

# Brave new world: biopharmaceuticals – the future

A report of a scientific symposium held on Wednesday, 25 March 2009 at the 14th EAHP Congress, Barcelona, Spain.

**B**iopharmaceuticals are becoming increasingly important in terms of healthcare. These medicines are used to treat serious diseases and long-term conditions, however, they also make a significant contribution to healthcare spending [1]. Treatment costs with biopharmaceuticals are considerably higher when compared with conventional pharmaceuticals. This is an important concern at a time when healthcare providers are trying to find ways to minimise expenditure. In the last few years the introduction of biosimilar products has offered healthcare providers, such as hospital pharmacists, an alternative when considering the use of biopharmaceutical medicines. The scientific symposium, *Brave new world; biopharmaceuticals – the future*, sponsored by Sandoz, provided delegates with the opportunity to learn about the issues surrounding the approval and use of biosimilar medicines.

### Is there a need for biosimilars?

Biopharmaceuticals are the fastest grow-

ing area of medicine today, representing a new generation of medicinal products. There are approximately 200 biopharmaceuticals on the market, with as many as 300 more in clinical trials. It is estimated that by 2010, 50% of all newly approved medicines will be biopharmaceuticals [2]. When the patented life-spans of these products expire, it is then possible for companies to produce biosimilar versions of these medicines [3]. Biopharmaceutical medicines are complex and cannot be copied exactly; therefore, the term biosimilar is used. The EMEA has a legal and regulatory pathway which, as Mr Vain Fenton-May (Vice Chairman, British Pharmacopoeia Commission, UK) explained in the first presentation of the symposium, was developed over six years and demands strict scientific and regulatory standards for biosimilars. When considering the use of biosimilars, this is one of the important factors the hospital pharmacist should keep in mind. They should also take into account other aspects in their evaluation of these medicines, such as the experience and heritage of the

manufacturing company; the quality, manufacturing and distribution processes; the traceability; the post market authorisation risk management plan and finally, of course, the cost savings. Technological developments mean advanced solutions for more diseases. However, this also comes with increasing financial costs, at a time when the EU faces challenges on spending and healthcare funding. Mr Fenton-May concluded that the crucial issue is now one of affordability and that healthcare systems across Europe need the competition and competitive pricing brought about by biosimilars.

### The development of a biosimilar

Following on, Dr Carsten Brockmeyer (Head of Global Biopharmaceuticals Project Management and Clinical Development, Sandoz, Germany) began by reminding the audience that biopharmaceuticals are complex large molecules, which are difficult to characterise, because they are derived from living cells. However, he too emphasised the quality, safety and efficacy of a biosimi-

Figure 1: Comparability is demonstrated at all levels

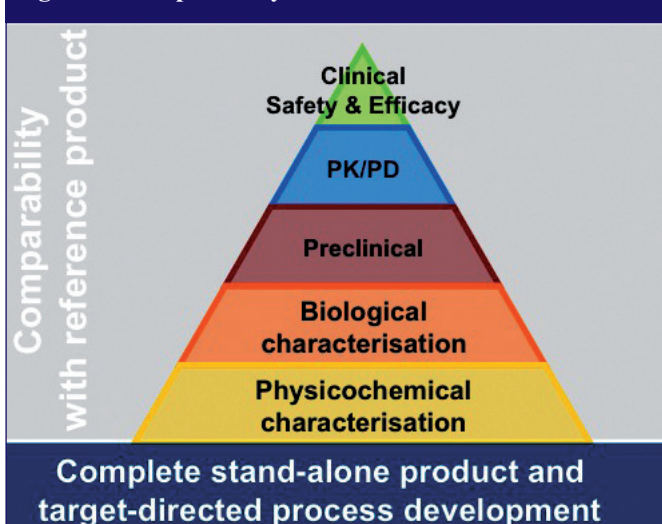
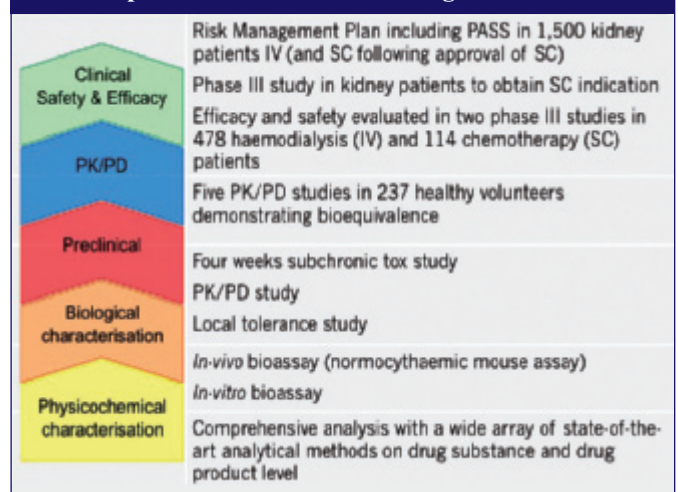


Figure 2: Comparability of Binocrit with the reference product established at all stages



lar is comparable to the reference product and has a clear legal basis in the European Union.

Comparable quality, safety and efficacy are considered during all stages of the development of a biosimilar and quality standards in manufacture apply equally to all biopharmaceuticals, including biosimilars (see Figure 1). Binocrit was the first complex biosimilar, approved in 2007, under the EMEA biosimilar pathway. It is an epoetin alfa biosimilar used for the treatment of renal and chemotherapy induced anaemia. The comparability of Binocrit to the reference product has been demonstrated at all levels of development (see Figure 2). Analytical and characterisation studies are a key part of the dossier on which EMEA approval for Binocrit was based. For example, isoelectric focusing gel electrophoresis of Binocrit and its comparator product epoetin alfa show a comparable isoform pattern [4]. Other techniques allow for further comparisons at the atomic level. Ultra violet circular dichroism (UV CD) spectra analysis techniques are modern methods of comparing protein structures. Binocrit and the reference product have been shown to have indistinguishable far- and near-UV CD spectra, indicating that both products have comparable secondary and tertiary structures. Dr Brockmeyer also described comparable Epo-receptor binding and *in vivo* bioactivity of Binocrit and the reference product [4]. A target directed approach to the development of biosimilars, therefore, results in highly comparable products, made to at least the same standards as existing biopharmaceuticals. State-of-the-

art manufacturing and analytical processes also demonstrate comparability to the reference product. In addition, clinical studies demonstrate therapeutic equivalence, comparable efficacy and safety profiles. For instance, the efficacy and safety of Binocrit were evaluated in two phase III studies in 479 haemodialysis and 114 chemotherapy patients. Biopharmaceutical medicines, Dr Brockmeyer concluded, are highly potent drugs that contribute significantly to healthcare spending and biosimilars, such as Binocrit, offer an important opportunity for patients, pharmacists, doctors, and payers to have greater access to these important medicines.

### Regulation of biosimilars

Professor Huub Schellekens (Departments of Pharmaceutical Sciences and Innovation Studies, Utrecht University, The Netherlands) in the final presentation of the symposium elaborated on the challenges for biosimilar approval in Europe. The EMEA definition of a biosimilar states that it is a medicine similar to a biological medicine that has already been authorised (the reference product). They are used in general at the same dose to treat the same disease but the name, appearance and packaging of a biosimilar differ from those of the biological reference product [5]. The development of a biosimilar requires preclinical investigation to confirm the pharmacokinetic, pharmacodynamic and safety profile of the drug, as well as a clinical programme to confirm comparative pharmacokinetics, safety and efficacy with the reference product. The biosimilar medicine must be shown to have been sufficiently characterised

and the manufacturing process validated. The challenges of gaining regulatory approval for a biosimilar, for example, interferon alpha-2a, are clear. Professor Schellekens then posed the question “Should the regulatory pathway be restricted to biopharmaceuticals?”, since there are other complex biological products, for example, Copaxone, as well as complex synthetic compounds (iron-sucrose complexes). These and the development of biosimilar monoclonal antibodies will mean that the regulatory legislation may need to be further adapted.

In conclusion, it is clear that the development of biosimilars are complex, but detailed European regulations ensure the quality, safety and efficacy of this new generation of medicines. This should allow hospital pharmacists to evaluate biosimilar medicines with confidence and also provides healthcare systems with the opportunity to provide effective treatments at reduced costs.

### References

1. Source: Estimatet, Express Scripts 2007.
2. Source: Scrip World Pharmaceutical News – 17th September 2007 (Ref. S00970766).
3. Drugs of the 21st Century: biopharmaceuticals and biosimilars. Eur J Hosp Pharm Pract. 2007; 13(3):26-7. Available from www.ejhp.eu
4. Brockmeyer C, Seidl A. Binocrit: assessment of quality, safety and efficacy of biopharmaceuticals. Eur J Hosp Pharm Pract. 2009;15(2): 34-40.
5. European Agency for the Evaluation of Medicinal Products. Questions and answers on biosimilar medicines (similar biological medicinal products) (EMEA/7456206/2006). <http://www.emea.europa.eu/pdfs/human/pcwp/7456266en.pdf> Accessed 2009 May 07.



Professor Huub Schellekens



Mr V'lain Fenton-May



Dr Allan Karr



Dr Carsten Brockmeyer