Exploring opportunities to develop a novel on-demand contraceptive: Request for Concept Memo

Concept Memo Deadline: April 28, 2017

Overview

Introduction

The Family Planning team at the Bill & Melinda Gates Foundation (BMGF) is committed to accelerating progress toward universal access to reproductive health and quality family planning (FP) supplies and services. BMGF would like to invite initial submissions (“Concept Memos”) from qualified organizations (“Applicants”) interested in receiving grant support to fill innovation and research gaps in the development of an on-demand contraceptive product. This potential investment will inform the feasibility of further product development of an on-demand contraceptive method that meets the needs of women who cannot or do not use continuous methods for a variety of reasons including but not limited to difficult access to family planning methods and services or infrequent sex. This group of potentially represents a market of up to 31 million women living in sub-Saharan Africa and South Asia regions. In this Concept Memo, we are looking for creative ideas for a non-hormonal, non-barrier, non-vaginally administered on-demand contraceptive product.

From those Concept Memos submitted, up to three Applicants may be invited to submit a full proposal for consideration for a 2-year grant award of up to $350,000.

Background

One-pill levonorgestrel (LNG) formulations have been promoted and studied for on-demand use. For various reasons including expensive clinical trials and lack of a business case for manufacturers, a dedicated product has never been marketed for on-demand use. BMGF invested in several projects to determine the product development pathway for a 1.5mg LNG on-demand pill. The results indicated that such a product may be feasible to develop as a dedicated, registered product, but the efficacy would be lower than that for other hormonal products potentially requiring exceptionally large clinical trials. This has only been examined for an LNG on-demand pill and not for other hormonal or non-hormonal on-demand products.

BMGF also recently invested in Ipsos Healthcare to conduct market research studies to estimate the potential market size for various novel contraception concepts including an on-demand pill (using LNG) and an on-demand bio-degradable, transdermal tape (patch-like material releasing LNG). The results indicated that, among the new contraceptive concepts examined, the tape and an injectable with a 6-month period of contraceptive efficacy have the largest market potential in the three sub-Saharan African countries studied (Chart: Women's Maximum Trial Potential: Africa). The results from two countries in Asia (Bangladesh and India) suggested the on-demand tape had the largest trial potential (Chart: Women's Maximum Trial Potential: Asia).

WOMEN’S MAXIMUM TRIAL POTENTIAL: AFRICA

- The 6 month injection and tape have biggest potential in African markets
- The film and gel have least potential

<table>
<thead>
<tr>
<th>Country</th>
<th>Long Acting Injectable</th>
<th>Tape</th>
<th>Ring</th>
<th>Pill</th>
<th>Film</th>
<th>Gel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kenya</td>
<td>21.9%</td>
<td>8.8%</td>
<td>6.9%</td>
<td>6.1%</td>
<td>3.6%</td>
<td>2.8%</td>
</tr>
<tr>
<td>Nigeria</td>
<td>8.1%</td>
<td>7.4%</td>
<td>5.7%</td>
<td>3.6%</td>
<td>3.3%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Senegal</td>
<td>9.7%</td>
<td>8.4%</td>
<td>4.4%</td>
<td>3.0%</td>
<td>1.9%</td>
<td>1.8%</td>
</tr>
</tbody>
</table>
Despite the promising market data on use and interest in on-demand products (pills and transdermal tapes/patches), the presumed efficacy of a hormonal product used in an on-demand fashion poses a challenge. Most hormonal contraceptive methods that are marketed today are ~99% efficacious when used consistently and correctly. Based on a WHO Phase III trial of a 1.5mg LNG on-demand pill, the observed pregnancy rate was 7.1 (3.8; 13.1, 95% CI) pregnancies per 100 woman-years of typical use. The study observed 7.5 (4.0; 13.9, 95% CI) pregnancies per 100 woman-years of sole use. This suggests an efficacy similar to that of non-hormonal barrier methods for contraception (e.g. male and female condoms).

BMGF also collaborated with the University of Washington to take a closer look at pharmacokinetic and pharmacodynamic (PK/PD) data available for on-demand hormonal contraception. Very little PK/PD data were found and the conclusions drawn were that the timing around ovulation when an on-demand hormonal contraceptive is taken impacts the product’s efficacy in preventing pregnancy. Of the products studied, LNG and Ulipristal Acetate (UPA) were the most common active pharmaceutical ingredients used, but proved to be ineffective when taken after the luteinizing hormone (LH) peak or follicular rupture. There was no published literature on the relationship of PK to ovulatory inhibition/delay for repeat use of LNG within one cycle in the last 25 years. In fact, most studies examined PK and PD outcomes of emergency contraception use (one time) with LNG and in a few cases, UPA.

Given this information, BMGF is seeking innovative ideas to develop novel on-demand products. The goal of this specific grant program is to determine feasibility of development of an on-demand method based on pre-clinical proof of concept data and/or modeling data including a target product profile for the proposed product. Selected applicants should demonstrate initial feasibility in the period of funding and develop a product development plan for possible future funding from BMGF or other donors if the idea looks promising upon completion of this initial phase.

**Anticipated Outcomes**

The following outcomes are examples of what could be achieved with this investment:
- Pre-clinical proof of concept to develop product determined;
- Target Product Profile and Product Development Plan developed;
- An overview of potential critical manufacturability, clinical and regulatory challenges and/or a plan presented as to when they would be determined;
- Estimated Cost of Goods Sold (COGS) determined;
- Modeled data to determine key parameters for product development for an on-demand contraceptive (e.g. Pharmacokinetic and Pharmacodynamic, PK/PD data).

This investment could consist of the following types of ideas:
- Modeling of the PK/PD parameters needed for a hormonal on-demand method to be as efficacious as other hormonal contraceptives;
- Design of a diagnostic for detecting or predicting ovulation sufficiently early for an on-demand method to be efficacious;
- Initial design and feasibility testing of a combined diagnostic and contraceptive product;
- Initial design and feasibility testing of a hormonal or non-hormonal on-demand method for female use;
- Novel mechanisms of action appropriate for immediate suppression of oocyte development or release.
Scope and Approach

**Approach:** There is a need to spur innovation in the contraceptive product development space, particularly for a class of products that meet the needs of women who have intermittent or irregular sex, have poor access to medical services, or cannot or do not want to take a method continuously. This Request for Concept Memos offers an opportunity for organizations to examine one or multiple new product ideas for quick evaluation. The idea is to be creative and fail fast.

**Target audience:** This initial idea is funded by BMGF, but is of interest to other donors who fund product development, possibly some companies and/or other partners interested in working in this sector. The data and information from this initial investment will inform future funding programs, either through BMGF or other entities to continue to develop promising leads.

**Scalability/replicability:** This investment is primarily focused on generating evidence of feasibility of novel on-demand contraceptive products. It is anticipated that a development plan will be one of the final deliverables of the grant to access future funding opportunities.

**Geography:** The primary population to ultimately be served by this technology will be women and girls living in the poorest countries (FP2020 countries). It is acceptable for Applicants to also consider potential for the product to be marketed in higher-income geographies.

Rules & Guidelines

**Eligibility**

**Funding Criteria**

This Request for Concept Memos is open to any organization that is able to complete the template within the required deadline for submission. Applicants can seek partnership with other organizations or individuals to complete the work. In the case of a multi-partner approach or consortium, it must be led by a prime organization and the prime organization will provide coordination and overall management of the project.

**Funding criteria:**

The selection of Applicant(s) to submit full proposals will be based on the technical merits of the concept memo, the organization’s capacity, strength of proposed partners (as applicable), and proposed budget.

**Exclusion Criteria**

We will NOT consider funding for:

- Projects that propose the development of an LNG oral on-demand product;
- Projects that propose the development of short-acting vaginal methods, vaginal products (spermicides, male or female condoms) or other female or male barrier methods;
- Male methods;
- Post-fertilization methods;
- Market research or operations research;
- Do not respond to the key goals of the Request for Concept Memos and/or
- Where the applicant or partners (if applicable) do not have demonstrable capacity in the areas of expertise defined in the request.

**Evaluation Criteria**

The following characteristics are required for a successful concept memo:

1. A clear description of the types of disciplines or approaches that will be used for the feasibility testing or other proposed research;
2. Demonstrated understanding of the issue presented and clear description of how the proposed work will respond;
3. Demonstrated innovation and willingness to try and test new approaches and/or work with new partners; and
4. Completion of full concept memo template and other requirements.

The ideal partner will have the following characteristics and experience:

1. Demonstrated capacity to conduct innovative research;
2. Experience with product development and particularly in the RH/FP space; and
3. An entrepreneurial, results-based mind-set and ability to develop innovative, creative ways for generating new ideas, evaluating them and making go/no-go decisions.
Activities and Timeline

Successful Concept Memos will be followed by an invitation to submit a full proposal according to the timeline presented below.

March 27, 2017: Request for Concept Memos announced
April 28, 2017: Deadline for submitting Concept Memos
May 19, 2017: Finalist(s) notified to submit full proposal
August, 2017: Anticipated date for final approval of grant and funding

How to Submit a Concept Memo

Response Requirements

To apply, please submit a concept memo in the format attached as well as additional appendices as requested below. Other attachments will not be reviewed.

- **Concept Memo Template** (5 page maximum) which includes the following sections:
  - General information: Summary with basic proposal information including names, address, contact information, proposed budget, etc.
  - Project Scope/Program description: Description of overall approach you will take to achieve the intended results of the project.
  - Investment Outcomes: Propose outcomes of the project and associated outputs needed to reach those outcomes. Describe how the proposed approach will achieve the desired outcomes and/or outputs and how this will be verified.
  - Organizational Fit: Describe your organization's experience to implement the proposed work.
  - Risks/Challenges: Describe the anticipated challenges to the success of the project and your proposed mitigation strategies.

- **High Level Budget** (1 page maximum; appendix) – no official template, but should include a high level understanding of how the proposed funding will be allocated

- **Bio-sketches of key personnel** (no page limit; appendix): Attach short biographies/CVs (1-2 paragraphs each) of key personnel and a proposed structure (consortium with prime organization, etc).

Submission Instructions

Submit your Concept Memo via the online portal. Please do not mail a duplicate hard copy after submitting your proposal online or send any additional attachments or information (videos, books, program materials, etc.).

The submission must be clear, concise and complete. The Gates foundation reserves the right to mark a submission down or exclude them from the process if its submission contains any ambiguities or lacks clarity. Applicants should submit only such information as is necessary to respond effectively to the request. Submissions will be evaluated on the basis of information submitted by the deadline.

Help Contact(s)

For programmatic clarification and questions, please contact Trisha Wood Santos, Program Officer, at trisha.wood@gatesfoundation.org. For template help or general RFP process guidance, please reach out to Marlo Hartung, Program Coordinator, at marlo.hartung@gatesfoundation.org directly with any questions you may have. Please see the “Activities and Timeline” Section for Q&A deadlines.

More Information

Frequently Asked Questions (FAQ)

**Who can participate?** This is an open solicitation. Applicants may choose to form consortia and consortia partners can be from organizations in all sectors (private, NGO, government, academic) and at all levels of expertise.

**Is there a preferred list of agencies to engage with for technical expertise?** There is no preferred list. We highly encourage applicants to refer to their own networks and contacts in terms of technical expertise.

**When are responses due?** Responses are due no later than 11:59pm PST on April 28, 2017.
When will proposals be selected? The finalist(s) will be selected to submit a full proposal by May 19, 2017. It is anticipated that the final grant/award approval will happen in June 2017.

Will I receive any compensation for submitting? You will not receive any compensation for your submission even if it is used by the foundation or third parties in any way.

What will the foundation do with my submission? The foundation will review all submissions. We may also share your submission, or ideas contained within it, with internal or external partners for technical review and comment.

What is the available budget for this work? The maximum award available is $350,000 per proposed project.

What is the proposed timeline for the project? The anticipated timeline to complete this project is 2 years, but this is flexible if the Applicant can rationalize an alternative timeline.

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**Key Terms and Conditions**

**A. Disclosure Notice**

To help the foundation with its review of RFP responses, the foundation may disclose proposals, documents, communications, and associated materials submitted to the foundation in response to this RFP (collectively, "Submission Materials") to its employees, contingent workers, consultants, independent subject matter experts, and potential co-funders. Please carefully consider the information included in the Submission Materials. If you (the "Applicant") have any doubts about the wisdom of disclosure of confidential or proprietary information, the foundation recommends you consult with your legal counsel and take any steps you deem necessary to protect your intellectual property. You may wish to consider whether such information is critical for evaluating the submission or if more general, non-confidential information may be adequate as an alternative for these purposes.

Notwithstanding the Applicants characterization of any information as being confidential, the foundation the foundation is under no obligation to treat such information as confidential.

**B. Disclaimer**

This RFP is not an offer to contract or award grant funds. The foundation assumes no responsibility for the Applicants cost to respond to this RFP. All responses generated by this RFP become the property of the foundation.

**C. Release and Verification**

In exchange for the opportunity to be awarded a grant or contract, the Applicant agrees that the foundation may, in its sole discretion: (1) amend or cancel the RFP, in whole or in part, at any time; (2) extend the deadline for submitting responses; (3) determine whether a response does or does not substantially comply with the requirements of the RFP; (4) waive any minor irregularity, informality or nonconformance with the provisions or procedures of the RFP; (5) issue multiple awards; (6) share responses generated by this RFP with foundation staff, consultants, contingent workers, subject matter experts, and potential co-funders; and (7) copy the responses.

Applicant agrees not to bring a legal challenge of any kind against the foundation relating to the foundation’s selection and award of a grant or contract arising from this RFP.

Applicant represents that it has responded to the RFP with complete honesty and accuracy. If facts provided in Applicant’s response change, Applicant will supplement its response in writing with any deletions, additions or changes within ten days of the changes. Applicant will do this, as necessary, throughout the selection process. Applicant understands that any material misrepresentation, including omissions, may disqualify it from consideration for a grant or contract award.

By responding to this RFP, you are representing: (i) that you have authority to bind the named Applicant to the terms and conditions set forth above, without amendment; and (ii) that you agree to be bound by them.

**D. Global Access and Intellectual Property**

Intellectual property (IP) rights and the management of IP rights are likely to play an important role in achieving the goals of this project. To this end, the foundation requires that, even at this stage, all applicants seriously consider their willingness to submit a response in compliance with the foundation’s response requirements, a portion of which may ask for certain information and intentions regarding intellectual property concerns and Global Access. Specifically, the foundation requires that:

You will conduct and manage the Project and the Funded Developments in a manner that ensures Global Access. Your Global Access commitments will survive the term of the Agreement. “Funded Developments” means the products, services, processes, technologies, materials, software, data, other innovations, and intellectual property resulting from the Project (including modifications, improvements, and further developments to Background Technology). “Background Technology” means any and all products, services, processes, technologies, materials, software, data, or other innovations, and intellectual property created by You or a third party prior to or outside of the Project used as part of the Project. "Global Access" means: (a) the knowledge and information gained from the Project will be promptly and broadly disseminated; and (b) the Funded Developments will be made available and accessible at an affordable price (i)
to people most in need within developing countries, or (ii) in support of the U.S. educational system and public libraries, as applicable to the Project.

The foundation will be selecting applicants based on the conclusion that their technologies and expertise will be most appropriate for the success of this RFP.

As part of the foundation’s review and evaluation of each response, the foundation will conduct due diligence with respect to each applicant's ability and commitment to manage intellectual property in a manner consistent with the stated scientific and charitable goals of the foundation. Due diligence activities may include inquiry into an applicant's:

1) Freedom to operate (FTO) and ability to freely use and acquire needed background technology;
2) Commitment to promote the utilization, commercialization and availability of Funded Developments for public benefit

The foundation encourages you to include this information in your response.

About the Bill & Melinda Gates Foundation

Guided by the belief that every life has equal value, the Bill & Melinda Gates Foundation works to help all people lead healthy, productive lives. We work with partner organizations worldwide to tackle critical problems in four program areas. Our Global Development Division works to help the world’s poorest people lift themselves out of hunger and poverty. Our Global Health Division aims to harness advances in science and technology to save lives in developing countries. Our United States Division works to improve U.S. high school and postsecondary education and support vulnerable children and families in Washington State. And our Global Policy & Advocacy Division seeks to build strategic relationships and promote policies that will help advance our work. Our approach to Grantmaking emphasizes collaboration, innovation, risk-taking, and, most importantly, results.

To learn more about the foundation's work, visit www.gatesfoundation.org.

Festin, M. et al. “A prospective, open-label, single arm, multicenter study to evaluate efficacy, safety and acceptability of pericoital oral contraception using levonorgestrel 1.5mg” Hum Repro 31.3 (2016): 530-540.