AN AUDIENCE WITH…

Thomas Lönngren

Thomas Lönngren, Executive Director of the EMEA
Thomas Lönngren is Executive Director of the European Medicines Agency (EMEA), a position he took up at the beginning of 2001. Before joining the EMEA, Lönngren was Director of Operations of the Swedish Medical Products Agency, where he later became Deputy Director-General. A qualified pharmacist with an M.Sc. in social and regulatory pharmacy, Lönngren was a lecturer at Uppsala University in Sweden before he served with the Swedish National Board of Health and Welfare from 1978 to 1990. During this time he also acted as a senior pharmaceutical consultant for the Swedish International Development Agency's health cooperation programme in Vietnam (1982–1984). Lönngren was elected an Honorary Member of the Pharmaceutical Society of Great Britain in 2003 and made an Honorary Fellow of the Royal College of Physicians in 2004.

What's the difference between a biogeneric and a biosimilar product?
There is no difference. 'Biogeneric' doesn't exist as a term; we have used the term 'biosimilar' in the legislation because these are not generic products, by definition. There is a new route for application and authorization of these products and it's quite different from generics. Generics are very well-defined chemical substances, and it's very easy to demonstrate that you can basically make the same product. But with biologics — complex proteins and molecular structures — it's not so easy. The European Commission (EC) investigated whether, once a branded biologic has gone off-patent, it's possible for another company to develop more or less the same product and, in the justification for the application, refer to the fact that a similar product has already been authorized. This means that you could reduce the data requirements for clinical and preclinical studies when evaluating regulatory documentation. So we have published guidelines for information required for different types of biological products.

If these drugs are similar, but not exact copies, how can you ensure their safety?
Studying aspects of safety is a data requirement that the industry must conform to according to our guidelines. The studies that accompany the filing have to be performed to demonstrate comparability of quality, efficacy and safety profiles.

But that's not as extensive as full-scale clinical trials is it?
Well, yes, probably there are clinical trials that are necessary to do for these products, but not large-scale clinical trials that were done for the original product. There is a careful examination of the safety and efficacy of biosimilars and this is supported by a comprehensive study of quality, with comparative data to evaluate differences with the original product. After extensive public consultation there is scientific consensus regarding the content of the guidelines developed by the EMEA and this should be enough to demonstrate safety and efficacy.

Will post-marketing surveillance be a requisite for these drugs?
The revised pharmaceutical legislation in Europe requires that companies submit risk-management plans for each drug, which will include a demonstration of the type of post-marketing surveillance they will do and what risk-minimization plans they have for post-marketing.

How will you ensure that industry complies?
There are new tools in the legislation concerning industry's responsibility for post-marketing studies, including pharmacovigilance inspections, to check that the company is complying. If a company does not comply, the new pharmaceutical legislation allows the possibility of issuing penalties. The implementation of this legislation has not been adopted yet by the EC and so the type of penalties is not quite clear yet, but the EC is working on guidelines for this.

How do you characterize a biosimilar drug? Have advances in technology made this easier?
There are continual advances with the analysis of complex protein structures, and technologies such as mass spectroscopy play an important role in the characterization of these molecules. However, the guidelines for biosimilars refer to existing requirements for characterization of other types of biological product. A biosimilar product must also be compared directly with the originator product in these characterization studies in order to identify differences between them.

What endpoints constitute efficacy, safety and similarity for a biosimilar?
The demonstration of similarity is based on an equivalence design versus the originator's product. Details on the requirements for these studies — for example, for somatropins — are included in specific guidelines that are available on the EMEA website and which are currently being finalized. In cases where no guidance is available, requests for scientific advice could be considered on a case-by-case basis. The European Public Assessment Report (EPAR) will reflect the studies, which form the basis of any marketing authorization.

Biopharmaceutical innovators have criticized the publication of guidelines that might make it easier for companies to copy their drugs. How do you respond?
We have not received any criticism here at the EMEA. It's obvious that the pharmaceutical industry has different interests, and everybody has to look after their own interests, so there is nothing wrong in that. But the EC made a policy decision that this route is open for companies to make applications, and we are simply executing that legislation.

Do you think we will now see a rapid increase in approvals of biosimilars?
A couple of years ago everybody was optimistic when this possibility arose in the legislation, and foresaw many applications. But now, because biosimilar products are compared with generics and we have more experience of biologics, biosimilar products need to fulfil more requirements, so it will take greater investment by companies to put these products on the market. Maybe as more biologics go off patent, more companies will invest in this area of drug development, but I don't expect to see an enormous amount of applications coming in soon.