PROJECT REVIEW

"Detection of Oxygen Delivery Enhancers using Dual Detection Methodology"

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The SLAB project will generate a comprehensive blood screening procedure capable of providing same-day feedback on the use of recognized methods of blood doping. These detection methodologies are designed to complement the 'SAFE mobile' project presented to the WADA Health and Medical Committee. Implementation of the strategies will deter athletes from experimenting with blood substitutes and other substances that enhance oxygen delivery. Researchers who were instrumental in the success of the EPO2000 project will collaborate with pharmaceutical companies to develop tests for yet-to-be-released pharmaceutical products. This pro-active approach will dissuade athletes who in the past have sought to 'stay ahead' of doping authorities by progressing to novel drugs before appropriate tests can be implemented.

Features of the SLAB proposal:

- Internationally-renowned scientists with a proven ability to undertake and successfully complete anti- doping research (incorporating both blood and urine matrices)
- Collaboration with the pharmaceutical companies who develop blood substitutes, as well as with medical experts and manufacturers of analytical instruments
- Substantial in-kind contributions from industry partners subsequent to appropriate negotiation and confidentiality agreements
- A Steering Committee (including invitees from the WADA and the IOC/Australian Olympic Committee Medical Commissions) and a Probity Officer to ensure appropriate transparency and propriety.

Detection of Oxygen Delivery Enhancers Using Dual Detection Methodology

Results and Conclusions

The SIAB research consortium seeks to deter blood doping in sport by combining the expertise of sports scientists, haematologists and analytical chemists with the knowledge and experience of industry partners, to proactively develop tests for novel pharmaceutical products that may be prone to abuse by athletes.

One important aspect of research focused upon haemoglobin-based oxygen carriers (HBOCs). The first requirement was to enter collaborative arrangements with each of the five pharmaceutical companies developing products, in order to obtain a sample for analytical chemists at the University of Montpellier and the Laboratoire Nationale Depistage du Dopage to develop analytical techniques to detect the different substances. Two manuscripts were drafted and subsequently accepted. These manuscripts describe an electrophoretic technique that was subsequently adopted by WADA for use as a screening method (Lasne et al. Clin Chem 50(2):410-5, 2004), and a high performance liquid chromatography technique that was adopted by WADA for use as a confirmation technique (Varlet-Marie et al. Clin Chem. 2004 Apr;50(4):723-31). Both methods were shown to be valid for each of the different HBOC products currently under development.

A second aspect of research was the Haematological Passport. A preliminary goal was to overcome the practical limitations inherent in the different proprietary technologies used to measure reticulocytes by different instrument manufacturers. This leads inevitably to inter-instrument bias which makes results collected on different instruments difficult to compare. We conceived and published an approach that allows reticulocyte percentage results derived on different platforms, at different times, and in different locations, to be compared directly. In keeping with SIAB's goal to provide strategies compatible with sport federations, it was recognised that the disparate approaches utilised by some international sport federations to blood testing of their athletes was detrimental to the widespread acceptance of blood testing as a valid strategy to fight blood doping in sport. Efforts were undertaken to liaise with key federations, to better understand their rationale and stance, and to seek to find a compromise approach that was both inclusive and an effective deterrent against doping. Having addressed these practical concerns, we focussed upon the statistical interpretation of longitudinal data collected from international athletes in order to understand the degree of biological variation inherent in key blood parameters. We proposed a third-generation approach to blood testing to assist authorities to detect EPO doping, in particular focussing on the need to detect cynical athletes who manipulated EPO injections in order to escape sanction with the existing urine test.

The research consortium also completed a pilot trial utilising a low-dose EPO regimen, which demonstrated that it is likely that an athlete could only be sanctioned for rHuEPO use if a urine test was conducted within 24 hours of the last injection if the athlete had resorted to 'maintenance' doses of the drug.

Publications

1: Ashenden MJ, Lacoste A, Orhant E, Audran M, Sharpe K.
Longitudinal variation of hemoglobin and reticulocytes in elite rowers.
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2: Ashenden MJ, Sharpe K, Schoch C, Schumacher YO.
Effect of pre-competition and altitude training on blood models used to detect erythropoietin abuse by athletes.
Haematologica. 2004 Aug;89(8):1019-20.

3: Ashenden M.
Contemporary issues in the fight against blood doping in sport.
Haematologica. 2004 Aug;89(8):901-3.

4: Ashenden MJ, Sharpe K, Damsgaard R, Jarvis L.
Standardization of reticulocyte values in an antidoping context.
Am J Clin Pathol. 2004 Jun;121(6):816-25.

5: Schumacher YO, Ashenden M.
Doping with artificial oxygen carriers: an update.
Sports Med. 2004;34(3):141-50. Review.

6: Varlet-Marie E, Ashenden M, Lasne F, Sicart MT, Marion B, de Ceaurriz J, Audran M.
Detection of hemoglobin-based oxygen carriers in human serum for doping analysis: confirmation by size-exclusion HPLC.
Clin Chem. 2004 Apr;50(4):723-31. Epub 2004 Feb 5.

7: Lasne F, Crepin N, Ashenden M, Audran M, de Ceaurriz J.
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Clin Chem. 2004 Feb;50(2):410-5. Epub 2003 Nov 21.

8: Ashenden MJ.
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Haematologica. 2002 Mar;87(3):225-32.