

Comment to: Recombinant erythropoietin found in seized blood bags from sportsmen. Haematologica 2008;93:313-4

We read with interest the article of Mallorquí *et al.* reporting a new immuno-purification method providing evidence for presence of recombinant erythropoietin (rEPO) in bags of human plasma confiscated during the *Operation Puerto* (OP).¹ The method developed by Mallorquí *et al.* seems sound and potentially useful to establish whether blood or plasma confiscated during antidoping controls contains rEPO. However, we do not agree with the conclusion that routine rEPO measurement in plasma could be a way to deter blood doping practices, given the difficulties in detecting autologous transfusions.¹ This new immuno-purification method followed by traditional isoelectric focusing (IEF) to separate rEPO from endogenous EPO is more expensive and labour intensive when compared to current urinary screening,² and it poses additional practical problems. First, the mean half-life of rEPO following repeated 50 IU/kg per day subcutaneous administrations is ~36 h (with a average clearance of 17 mL/h/kg). However, half life is reduced to 4-7 h following intravenous administration and total clearance is nearly three times higher in athletes than in untrained subjects (6.5 mL/h/kg).³ Due to this particular kinetics, intravenous administration of rEPO in athletes would lead to undetectable plasma levels after 2-3 h. Furthermore, due to the long lasting effects of rEPO and derivatives on erythrocyte biology, it is unlikely that athletes will use rEPO or similar compounds close to competitions.⁴ Finally, athletes preparing to dope with autologous transfusions can do without rEPO administration by extracting blood without prior "boosting".⁵ Another specific concern on the analytical efficiency of the new method is the use of epoetin delta and CERA (continuous erythropoietin receptor activator). Due to innovative production technology, these new EPO analogues are as yet undetectable by the traditional IEF approach, both in urine and in plasma.⁴

Therefore, we consider that in- or near-competition testing for plasma rEPO would primarily waste human and economical resources, whereas the revenues in terms of doping prevention are as yet unpredictable. Even in out-of-competition settings, the specific kinetics of rEPO would make detection rather unlikely, provided that blood is collected in the immediate period following rEPO administration. Current antidoping policy, essen-

tially a costly repressive zero-tolerance approach in elite sport, will continue to be hampered by the limits of technology. False negatives and false positives are inherent possibilities with testing technology and current protocols do not adequately address the problem of biological and pre-analytical variability, which both may lead to unreliable test results. This uncertainty is acceptable in the field of therapeutic medicine but problematic in sport because athletes can never be considered truly clean, whereas false accusations should be avoided at all cost. Pragmatically, the introduction of additional analyses to the already huge armamentarium of antidoping tests is questionable, both in ethical and economical terms, especially when the diagnostic efficiency of the new tests is not proven. Contributions: GL (ulippi@tin.it): conceived and wrote the article. MF (massimo.franchini@azosp.vr.it): helped to write the article. BK (Bengt.Kayser@medecine.unige.ch): helped to write the article and revised it for important intellectual content.

Giuseppe Lippi,¹ Massimo Franchini,² Bengt Kayser³

¹Sezione di Chimica Clinica, Università degli Studi di Verona, Italy;

²Servizio di Immunoematologia e Trasfusione, Azienda Ospedaliera di Verona, Italy; ³Institute of movement sciences and sports medicine, University of Geneva, Switzerland.

Correspondence: Prof. Giuseppe Lippi, MD, Sezione di Chimica Clinica, Dipartimento di Scienze Morfologico-Biomediche, Università degli Studi di Verona, Ospedale Policlinico G.B. Rossi, Piazzale Scuro, 10 37121 - Verona Italy

Tel. 0039-045-8124308 Fax: 0039-045-8201889

E-mail: ulippi@tin.it, giuseppe.lippi@univr.it

Key words: antidoping testing, doping, erythropoietin, blood.

Haematologica 2008; 93:e55. DOI: 10.3324/haematol.13179

References

- Mallorquí J, Segura J, de Bolòs C, Gutiérrez-Gallego R, Pascual JA. Recombinant erythropoietin found in seized blood bags from sportsmen. *Haematologica* 2008;93:313-4.
- Lasne F, Martin L, Crepin N, de Ceaurriz J. Detection of isoelectric profiles of erythropoietin in urine: differentiation of natural and administered recombinant hormones. *Anal Biochem* 2002;311:119-26.
- Varlet-Marie E, Gaudard A, Audran M, Gomeni R, Bressolle F. Pharmacokinetic-pharmacodynamic modelling of recombinant human erythropoietin in athletes. *Int J Sports Med* 2003;24:252-7.
- Lippi G, Franchini M, Salvagno GL, Guidi GC. Biochemistry, physiology, and complications of blood doping: facts and speculation. *Crit Rev Clin Lab Sci* 2006;43:349-91.
- Lippi G, Banfi G. Blood transfusions in athletes. Old dogmas, new tricks. *Clin Chem Lab Med* 2006;44:1395-402.