Regulatory frameworks in developing countries

To the editor:

Although we appreciate that the recent *Nature Biotechnology* supplement 'Health Biotechnology Innovation in Developing Countries' was concerned largely with the economics of biotech manufacturing in developing countries, we feel there were some serious gaps in the coverage presented.

It is true that governments have a role in creating the correct environment to enable biotech companies to flourish, but there must also be some regulatory framework to oversee licensing of new products and to monitor the quality of products released into the marketplace. Our experience is that this regulation is often lacking; as a result sub-standard products are reaching the market with potentially seriously damaging effects on patients.

Our laboratory has a long-standing interest in streptokinase and maintains the International Standard for Streptokinase, which is used as the global reference preparation to quantify streptokinase potency. Over the past two years or so, we have used this standard to survey a number of products from developing countries and the results are not good[1]. For example, of 17 routine batches tested (made up of 12 different products) consisting of streptokinase manufactured or sold in India, South Korea, Egypt or Brazil, 15 would fail to meet current European Pharmacopoeia standards and would not be approved for use in Europe. Many had activities below 50% of the labeled potency. In particular, one batch from India contained no detectable streptokinase protein or activity and a further two batches from the same manufacturer had only 10% and 20%, respectively, of the labeled potency.

Furthermore, as your report pointed out, several countries including China, Cuba, Egypt and India are producing recombinant streptokinase. We have grave concerns over how these products should be licensed and regulated since streptokinase activity is very sensitive to small changes in amino acid sequence; it is our experience that the current International Standard for Streptokinase is not a suitable reference for some recombinant products. As a result patients may receive significantly different doses of streptokinase in different products, which could lead to ineffective treatment or, alternatively, cerebral hemorrhage. Thus, although the "regulatory processes in India may be unnecessarily burdensome" for a variety of reasons, there are serious scientific questions that need to be addressed if safe products are to be released onto the market.

Rates of cardiovascular disease are rising rapidly in developing countries and there is a need for increased access to thrombolytic therapy. Streptokinase is a cheap and effective treatment and is an obvious target for biotech companies. However, if we adopt streptokinase as a marker for the quality of biotech products generated in developing countries, then our survey is very disturbing. Appropriate regulatory mechanisms should not be ignored simply to create a free market where biotech companies can flourish at the expense of patient well-being.

Colin Longstaff, Craig Thelwell & Colin Whitton

Division of Haematology, National Institute for Biological Standards and Control, Blanche Lane, South Mimms, Hertfordshire, EN6 3QG, UK.
e-mail: clongstaff@nibsc.ac.uk

1. Longstaff, C., Thelwell, C. & Whitton, C. J. *Thrombosis Haemostasis* **3**, 1–2 (2005)

Halla Thorsteinsdóttir and Abdallah S. Daar respond:

We agree with Longstaff *et al.* that the development of appropriate regulatory mechanisms is necessary to ensure that the growth of a biotech industry goes hand in hand with patient well-being. Indeed, the countries we surveyed in Health Biotechnology Innovation in Developing Countries did focus on developing their regulatory systems so that their biotech products would conform to acceptable standards of quality, safety and efficacy. They have used World Health Organization recommendations and guidelines, Food and Drug Administration guides, European Union guidelines and International Conference on Harmonization guidelines to draft mechanisms for unified and systematic registration and rigorous quality monitoring of biotech products. They have also set up systems to ensure that Good Laboratory Practices, Good Clinical Practices and Good Manufacturing Practices are all followed.

Some of the countries in our study have had their vaccine production prequalified to be used by the United Nations purchasing agencies. That is the case, for example, for the hepatitis B vaccines from Cuba, India and South Korea[1]. When we state that the regulatory process is unnecessarily burdensome in India, we base that on interviews with 38 experts in the health biotechnology sector in India. We and the Indian experts do not argue for a less stringent regulatory system but for increased coordination between the different regulatory bodies and more efficiency.

We recognize that setting up a regulatory system is only the first step towards the production of safe, efficient and high quality medicinal products but well-organized operation of the system is vital for its success. It is possible that the operation of the regulatory systems in Brazil, Egypt, India and South Korea needs to be improved at least with regard to quality monitoring of streptokinase. As such the work of