

## **Partnership for Clean Competition Request for Proposals for the Detection of Human Growth Hormone Use**

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 priority research areas to the PCC, the organization may encourage specific research topics by calling for requests for proposals.

Growth hormone (GH) is believed to be used by professional and amateur athletes as a performance-enhancing agent, yet its use in competitive sports is prohibited by the World Anti-Doping Agency (WADA). The PCC is requesting proposals for new and innovative approaches for detecting the use of human growth hormone.

### **Background**

Growth hormone, also known as somatotropin, is a protein hormone made and secreted by the pituitary gland. Growth hormone is considered an anabolic hormone and also mobilizes fat from adipose tissue. There are several isoforms of naturally occurring growth hormone, including 22K-GH (the most abundant), 20K-GH, placental GH and several other minor isoforms, including aggregates of two or more GH molecules (dimers and oligomers).

The pharmaceutical form of growth hormone is used for the treatment of growth hormone deficiency in children and adults. Because of its availability in the marketplace, the 22K-GH form is the form thought to be abused by athletes.

While the greatest effects of growth hormone occur in individuals deficient of naturally produced growth hormone, some believe that growth hormone demonstrates qualities of an ergogenic substance and could enhance athletic performance. Although the effect of human growth hormone on athletic performance has not been proven, it is thought that growth hormone is being abused by many athletes across a range of sports.

Several aspects of growth hormone have made it difficult to detect its use.

- The pharmaceutical form of growth hormone is identical with the natural 22K-GH
- GH in blood is very short-lived (half-life of 15-18 minutes). A typical elevation in GH concentration may no longer be detectable after 2 hours

- The time period for detection based on suppression of endogenous GH secretion is limited to about 24 hours

### **Areas of Opportunity**

Despite the difficulties of detection, there are several areas of opportunity that should be further explored. Current approaches for detection of GH abuse include the isoform test and the biomarker approach.

The currently used WADA-sanctioned test combines the direct identification of the doping substance (22K-GH) and assessment of a biological response (suppression of endogenous GH production). In principle, this is an excellent and robust test but it suffers from a short time period for detection. The test is effective when applied within one day of the last GH dose, which limits its practicality to primarily out-of-competition testing.

The biomarker approach is an indirect test that measures substances known to be increased in response to GH. Its main advantage over the isoform test is predicated upon GH treatment inducing a number of downstream biomarkers. These biomarkers are relatively specific for GH action and have been selected for anti-doping purposes; they are insulin-like growth factor (IGF-I) and N-terminal peptide of procollagen III (P-III-NP). Difficulties still exist because of reagent availability and standardization issues and the lack of normative data for P-III-NP in particular. It is possible that other biomarkers may be equally suitable for anti-doping testing.

### **Proposals Requested**

In addition to projects addressing the ongoing research priorities, the Partnership for Clean Competition welcomes proposals that would improve the detection methods for misuse of hGH. Projects covering the topics below will receive special consideration:

1. Development of approaches that cannot be easily circumvented, such as the feasibility of circulating GH mRNA or miRNA measurement as a detection tool.
2. Techniques to minimize the amount of blood needed for assays to detect the use of human growth hormone and other performance enhancing substances.
3. The development of a robust, preferably MS-based, assay for IGF-I.
4. Research into other biomarkers for GH and/or IGF-I use. Encourage documentation of why some biomarkers are better for anti-doping purposes than others.
5. Research into measurement of P-III-NP, including developing an international standard, robust assay reagents, and possibly measurement techniques that do not rely solely on immunoassay.
6. Research into secretagogue use and methods for secretagogue detection.
7. Construction of a database of GH and IGF-I use and real doping practices among athletes and body builders in order to aid in the interpretation of scientific studies.

## Key Evaluation Criteria

- **Impact on anti-doping:** Proposal demonstrates novel, improved approach to meeting an important need for anti-doping efforts.
- **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 outcomes 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, especially those who have experience in growth hormone research. Applicants do not need to have undertaken anti-doping projects previously; however, collaboration between growth hormone experts and anti-doping experts will be viewed favorably. Nonprofit institutions will be granted priority.

## Funding

Funding will be commensurate with demonstrated approach to achieve identified results. The PCC encourages robust 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-applications 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)

All grants will be subject to execution of the PCC's standard Grant Agreement.

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