



## Request for Proposals: Investigations Needed for Future Clinical Trials and Secondary/Exploratory Study Objectives

**Background/Goal:** The primary purpose of this RFA is to encourage and support investigations that will contribute to the knowledge base necessary for future clinical trials within the network's research agenda. Investigators are invited to submit a brief (2-page) proposal for funding of work that can be completed by 30 October 2020. This work may be 1) associated with secondary or exploratory study objectives specified in selected IMPAACT studies that were closed to follow-up within the last five years and for which the primary analyses have been completed (list provided below) or 2) associated with completed non-network studies (with appropriate permissions). Priority will be given to investigations considered foundational for future clinical trials within the network's research agenda.

*Note that this is not the only opportunity for study teams to carry out protocol-specified secondary or exploratory objectives; approval from the IMPAACT Management Oversight Group may be sought at any time for associated investigations requiring additional resources.*

### Eligibility:

- Proposals may be submitted for investigations using existing data and/or specimens from studies outside of the IMPAACT network (with appropriate permissions from sponsor, protocol chair, IRBs/ECs) or from the following IMPAACT studies: P1020A, P1058A, P1060, P1063, P1065, P1070, P1073, P1074, P1079, P1080, 1077HS, 1085, P1094, P1104s, P1041, P1066, P1068s, P1076, P1083, P1086, P1097; full titles are provided at the end of this solicitation. Note that investigations using data from 1077BF/FF, P1084s and P1078 may be proposed; however, due to the number of ongoing/planned analyses for these studies, the timeline for beginning new analyses may be delayed for several months. These protocols may be accessed on the IMPAACT website: <http://impaactnetwork.org/studies/index.asp>. MS Word versions may be requested from the IMPAACT Operations Center at [IMPAACT.OperationsCenter@fstrf.org](mailto:IMPAACT.OperationsCenter@fstrf.org).
- Priority will be given to investigators who have served as members of the respective protocol teams.

### Limitations/Parameters:

- This program will **not** support collection of prospective data.
- This program will **not** support objectives/investigations associated with ongoing studies.
- This program will support investigations specifically identified in an IMPAACT protocol as a secondary or exploratory objective or other investigations that are considered foundational for future clinical trials within the network's research agenda.
- Investigations using data and/or specimens from studies completed outside of the network will require a letter of support from the relevant protocol chair, written permission from original sponsor and evidence that the informed consent obtained would allow their use for the proposed purpose.

- Secondary objectives as stated in IMPAACT or other protocols approved by IRBs/ECs cannot be changed; proposed work must be consistent with the relevant protocol document and associated informed consent forms. Depending on the specificity of the language, there may or may not be leeway to use more up-to-date assays/methods than originally planned.
- The proposed work must be completed by 30 October 2020. Therefore, location of specimens (if applicable) and required time for obtaining approvals for shipping (e.g. Materials Transfer Agreements), especially internationally, should be considered and will be included in the review process.
- IMPAACT Statistical and Data Management Center statistical support may be requested for analyses.
- For proposals involving secondary or exploratory objectives in IMPAACT studies, a brief statement of support from the protocol chair(s) is required. If the analyses associated with an objective in which a potential applicant is interested have already been completed or are currently underway, the protocol chair will inform the investigator, as that objective would not be considered eligible for support through this award. For this reason, interested investigators must contact the protocol chair **before** preparing a proposal.

**Funding:** A maximum **total** dollar amount of \$150,000 is available for each award. Funding may include LoE support for the investigator and, if applicable, laboratory assays and materials, and shipping of samples to the laboratory of interest. Equipment costs cannot be supported. IMPAACT statistician time should not be included in the budget.

**Inquiries:** Inquiries regarding eligibility or other aspects are strongly encouraged prior to submission of applications. Questions may be submitted through the IMPAACT Operations Center at [IMPAACT.OperationsCenter@fstrf.org](mailto:IMPAACT.OperationsCenter@fstrf.org).

**Key Dates:**

- Proposal Submission Due Date: 7 June 2019 at 5:00 PM ET
- Anticipated Funding Start Date: 1 August 2019

**Submission of Proposals:** Proposals must be submitted through the IMPAACT Operations Center at [IMPAACT.OperationsCenter@fstrf.org](mailto:IMPAACT.OperationsCenter@fstrf.org) by 5:00 PM ET on the due date.

**Application Format/Outline (Maximum 2 pages, exclusive of appendices)**

**Title of Proposed Investigation** (to include relevant protocol number)

**Investigator Information**

- Name and Contact information (include institution, e-mail address)
- Affiliation with protocol team

**Research Proposal**

- Relevant secondary/exploratory objective(s) exactly as stated in the approved study protocol, if applicable.

- Rationale for pursuit of this objective: Include both a) the original rationale included in protocol, b) rationale for why the investigation is still considered a priority (noting any more recent references) and c) how the investigation may contribute to the knowledge base needed for future clinical trials within IMPAACT's research agenda.
- Summary of the proposed investigation, including time points for relevant data/specimen required from the protocol, shipment plan for specimens (if any), and any associated analysis plans that may have been included in the protocol document.
- Note any specific institutions/laboratories that were identified or designated for this work in the approved protocol.
- Note whether the investigators have their own statistician or would like an IMPAACT statistician to work on the project.
- Expected deliverables/timeline for completion within the funding period. This should, ideally, include completion of laboratory assays (if any), data analysis and manuscript preparation. Note that if SDMC resources are requested, the timeline should allow 3-6 months for SDMC data cleaning/data analysis depending on whether the data have been cleaned/analyzed for another analysis.

### **Budget and Justification**

- For evaluation/illustrative purposes, provide the budget and justification for the entire funding period (total costs of maximum \$150,000 – 1 August 2019 through 30 October 2020, as Appendix 1. IMPAACT statistician time should not be included in the budget.
- *Optional:* Note any outside resources that are available to the investigator that may contribute to the success of the investigation; e.g., institutional support, grant or foundation support.

### **Letter of Support/Other Documentation**

- A brief statement of support from the Protocol Chair/PI of the study through which the data/specimens were obtained must be included as Appendix 2.
- For investigations associated with studies completed outside of the network, permission from original sponsor and evidence that the informed consent obtained would allow use of data/specimens for the proposed purpose must also be included in Appendix 2 (in addition to the letter of support from the Protocol Chair/Principal Investigator).

### **Eligible IMPAACT Studies**

As noted above, proposals may be submitted for the studies listed below or for other investigations as noted above. The protocols may be accessed on the IMPAACT website:

<http://impactnetwork.org/studies/index.asp>. MS Word versions may be requested from the IMPAACT Operations Center at [IMPAACT.OperationsCenter@fstrf.org](mailto:IMPAACT.OperationsCenter@fstrf.org).

- P1020A: A Phase I/II, Open-Label, Pharmacokinetic and Safety Study of a Novel Protease Inhibitor (BMS-232632, Atazanavir, ATV, Reyataz) in Combination Regimens in Antiretroviral Therapy (ART) Naive and Experienced HIV-infected Infants, Children and Adolescents
- P1058A: Intensive Pharmacokinetic Studies of New Classes of Antiretroviral Drug Combinations in Children, Adolescents, and Young Adults
- P1060: Phase II, Parallel, Randomized Clinical Trials Comparing the Responses to Initiation of NNRTI-Based Versus PI-Based Antiretroviral Therapy in HIV-Infected Infants Who Have and Have Not Previously Received Single-Dose Nevirapine for Prevention of Mother-to-Child HIV Transmission
- P1063: Phase I/II Safety and Efficacy Investigation of Atorvastatin for Treatment of Increased LDL-

#### Cholesterol in HIV-Infected children, Adolescents, and Young Adults

- P1065: Phase I/II Study of Safety and Immunogenicity of Quadrivalent Meningococcal Conjugate Vaccine in HIV-Infected Youth (Versions 1.0 - 3.0) and Open Label Immunogenicity Study of a Booster Dose of MCV4 in Previously Immunized HIV-Infected Children and Youth (Version 4.0)
- P1070: Dose Finding and Pharmacogenetic Study of EFV in HIV-Infected and HIV/TB Co-infected Infants & Children  $\geq 3$  months to  $< 36$  Months of Age
- P1073: Study of Immune Reconstitution Inflammatory Syndrome (IRIS) for International Sites Initiating Highly Active Antiretroviral Therapy (HAART) in Infants and Children  $< 72$  Months of Age
- P1074: A Prospective Surveillance Study of Long Term Outcomes in HIV-infected Infants, Children and Adolescents
- P1079: Pharmacology of Artemisinin-Based Antimalarial Therapy Within the Context of Antiretroviral Therapy
- P1080: A Pilot Study of Psychiatric and Antiretroviral Medication Concentrations in HIV-1 Infected and Uninfected Children and Adolescents
- 1077HS: HAART Standard Version of the PROMISE Study: Promoting Maternal and Infant Survival Everywhere
- \*1077BF/FF: Breastfeeding/Formula Feeding Versions of the PROMISE Study: Promoting Maternal and Infant Survival Everywhere\*
- \*P1084s: Maternal and Infant Monitoring for Evidence of Toxicity Related to Tenofovir Exposure: The Bone and Kidney Health Substudy of PROMISE Protocol: Promoting Maternal and Infant Survival Everywhere\*
- P1085: Duration of Human Papilloma Virus (HPV) Type-Specific Antibody After Administration of Quadrivalent HPV Vaccine to HIV-infected Children
- P1094: Evaluation of 3TC or FTC Monotherapy Compared to Continuing HAART as a Bridging Antiretroviral Strategy in Persistently Non-Adherent Children, Adolescents, and Young Adults Who Are Failing HAART and Have the M184V Resistance Mutation

#### ***Additional studies since last solicitation:***

- P1104s: Longitudinal Developmental and Neuropsychological Assessments of HIV-Infected Participants of P1060 and HIV-Uninfected Controls
- P1041: Randomized Double Blind Placebo Controlled Trial to Determine the Efficacy of Isoniazid in preventing Tuberculosis Disease and Latent Tuberculosis Infection among Infants with Perinatal exposure to HIV
- P1066: A Phase I/II, Multicenter, Open-Label, Noncomparative Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Antiretroviral Activity of Raltegravir (Isentress™, MK-0518) in HIV-1 Infected Children and Adolescents
- P1068s: P1060 Substudy Comparing Differences in Malaria Parasitemia by Real-Time Quantitative PCR in HIV-Infected Infants and Children on PI-Based HAART Versus NNRTI-Based HAART
- P1076: Impact of Oral Alendronate Therapy on Bone Mineral Density in HIV-Infected Children and Adolescents with Low Bone Mineral Density at Baseline
- \*P1078: Phase IV Randomized Double-Blind Placebo-Controlled Trial to Evaluate the Safety of Immediate (Antepartum-Initiated) Versus Deferred (Postpartum-Initiated) Isoniazid Preventive Therapy Among HIV-infected Women in High TB Incidence Settings\*
- P1083: A Phase II/III Trial of Lopinavir/Ritonavir Dosed According to the WHO Pediatric Weight Band Dosing Guidelines

- P1086: A Phase II Study to Assess the Safety and Immunogenicity of an Inactivated Swine-Origin H1N1 Influenza Vaccine in HIV-1 Infected Pregnant Women
- P1097: Raltegravir Pharmacokinetics and Safety in Neonates

*\*As noted above, investigations using data from **1077BF/FF**, **P1084s** and **P1078** may be proposed; however, due to the number of ongoing/planned analyses for these studies, the timeline for beginning new analyses may be delayed for several months.*