

## **PROJECT REVIEW**

### **“Identification/detection of novel anaemia drugs”**

**M. Ashenden** (SIAB Research Ltd, Australia), **I. MacDougall** (Kings College, London, UK), **J. de Ceaurriz** (Laboratoire du Depistage du Dopage, France)

Despite a committed antidoping movement, abuse of recombinant human erythropoietin (rHuEPO) continues. Clandestine use extends to the use of novel rHuEPO products in the hope these may be undetectable via the electrophoresis test which distinguishes endogenous EPO from the synthetic versions based on different electric charges on the respective molecules.

Recombinant erythropoietins are the number one revenue-generating class of biological products on the market, with worldwide sales exceeding US \$12 billion. The lapse of European patents in 2004 has opened the door for approval of biosimilar versions of rHuEPO, and multiple pharmaceutical companies are now embarked on the development of viable alternatives for this lucrative market. In order to maintain an effective screening process it is vital for laboratories to obtain pre-emptive information regarding the structure and detectability of these novel anaemia drugs.

Several classes of products are being developed: biosimilar rHuEPOs (same molecular structure but produced using different procedures), long lasting EPOs (molecule modified to extend half-life in circulation), synthetic EPO receptor agonists (completely different molecular structure which nonetheless stimulates the EPO receptor) and EPO replacements (stimulate red cell production via non-EPO receptor pathways).

The aim of this research is to validate the capacity for isoelectric focussing to discriminate between novel anaemia drugs and endogenous EPO, and where this proves impractical to develop new detection methodologies. We will enter collaborative arrangements with the pharmaceutical companies to seek access to their products prior to commercial release in order to thwart attempts to use novel drugs before an appropriate test has been introduced by antidoping authorities. The drugs will be screened at the WADA-accredited laboratory in Paris who developed the isoelectric test and are world leaders in its application to doping control.

## **"Identification/detection of novel anaemia drugs"**

**M. Ashenden** (SIAB Research Ltd, Australia), **I. MacDougall** (Kings College, London, UK), **J. de Ceaurriz** (Laboratoire du Depistage du Dopage, France)

### **Results and Conclusions**

An extensive network including pharmaceutical company representatives and their expert consultants was activated in order to identify and detect novel anaemia drugs.

A comprehensive market appraisal and *de novo* interrogation of literature and websites dramatically expanded upon the initial estimate made in 2007 that around one dozen copy EPOs were available. The most recent estimate suggests this number to be in excess of 100 in 2010. A significant number of these products have been procured and analysed by an anti-doping laboratory; several unusual profiles, and in a small number of cases inexplicable characteristics, have been reported.

An important emphasis of the project has been to facilitate collaboration between pharmaceutical manufacturers and the WADA. Introductions were made to different pharmaceutical and biotechnology companies which enabled WADA to commence discussions and in several cases in-depth collaboration to develop detection methods for novel ESAs considered of high interest.

In 2009 the ESA industry experienced considerable upheaval following the publication of results ('TREAT" study) indicating that administration of exogenous EPO posed previously unrecognised health risks. Subsequently it is anticipated that substantially greater research emphasis will be placed in the foreseeable future on development of novel ESA agents.