

Partnership for Clean Competition Request for Proposals for the Detection of Performance Enhancing Drugs (PEDs) using low volume and alternative specimens

The Partnership for Clean Competition (PCC) supports high-quality, high-impact, novel research that has a high likelihood of success and of resulting in methods or products that will advance the anti-doping field and ensure integrity in sport. Funded projects typically address the improvement of existing analytical methods for detecting particular drugs, the development of analytical methods to test for performance-enhancing drugs not currently detectable, and discovering cost effective approaches for testing widely abused substances across all levels of sport. The ongoing research priorities of the PCC can be found listed at:

<http://www.cleancompetition.org/research-priorities.aspx>

In an effort to address research areas that are priorities for the PCC, the organization may encourage submission of projects on specific research topics by calling for requests for proposals.

The PCC is requesting proposals for new and innovative approaches for collecting smaller volumes, whether blood, urine, saliva, or other specimens, and for methods necessary to detect known performance enhancing drugs in these samples. The forensic nature of the testing process must be considered when developing new collection approaches so that irrefutable linkage of the sample to the donor can be achieved and that no potential for tampering with the sample after collection exists. Stability of the drugs in the proposed collection matrix or medium should also be considered. Blood collection approaches that eliminate the need for phlebotomy are of particular interest.

Overview of current sample collection process

Across sports drug testing programs, the processes for collection are similar although the banned substances as well as the tested specimens (i.e., blood, urine) may differ.

The drug testing process begins with sample collection, which may be conducted either in-competition or out-of-competition. The responsible anti-doping organization (ADO) selects an athlete to be tested and a collection officer is dispatched to perform the collection. The athlete is then required to provide a sample of urine or blood. A urine sample typically requires 90 ml, and the sample is separated into an "A" and "B" sample. For urine samples, full frontal observation during provision of the urine sample is generally required. Any collection system needs to address the potential for adulterated or substituted samples.

The athlete usually handles the urine and collection containers until they are sealed. The athlete selects the pre-labeled transport container from several possible kits. After the urine is transferred to the containers, they are sealed with a tamper-evident mechanism, placed inside other sealed containers, and shipped to a WADA-accredited laboratory. Once custody of the sample is transferred to the collection officer, a chain of custody is maintained. The purpose of

the chain of custody is to ensure that the sample can be indisputably associated with the athlete and that the sample could not have been tampered with after collection. From a historical perspective, the athlete has been afforded the opportunity to view the part of the collection process that involves any manipulation of the sample (e.g., centrifugation of blood).

The cost of collection of a single no-notice out-of-competition sample can run as high as \$400. For this reason, collection methods that could minimize the use of a collection officer or phlebotomist could have appeal as long as the potential for adulterating and unambiguously identifying the sample donor can be maintained. In addition, decreasing the weight of the sample to be shipped could result in substantial savings.

From the site of the sample collection, the sample is then shipped to a laboratory to detect any prohibited substances or methods contained in the sample. The list of prohibited substances includes a wide variety of chemicals, ranging from small molecules like stimulants (e.g., amphetamine) and anabolic steroids (e.g., testosterone) to peptides like insulin-like growth factor 1 (IGF-1) and proteins like erythropoietin (EPO) and human growth hormone (hGH). The samples must be handled in a way that preserves the integrity of this wide range of compounds. As a general consideration, the urine samples are not frozen before shipment.

Blood samples have been routinely transported to laboratories under refrigerated conditions and delivered and analyzed within 48 hours. This is primarily due to the in vitro maturation of reticulocytes during shipping and storage. Other blood analytes, such as GH or IGF-1, may not have the same shipping and storage requirements.

Historically, two separate blood tubes have been collected during venipuncture to provide a “A” and “B” sample. If a prohibited substance is detected in the “A” sample, the athlete may ask for an analysis of the “B” sample to determine whether it confirms the findings from the “A” sample.

Opportunity

If targeted performance-enhancing drugs were to be sensitively and accurately detected through collection of smaller volumes, whether blood, urine, saliva, or other specimens, several benefits could be achieved:

- The cost for shipping to laboratories could be reduced, allowing for more tests to be conducted at all levels of sport
- Tests for specific substances could potentially be conducted onsite, reducing the time required to analyze samples and allow for more intelligent lab analysis
- Stability of analytes could be better maintained without the need for refrigeration or freezing
- Maximize efficiency and minimize burden of sample collection

The detection of prohibited substances in biological fluids generally requires methods that can identify the compound, for example, mass spectrometry or antibody-based techniques in which the specificity of the epitope recognized is well characterized. In general, only a few naturally-occurring prohibited substances are quantified.

Proposal Concepts

New technologies have already been applied to analogous fields and other opportunities may exist or be under development. For instance, a newborn screening test for metabolic disorders may be performed on a dried blood spot. By critically reviewing approaches that have been used by other areas of science or by developing novel approaches for sample collection, innovation in sample collection may be achieved.

Several ideas have been considered that could be supported for further development. Additional projects which meet the key considerations would also be considered.

- Saliva test for common metabolites from PEDs.
- Blood spot to detect known substances that can be detected in blood (e.g., hGH). Collection strategies that allow detection of only one Prohibited Substance will be considered.
- Using DNA for verification of the individual who provided the sample and the time of sample collection.
- Using a solid phase extraction technique to concentrate analytes into a smaller, lighter form before shipping to the laboratory.

Key Considerations

- Indisputable evidence must link the sample to the individual sample donor
- Test must stand up to forensic levels of sensitivity
- Proposed method should allow for quick, efficient collection from donor
- The approach must be cost effective
- Separation of the sample into two portions (A & B) or convenient collection of two samples simultaneously at the time of collection is preferred
- Cost implications of the suggested process should be considered. Lowering costs may allow for increasing the number of tests or rolling out testing more broadly to other sports entities

Key Evaluation Criteria

- **Impact on anti-doping:** Proposal demonstrates novel and improved approach to meeting an important need to anti-doping.
- **Quality of proposal:** Proposal shows significant scientific merit, clear and defined objectives and ability to achieve results within given timeframe.
- **Personnel, resources and budget:**
 - Reputable and credible experience and expertise of investigators
 - Access to resources to enable high quality research
 - Reasonable cost projections and efficient use of funds
- **Likelihood of success to the field:** Analytical support for anticipated results and likelihood of transferability of results for practical use in the anti-doping field.

Eligibility and Considerations

Project investigators from academic institutions inside and outside the United States are encouraged to submit proposals. Applicants do not need to have undertaken anti-doping projects previously; however, collaboration between experts in relevant fields and anti-doping will be viewed favorably. Nonprofit institutions will be given priority.

Funding

Funding will be commensurate with demonstrated approach to achieve identified results. The PCC encourages projects with ambitious yet realistic aims. It is not uncommon for the PCC to fund 2-year to 3-year projects ranging in funding between \$100,000 and \$1,000,000. Longer-term or a higher project budget would be considered if the proposal justifies that level of commitment.

Individuals are also allowed to submit pilot project applications for topics in which preliminary data may be limited.

Application Process

Applicants must complete a pre-application before submitting a full proposal. The screening of pre-applications is meant to ensure alignment between the research project and the PCC's objectives and to ascertain basic scientific merit of the approach.

The PCC considers applications three times per year, with pre-application due March 1, July 1 and November 1.

Investigators whose pre-applications are consistent with the PCC's priorities will be asked to submit a full proposal. The full proposal will be e-mailed to those applicants and includes the following sections:

- Abstract
- Background/Significance
- Specific Objectives
- Preliminary Data
- Experimental Design, Methods and Data Analysis
- Applicability to Anti-Doping
- Facilities and Equipment
- Personnel
- Budget and Justification
- Other Support
- Biographical Sketches
- Statement of Potential Conflicts of Interest
- Letters of Support (if necessary)

To apply for PCC funding, please visit the PCC website at www.cleancompetition.org. Please contact PCC President, Jill Zeldin, at (719) 866-3306 or jzeldin@cleancompetition.org with further questions.