regulatory-required animal safety, toxicity, and pharmacology testing necessary to advance an MPT candidate to Investigational New Drug (IND) filing. Once an IND is obtained, additional support is required to initiate and complete multiple phases of clinical testing, which is typically beyond the scope of most governmental funding. The pharmaceutical industry traditionally avoids licensing and funding products until after phase two clinical development stages have been successfully completed to "derisk" the product. Further, preventative products, like contraceptives and MPTs, are designed to be used by healthy individuals over long periods of time, which further changes the risk calculus compared with the development of therapeutic products designed to treat cancers or other life-threatening diseases.

Thus, a commonly encountered challenge for MPT product development is the progression from the end of preclinical drug discovery through phase I–II clinical evaluation. This process is often referred to as the "Valley of Death" because many preclinical products never reach clinical development [6]. While some of this

© The Author(s) 2020. Published by Oxford University Press on behalf of Society for the Study of Reproduction.
This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

Downloaded from https://academic.oup.com/biolreprod/article/103/2/286/5843376 by OUP site access user on 26 August 2020

Downloaded From: https://bioone.org/journals/Biology-of-Reproduction on 11 Oct 2024
Terms of Use: https://bioone.org/terms-of-use

loss is due to attrition, the development of many innovative and promising product candidates by academic laboratories and smaller companies often stalls without appropriate financial resources, training, and expertise, resulting in major losses to drug development efforts. Providing product development and commercialization training for MPT developers can assist with some of this transition. For example, the NIH Commercialization Accelerator Program is available to NIH and Health and Human Services Small Business Innovation Research and Small Business Technology Transfer awardees [7]. Open-source access to technical resources and trainings, such as webinars on regulatory guidance and vaginal microbiome, could also benefit developers.

Developing clear guidance by which the most promising preclinical MPT product candidates can expediently advance through clinical development and eventually to the hands of end users would stimulate ongoing MPT support and scientific innovation. Given the accumulation of preclinical MPT products currently in development, establishment of clear scientific, regulatory, and target product profile (TPP)-driven criteria to serve as benchmarks for these candidates may be valuable. For products that meet these benchmarks, a non-biased, standardized evaluative process could then efficiently identify priority MPT candidates and support their progression through the development pipeline. For this, we recommend convening a global authoritative committee comprised of multidisciplinary experts with reputable track records and a broad range of expertise. Expert panelists could include those with scientific (medicinal chemistry, reproductive biology, virology, microbiome, contraceptive pharmacology), pharmaceutical development (compound screening, medicinal chemistry, toxicology), CMC (chemistry, manufacturing, controls), clinical trial, socio-behavioral and market research, sociology, intellectual property, and regulatory and logistical expertise (manufacturing, commercialization, supply channels, product introduction, regulatory issues in developed and low- and middle-income countries). Committee members may also include those with executive level pharmaceutical company backgrounds. Similar to the evaluative process of an NIH study section, we envision that such a global authoritative committee could review MPT candidates rigorously and comprehensively.

This expert committee would identify global criteria and benchmarks that product developers could incorporate into their MPT development plans. From this, a checklist of preclinical testing criteria, often required by the Food and Drug Administration, that outline the critical data needed for evaluation could be developed and made available to developers, funding agencies, industry, and other interested stakeholders. These criteria and benchmarks for MPT product development would also certainly draw upon prior work, including the Strategic Evaluation Framework comprised of the Target Market Profile (TMP), Strategic Target Profile (STP), and a generalized MPT TPP [8]. The TMP includes data-informed assessments of market needs and factors that are predicted to impact product viability. The STP would describe ideal MPT products by listing optimal and minimal target attributes based on market predictions. The generalized MPT TPP is structured as a regulatory-licensed commercial product label and sets minimal and optimal clinical targets for product indications and usage. Generalized TPPs for two MPT product types have been previously developed through expert consultations and could inform this process [9,10].

Recognizing that funder mandates and decision processes vary (e.g., board priorities and peer-review processes), if done well, a benchmark checklist potentially could be incorporated into various review processes and provide a framework to directly compare various MPT concepts and formulations. Taking this idea one step further, a subset of members of the global authoritative committee could undertake a robust evaluation of the array of preclinical MPT products that have fulfilled all items on the specified benchmark checklist. Critically, this group would be comprised only of members free of ties to any MPT product to minimize bias and provide product neutral guidance. The resulting objective, data-driven priority list of MPT product candidates could be made available for funding agencies, industry, and other interested stakeholders to help guide MPT product candidate investments. The World Health Organization (WHO) has experience moderating these processes in other sectors of global health and could be similarly called upon here. For example, the WHO has convened the Paediatric Antiretroviral Drug Optimization group to establish medium- and long-term priorities for drug development and to accelerate access to optimal formulations in the context of fragmented markets for antiretroviral drugs in children [11].

Finally, critical to the realization of such an authoritative panel is both funding to support the development and sustainability of the panel and commitment from funding agencies to support the panel recommendations. Ideally, support would come from a diverse set of funders or perhaps a consortium of pharmaceutical companies who could benefit from the process and outcomes. Existing funder collaborations with similar missions include:

- The European & Developing Countries Clinical Trials Partnership [12], created as a European response to the global health crisis from poverty-related infectious diseases.
- The Global HIV Vaccine Enterprise [13], created as an alliance of organizations working to accelerate development of an HIV vaccine.
- The Coalition for Epidemic Preparedness Innovations [14], created to finance and coordinate development of new vaccines to prevent and contain infectious disease epidemics.
- The Reproductive Health Investors Alliance [15], created to bring investment capital and enterprise to the reproductive health and reproductive justice fields in the United States.

To realize the full potential of MPTs, we must strategically and objectively work to forge a path that promotes the most promising preclinical products through the development pathway given the finite resources available. Creating agreed upon benchmark criteria will ensure availability of all essential data for each MPT candidate on which to directly compare MPT candidates by a multidisciplinary committee with no financial stakes in the outcomes. A nascent infrastructure of stakeholders exists [16] and more focused collaborations, optimization, and organization of resources such as outlined here could help fill resource gaps, add rigor, and work to advance the most promising products. Our proposed approach will add credibility to the MPT field and facilitate a process for moving promising products from the lab to end users, improving the health and well-being of women and their families.

Conflict of interest

SLA has served as a consultant to Merck Sharp & Dohme Corp and has received research grants from The National Institutes of Health, The U.S. Food and Drug Administration, The Bill & Melinda Gates Foundation, Mithra and Evofem. Other authors have no conflict of interest.

Downloaded from https://academic.oup.com/biolreprod/article/103/2/286/5843376 by OUP site access user on 26 August 2020

Downloaded From: https://bioone.org/journals/Biology-of-Reproduction on 11 Oct 2024
Terms of Use: https://bioone.org/terms-of-use

Acknowledgments

The authors would like to thank Daniel Johnston, Thesla Palanee, Joseph Romano, and Jim Turpin for their valuable discussions and feedback on the ideas outlined in this commentary.

References

1. Weinrib R, Minnis A, Agot K et al. End-users' product preference across three multipurpose prevention technology delivery forms: Baseline results from Young women in Kenya and South Africa. *AIDS Behav* 2018; **22**:133–145. doi: 10.1007/s10461-017-1911-6.
2. Anderson DJ. Population and the environment — Time for another contraception revolution. *N Engl J Med* 2019; **381**:397–399. doi: 10.1056/NEJMp1906733.
3. Karim S, Baxter C, Frohlich J, Karim QA. The need for multipurpose prevention technologies in sub-Saharan Africa. *BJOG* 2014; **121**. doi: 10.1111/1471-0528.12842.
4. Norick P. Meet the intrepid doctors and scientists who are viewed as the 'Zena warrior princesses of women's health. *Women in the World Published November* 2017. Accessed February 10, 2020; **30**. https://womenintheworld.com/2017/11/30/meet-the-intrepid-doctors-and-scientists-who-are-viewed-as-the-zena-warrior-princesses-of-womens-health/.
5. Initiative for MPTs. MPT product development database. http://mpts101.org/mpt-database. Published 2019. Accessed February 15, 2020.
6. Parrish M, Yuan JT, Grimes K, Mochly-Rosen D. Surviving in the valley of death: Opportunities and challenges in translating academic drug discoveries. *Annu Rev Pharmacol Toxicol* 2019; **59**:405–421.
7. National Institutes of Health. Commercialization accelerator program. https://sbir.nih.gov/cap Published February 6, 2020. Accessed February 15, 2020.
8. Tebbey PW, Rink C. Target product profile: A renaissance for its definition and use. *J Med Mark Device Diagn Pharm Mark* 2009; **9**:301–307.
9. Romano J, Manning J, Hemmerling A, McGrory E, Young Holt B. Prioritizing multipurpose prevention technology development and investments using a target product profile. *J Antiviral Research* 2013; **100**:S32–S38.
10. Initiative for MPTs. MPT dosage-form specific target product profiles (TPPs). http://www.theimpt.org/resource-results. 2014. Accessed February 15, 2020.
11. World Health Organization Paediatric Antiretroviral Drug Optimization (PADO). Accessed February 15, 2020. https://www.who.int/hiv/pub/meetingreports/paediatric-arv-optimization-pado3/en/
12. European & Developing Countries Clinical Trials Partnership (EDCTP). Accessed April 30, 2020. https://www.edctp.org/
13. Global HIV Vaccine Enterprise. Accessed April 30, 2020. https://vaccineenterprise.org/
14. Coalition for Epidemic Preparedness Innovations (CEPI). Accessed April 30, 2020. https://www.glopid-r.org/coalition-for-epidemic-preparedness-innovations-cepi/
15. Reproductive Health Investors Alliance. Accessed April 30, 2020. https://rhiaventures.org/
16. Ehrlichman D, Sawyer D. Learn before you leap: The catalytic power of a learning network. *Stanford Social Innovation Review Published July* 2018. Accessed February 10, 2020; **27**. https://ssir.org/articles/entry/learn_before_you_leap_the_catalytic_power_of_a_learning_network.

Downloaded from https://academic.oup.com/biolreprod/article/103/2/286/5843376 by OUP site access user on 26 August 2020

Downloaded From: https://bioone.org/journals/Biology-of-Reproduction on 11 Oct 2024
Terms of Use: https://bioone.org/terms-of-use