

**Call for Concepts for the NIH HIV Prevention Trials Network: January 2021**

Dear Colleagues:

The HIV Prevention Trials Network (HPTN) is committed to advancing non-vaccine HIV prevention research agenda globally. The Network’s focus is on the design and implementation of trials for the prevention of HIV acquisition and transmission among all population at risk for HIV. Its mandate is centered on four aims along the following research pillars:

1. Identifying **novel antiretroviral (ARV)-based methods and delivery systems** for HIV prevention;
2. Developing **multi-purpose technologies** for HIV prevention as well as for contraception, prevention of other sexually transmitted infections or opioid dependence;
3. Evaluating **broadly neutralizing antibodies** alone or in a combination that prevent HIV acquisition, in collaboration with the HIV Vaccine Trials Network; and
4. Designing and conducting population-specific **integrated strategy studies** that combine biomedical, socio-behavioral, and structural interventions for HIV prevention to maximize their effectiveness.

The HPTN trials span across diverse at-risk populations and vary from exploratory vanguard studies designed to guide further development of relevant studies to phase 3 randomized controlled trials. For further information, please visit the HPTN website at [www.hptn.org](http://www.hptn.org).

We are writing to solicit the submission of new research concepts that fit within the HPTN scope of work.

Concepts are welcomed from HPTN and non-HPTN affiliated investigators and can focus on any of the aims outlined above and in the objectives outlined in Attachment 1. Further, we are including a FAQ (Attachment 2) that we hope you find useful to guide the development of your concept.

As outlined in the FAQ, the following steps outline the process for facilitating the review and to ensure that the proposed topic fits within the Network’s mission:

1. Submit a brief **letter of intent** no later than **March 1, 2021** to concepts@hptn.org. The letter of intent will be reviewed by the HPTN leadership to ensure that proposed research is consistent with the mission, objectives and scientific priorities of the HPTN as indicated above. The letter of intent should include the following:
* Descriptive title
* Letter of intent authors (for primary point of contact, including email address)
* **One** brief paragraph describing aims/objectives/type of study/population of focus
1. An email confirming next steps will be sent within five working days to the primary author with feedback and indicating whether a concept submission is invited. If so, the concept team will be directed to submit a concept proposal.

In the event that similar letters of intent are submitted, the HPTN leadership may suggest for various research teams to work together in the development of a concept.

1. Concepts **must be limited to five pages** using the template in Attachment 3. Failure to comply with this requirement could result is not being considered.
2. Concepts should be submitted **by April 12, 2021 to concepts@hptn.org.**
3. The concepts will be forwarded to the relevant HPTN scientific committee and working group for review and prioritization. To facilitate, we are asking each concept to identify the committee for primary review, and if appropriate the committee for secondary review. Refer to the HPTN website ([HPTN Committees](https://www.hptn.org/index.php/about/network-groups-committees)) for description of the HPTN scientific committees and working groups is most appropriate
4. Following the scientific committee review process, the concepts may undergo further reviews by an external group as directed by the HPTN Leadership. This process is anticipated to take place during the 2nd quarter of 2021 and will include provision of feedback to the concept authors.
5. It is important to note that selection of a concept for further development is not a guarantee of funding. Fundraising efforts will be pursued as per usual HPTN processes.

Should you have any questions, please send your queries to concepts@hptn.org. We look forward to hearing from you.

Sincerely,

Myron S. Cohen, MD Wafaa M. El-Sadr, MD, MPH, MPA

Co-Principal Investigator Co-Principal Investigator

HIV Prevention Trials Network HIV Prevention Trials Network

**Attachment 1: HPTN Specific Aims**

The goal of the HIV Prevention Trials Network (HPTN) is to reduce HIV incidence worldwide. We aim to identify novel effective, safe, acceptable, and scalable HIV prevention tools and integrated strategies, informed by biomedical and socio-behavioral research. The HPTN will collaborate with a broad range of partners including clinical research sites, community members, other DAIDS Networks, NIH Institutes and Centers, other governmental agencies and pharmaceutical companies to achieve the following Specific Aims:

**Specific Aim 1. To design and conduct studies of long-acting antiretroviral (ARV) agents and delivery systems for pre-exposure prophylaxis (PrEP)**

*Rationale: Long-acting systemic ARV agents will facilitate adherence with PrEP, a major limitation to PrEP effectiveness.*

1a. To design and conduct Phase 1 and 2 studies to evaluate the safety, acceptability and pharmacokinetic/pharmacodynamic (PK/PD) characteristics of long-acting ARV agents and novel delivery methods.

1b. To design and conduct Phase 3 studies to evaluate the safety and efficacy of novel long-acting ARV agents for HIV prevention. These may be delivered orally, by injection or infusion, or via devices such as implants or microneedle patches.

1c. To design and conduct bridging studies to evaluate the safety and acceptability of long-acting ARV agents among specific populations such as adolescents and pregnant women.

**Specific Aim 2. To design and conduct studies to evaluate multipurpose prevention technologies (MPTs) that concurrently prevent HIV and pregnancy, sexually transmitted infections (STIs) or opioid dependence.**

*Rationale: HIV prevention products are likely to achieve greater and more durable coverage with more significant health impact if they have a broader prevention profile for specific populations.*

2a. To design and conduct Phase 1 and 2 studies to evaluate the PK/PD, drug interactions and safety of MPT candidates (e.g., injectable, implants, patches, rings) for HIV and contraception, STIs or opioid dependence.

2b. To design and conduct Phase 3 studies to evaluate the safety and efficacy of an MPT or other novel drug delivery systems for prevention of HIV and pregnancy which may be delivered by an injection, implant, microneedle patch or intravaginal ring.

2c. To design and conduct studies to determine the acceptability and adherence with a co-formulated TDF/FTC-contraceptive oral agent; as an attractive option for women seeking contraception and HIV prevention. A Phase 3 study may not be required as efficacy of each component is known.

**Specific Aim 3. To design and conduct studies in collaboration with the HIV Vaccine Trials Network to evaluate broadly neutralizing antibodies (bnAbs), alone and in combination, for PrEP**

*Rationale: A combination of bnAbs, if proven to be safe, effective and scalable, would be an additional option to ARV-based PrEP.*

3a. To design and conduct Phase 1 and Phase 2 studies to evaluate PK/PD, safety and the *ex vivo* viral neutralization activity of bnAbs with different specificities and binding sites.

3b. To design and conduct Phase 3 studies of a multi-target bnAb or combinations of bnAbs to evaluate their efficacy and safety for PrEP.

**Specific Aim 4. To design and conduct integrated strategies for HIV prevention**

*Rationale: Effective HIV prevention requires an integrated package of interventions tailored to the needs of populations at risk*

4a. To design and conduct integrated strategies studies consisting of biomedical, socio-behavioral and structural interventions appropriate for priority populations at risk for HIV.

4b. To use diverse designs for integrated strategies studies including cluster randomization, factorial, and step-wedge to evaluate the effectiveness of package and individual components for HIV prevention.

4c. To identify geographic “hotspots” and clusters of HIV transmission using HIV recency testing, HIV molecular phylogeny and phylogeography, enabling focused HIV prevention interventions.

4d. To include robust process measures to determine reasons for success or failure of integrated HIV prevention strategies.

4e. To utilize mathematical modelling of data from integrated strategy studies to estimate impact at a population level.

**Attachment 2: FAQ**

Concepts for the NIH HIV Prevention Trials Network – March 2021

Frequently Asked Questions (v. 0.2)

*Q1. What is the due date for submission?*

A. All concepts must be submitted to concepts@hptn.org by COB **April 12, 2021**.

*Q2. What criteria are considered in evaluating an HPTN concept?*

A. The criteria listed below are used for evaluation of HPTN concepts. In addition, innovation is essential.

|  |  |
| --- | --- |
| Scientific Merit (50%) | * hypothesis is scientifically sound and answerable by the proposed design
* study design and methods will yield the proposed outcomes
* plan for analysis of data is adequate and appropriate
* population is appropriate for the research; relevance of research to the community is considered
 |
| Public Health Impact (30%) | * relevance of the planned research to the prevention of HIV infection
* proposed study is part of a critical path of research
* proposed study is or would potentially lead to an efficacy trial
 |
| Research Advantage of the HPTN (20%) | * study is aligned with the scientific agenda and priorities of the Network (i.e., integrated strategies and PrEP)
* proposed research will benefit from a multi-site, multidisciplinary collaboration involving different populations either in the initial phase or in a subsequent phase
 |

*Q3. Where can I locate a template of the concept form for submission? Is this the normal template used for concept submissions?*

A. A copy of the template for this solicitation is attached and can also be found on the HPTN website: [Call for Concept Template](https://www.hptn.org/news-and-events/announcements/hptn-call-for-concepts). This **five-page** template is shorter than the previously used ten-page template. This abbreviated version focuses on the scientific aspect with the following key sections: title, purpose/rationale, study aim, objectives, design, description of intervention(s), endpoints, study population, product-related considerations, and timeframe.

*Q4. Who can submit a concept? Can different individuals from the same group/organization submit more than one concept? If yes, would we compete against each other?*

A. Concepts are welcome from either HPTN or non-HPTN investigators. Individuals within the same organization can submit concepts. See the response below about the review process in terms of the competition.

*Q5. What is the review process for these concepts?*

A. Concepts will be sent to concepts@hptn.org by April 12, 2021. These concepts will then be forwarded to the relevant HPTN scientific committee for review and prioritization. Following the scientific committee review, the concepts will undergo the Network review by the HPTN Executive Committee as per HPTN’s established process. This process is anticipated to take place during the Spring/Summer 2021. The process will include feedback to the concept authors. The feasibility and funding is not guaranteed for the approved concepts will be discussed with NIH partners.

*Q6. Can I receive the template in a word document?*

A. See the attached announcement and template as a word document (see below).

*Q7. How can I get input for a concept under development?*

A. Concept authors can solicit input from the existing scientific committees (see committee and working group information on the HPTN website ([HPTN Committees](https://www.hptn.org/about/network-groups-committees/scientific-committee-scs)) or from topic area experts within and outside the HPTN.

*Q8. Do all concepts need HIV as an endpoint?*

A. The endpoint(s) for specific concept will be dependent on the nature of the proposed study. For vanguard and phase 1 studies, HIV incidence is not required as the endpoint. However, for phase 2 and phase 3 studies, HIV incidence is the preferred endpoint. The vanguard studies should describe how the data obtained will inform the design of the potential phase 2 or 3 studies.

*Q9. Do all concepts have to be a randomized controlled trial (RCT)?*

A. Proposed concepts should propose the preferred methodology to answer the research question.

*Q10. Can I withdraw my concept after it has been approved to move forward to protocol development?*

1. Concepts can be withdrawn at any time. However, the concept chair should inform the HPTN promptly, if they decide to withdraw a concept from consideration.

*Q.11. Are biosketches, budgets, and letter of support required with the submission?*

A. Please use the concept template for the information provided. No additional supporting documentation like biosketches, letters of support, or budgets are required at the time of submission.

*Q.12. Can individuals submitting concepts get statistical and design support from the HPTN?*

A. Network resources including statistical, laboratory or operational support are not provided for concept submission. Should the concept be approved, dedicated Network resources will support continued development.

*Q13. Can proposals include products that do not have GMP manufacturing or is the Network entertaining only purely research products?*

1. *Proposals involving new or investigational products must be GMP manufactured to facilitate use in human trials.  While products should be scalable for use in subsequent clinical studies, this is not required at the time of solicitation.  This solicitation is not intended for pre-clinical trial work.*

*Q14. What about COVID-19-based trials? What types of trials will be considered, vaccines? PreP adherence in COVID-19 patients?*

1. *Concepts that include an intersection of SARS-CoV-2 and HIV infection will be considered in this solicitation.  Concepts focused only on COVID-19 will not be considered in this solicitation.*

*Q15. Can any investigator submit more than one concept or be part of an investigative team on more than 1 concept?*

1. *Yes, an investigator can have multiple submissions, as an individual or as part of a team.*

*Q16. What is the timeline for communicating whether my proposal has been approved?*

1. The following timeline is tentative and is a guide for planning purposes.

|  |  |
| --- | --- |
| Disseminate concept solicitation | January 5, 2021 |
| Submit letter of intent  | March 1, 2021 |
| Receive concept proposals | April 12, 2021 |
| Review, triage and distribute proposals for review that fit within Network mission | April 15, 2021 |
| Review and prioritization of proposals by Scientific Committee | May 10, 2021 |
| Review and prioritization by Executive Committee and/or External Panel | +/- May 26-7, 2021 |
| Communications to all concept authors | Early June |

Q17. Is there an estimated budget? Or other budget considerations that we should be aware of.

A. At this stage, a budget is not required. If your concept will involve use of non-approved tools, it is required that you obtain letter from the pharmaceutical company indicating their interest in the concept.

Q18. Which HPTN sites have relationships with correctional facilities specifically county jails?

A. It is the responsibility of the concept author(s) to identify capacity for specific populations. The concept should propose brief context for reaching a specific population or site.

Q19. Can non-HPTN sites be participating sites in this study?

1. The HPTN has a site selection process (see [HPTN MOP](https://www.hptn.org/resources/manual-of-operations)) that provides preference to sites that are affiliated with the HPTN.

Q20. Do I need to state which sites?

A. Specific sites are not necessary at the concept stage given the HPTN’s site selection process. However, a descrption of the population and country or region is sufficient.

Q21. Is there a list of HPTN sites?

1. A list of HPTN sites can be found on the HPTN website: [www.hptn.org](http://www.hptn.org)

Q22. What is a vanguard study?

A. A vanguard study is a study that is smaller in nature to address the feasibility issues before launching into a larger trial. Such a proposed study should lead to a future Phase III trial.

**ATTACHMENT 3:**

HIV Prevention Trials Network

## STUDY CONCEPT PLAN

## TITLE

## DATE

##  HPTN STUDY CONCEPT PLAN

## TITLE

**CONCEPT DEVELOPMENT TEAM**

**(names and affiliations)**

**To facilitate review, please indicate the primary HPTN committee or cross-cutting working group that should review this concept**

[ ]  Adolescent at Risk Committee

[ ]  Sexual and Gender Minority Committee

[ ]  Substance Users Committee

[ ]  Women at Risk Committee

[ ]  Community Working Group

[ ]  Ethics Working Group

[ ]  Biomedical Sciences Working Group

[ ]  Socio-Behavioral and Structural Working Group

**CONCEPT NOT TO EXCEED 5 PAGES (the five pages does not include the title page;**

**numbering should start from this page onward)**

**STUDY TITLE**

**SUMMARY OF PURPOSE AND RATIONALE**: This should include introduction and background literature to set the context of the proposed research. Specify the principal aim(s), rationale, relevant background, overall design for Phase I/II trials describe critical pathway to efficacy evaluation; indicate relevance to the long-term global goals of HPTN.

**STUDY AIM**

**STUDY OBJECTIVES**

**STUDY DESIGN**

Specify the type of study proposed, e.g., whether it is a Phase I, IIA, IIB, or III randomized clinical trial, observational, nested case control study, etc.

**Description of the INTERVENTION**

Describe intervention (e.g. drug/regimen, counseling program), specify study arms, including control if applicable.

**ENDPOINTS**

Specify the primary endpoints such as seroconversion, dose-limiting toxicity, specific behavioral outcomes (either primary or secondary endpoints).

**STUDY POPULATION**

Specify sample size, the principal inclusion and exclusion criteria, recruitment source (s), appropriateness of the proposed study population for the proposed concept, and other salient characteristics.

**PRODUCT-RELATED CONSIDERATIONS:**

Is an IND needed? Is the product and placebo available in sufficient quantity for the proposed study? From whom? Is there a plan to manufacture sufficient quantities for any proposed follow-on studies?

**TIMEFRAME:**

Specify expected duration of accrual and follow-up, and any contingencies for development/implementation (e.g. final product selection/dosage to await results of ongoing study)