# Biosimilars to Biobetters - the paths forward

Thursday, 16 May 2013
The Stevenage Bioscience Catalyst, United Kingdom

Whilst biopharmaceuticals remain a major component of the global therapeutics market, the ever expanding portfolio of products losing patent protection and with increasing healthcare costs remaining a poignant issue, the opportunity for development of competing, follow on biologics remains an attractive proposition for both Biotech and Pharma companies alike. However, as these biosimilar markets are captured how we manage the life cycle of these products and target specific patient and commercial benefits to maximise our product development strategies becomes increasingly important.

This Euroscicon biosimilars conference will focus on multiple aspects of biosimilar product development to successfully deliver safe, biosimilar products to the market place.

This event has CPD accreditation

***Who should attend***
Specialists in regulatory strategy and affairs, Biopharmaceutical developers/manufacturers including analytics/characterisation, marketing professionals, product enabling technology development companies

Meeting Chair: Dave Simpson PhD, Director, Virodigm Ltd

This event is part of the 2013 ***Euroscicon BioTherapeutics Week***,
to find out more see www.biotherapeutics2013.com

9:00 – 9:45 Registration

9:45 – 10:00 **Introduction by the Chairs**: Dave Simpson PhD, Director, Virodigm Ltd

10:00 – 10:30 **Novel Substituable Glycans in Biobetter Development**
*Jenny Thirlway,* Glythera
With multiple products facing the prospect of market erosion as they approach their patent cliffs, efforts have increased to capture markets through development of biosimilars or through further improvement to the originator into next generation products. Half-life extension using PEGylation or cell lines / strains developed to modulate naturally occurring N-linked glycans have enjoyed notable success however, the latter can often be difficult to control during scaled up production. More recent strategies have included the direct substitution of the natural glycan with a modified version resulting in a similar product profile to the originator, characterisable by the same methods.

10:30 – 11:00 **Critical steps in the development of Biosimilars**
*Dr Robert E. Zoubek,* Formycon AG, Germany
The proof of safety and efficacy of a Biosimilar is demonstrated by its comparability to the reference medicinal product in extensive biochemical and specially designed non-clinical and clinical studies. Therefore, Biosimilar development differs from the development of Novel Biopharmaceuticals and its requirements on the Chemistry and Manufacturing Control (CMC) exceed those of Novel pharmaceuticals.

11:00 – 11:30 **Speakers' photo then mid-morning break and trade show**
*Please try to visit all the exhibition stands during your day at this event. Not only do our sponsors enable Euroscicon to keep the registration fees competitive, but they are also here specifically to talk to you*

11:30 – 12:00 **The Challenges of Developing and Manufacturing Biosimilars**
*Adam Bentley*, Eden Biodesign, UK

12:00 – 12:30 **Rational design of biobetters**
*Manuel Carballo-Amador,* Faculty of Life Sciences, University of Manchester, UK.
Protein design is a potent approach for improving protein physicochemical properties with potential consequences for stability, activity, and solubility of proteins. Protein solubility plays an important role for recombinant therapeutic

proteins during protein expression, purification, long-term storage and drug administration. Based on protein structure, Chan and Warwicker developed an algorithm to predict protein solubility, defining polar and non-polar patches on the protein surface. Using this algorithm, we predicted amino acid changes that would facilitate expression of forms of human erythropoietin (HuEPO) of directed solubility in *E. coli*. We found that a single point mutation (changing a single amino acid from positive to negative charge) verified the predicted effect on HuEPO solubility (the distribution between soluble and inclusion body fractions) in three different *E. coli* strains (Bl21 (DE3), CodonPlus and SHuffle). Further application of this algorithm will provide a powerful tool for the design of biobetters, with enhanced solubility and stability.

12:30 – 13:30 **Lunch and trade show**

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13:30 – 14:00 **Enabling Less Frequent, Self-administration Blood Factors – Better for Haemophilia Patients**

*Dr Ji-won Choi,* Polytherics¸UK

Blood factors such as FVIIa, FVIII and FIX are life-saving treatments for Haemophilia A, B and trauma patients with uncontrolled bleeding. Current treatments can only be given as IV infusion, which is costly and inconvenient for haemophilia sufferers. Improved "immune-silent" forms of FVIIa, FVIII and FIX have been developed using site-specific PEGylation. In preclinical studies, PEGylated blood factors showed extended haemostatic cover for reduced dosing frequency. PEGylation also enabled previously unachievable subcutaneous injection for self-administration at home.

14: 00 - 14:30 **Regulatory & Clinical Development Considerations for Biosimilars**

*Gerry McGettigan,* Kinesys Consulting Ltd

The idea is to provide background to the legislation and guidance, followed by discussion of some of the typical development challenges and decisions.

14: 30 - 15:00 **Biosimilars: Clinical and Commercial Advantages Through The Application of Manufacturing Technologies**

*Mr John Mcguire*, DSM¸UK

- Key considerations in the development of Biosimilars
- The application of technologies to Biosimilar development and manufacturing
- The competitive edge that technologies bring including CMC risk management and improved Cost of Goods

15:00– 15:30 **Afternoon break and trade show**

15:30 - 16:00 **Molecular Characterization of Biotherapeutics: Possibilities and Practicalities**

*Eric Chang,*Faculty of Life Sciences, University of Manchester, Michael Smith Building, Oxford Road, M13 9PT, UK.

The molecular characterization of protein therapeutics is very difficult due to the presence of a wide variety of post-translational modifications. Two of the main tools available for biopharmaceutical analytics are chromatography and mass spectrometry. In this presentation, we describe our work applying these approaches, especially with a view to the investigation of modifications such as phosphorylation, methylation, methionine oxidation, glycosylation and other charge variants.

16: 00 - 17:00 **Question and Answer Session**

Delegates will be asked to submit questions to a panel of experts. Questions can be submitted before the event or on the day plus Afternoon Tea/Coffee and trade show

17:00 Chairman's summing up

Keywords: biopharmaceutical, drug delivery, Biosimilar, Regulatory, CMC,EU, Product registration, Biosimilars, Biologicals, Regulatory, Monoclonal antibodies, process development, automation, cell line, bioreactor, Characterisation, Biosimilarity, Comparability,biobetters, next generation biologics, technologies,CMC, Biosimilar, Comparability, Similarity, CTD,Biobetter, enabling, technologies, glycan, characterization, chromatography, mass spectrometry, post-translational modifications, variants, PEGylation, FIX, FVIIa, FVIII, haemophilia

About the Chair

**David's** background is in cell line, process and analytical development, Tech Transfer and manufacturing of clinical products. Formerly of Eden Biodesign, David led the process development capabilities and post-acquisition by Watson Pharmaceuticals led the development and manufacturing of a recombinant FSH biosimilar product. David now owns an independent consultancy supporting all aspects of biopharmaceutical product and commercial development needs.

About the Speakers

**Gerry McGettigan**, a molecular biologist, has twenty years' experience in the biotechnology and pharmaceutical industries, in regulatory affairs, clinical development and business development. He has worked with large and medium pharma companies (Almirall and Glaxo) and was Regulatory & Scientific Affairs Director of The Liposome Company, a US biotechnology firm.

He founded the European regulatory affairs and product development consultancy company, GMG BioBusiness Ltd, which was sold to a top 5 CRO in 2005. He also set up and was CEO of the Catalan biotechnology development agency, Biocat. Gerry has worked directly with many clients on projects ranging from early stage regulatory strategy and complex biotechnology products, to MAAs for novel healthcare products.

Gerry has excellent relationships with top level business, science and governmental executives. Gerry is a member of TRI Cap, a group of independent investors, through which he invests in biotech / pharma and other companies. Gerry is Non-Executive Director of two biotech companies, Syntropharma and Biopta.

**Robert Zoubek** is Director for Scientific Affairs at Formycon, a company which offers and performs Biosimilar development since 2003 (formerly as Scil Biopharma Services). As a passionate biochemist with more than 10 years of experience in protein chemistry, he squired numerous development projects thus knowing the needs in biosimilar development. Robert studied biology at the LMU Munich and business administration at the University of Manchester. He attained his PhD from the Medical School of Erlangen for his studies on therapeutic peptides. After the following postdoc fellowship he joined GlycoForm in Abingdon/ UK, where he developed platform technologies for Biobetters. Robert joined Formycon (former Scil Technology) in 2009. He supervised the analytical laboratories and implemented new sensitive methods for protein characterisation and comparability exercises.

**Eric Chang** is a PhD student in Biotechnology at the University of Manchester working with Prof Alan Dickson, Dr David Knight and Dr Kenneth Cook. He is sponsored by Dionex of Thermo Scientific. His work involves the characterisation of therapeutic proteins. Having completed a biochemistry PhD at the University of Nottingham,

**Jenny Thirlway** began a Post Doc at the University of Manchester studying Calcium Dependent Antibiotics from S. coelicolor. Jenny then joined Eden Biodesign where she was responsible for the cell line / strain and fermentation development teams. Post-acquisition by Watson Pharmaceutical (now Actavis) she was involved in development, scale up and manufacture of an FSH biosimilar product. Jenny joined Glythera immediately after an investment of £2M to spin the company out from Bath University and now oversees the development of Glythera's core technologies centred on stable linker and glycan chemistries.

**Ji-won Choi** joined the founding team in 2003 to establish and lead the biology department responsible for the in vitro and in vivo assessment of PEGylated and ADC-based therapeutics. He is also a co-inventor of several PolyTherics technologies. As Director of Scientific Evaluation, Ji-won is currently responsible for the evaluation of internal and external product and technology concepts. His role also covers grants, project management and steering. Ji-won awarded a PhD in Virology from Imperial College London, UK.

**John McGuire** studied as an undergraduate and post graduate at University of Strathclyde and has been a registered pharmacist since 1992. He has more than 15 years experience in various companies and roles in the biopharmaceutical industry. These roles have included analytical development, characterization and QC, as well as clinical and commercial manufacture of drug substance and drug product. John's roles have encompassed a wide scope of products including recombinant, vaccines and traditional chemicals. John also has extensive project/program management experience across a number of areas, including pre-clinical, clinical and commercial projects. Furthermore, John has a keen interest in Biosimilar development and has direct experience in a previous role where he managed the CMC aspects of a number of programs. This experience has been gained within GW/GSK, WyethBiopharma, UCB and Lonza Biologics. John joined the Business Development group in DSM Biologics in May 12 and has responsibilities across a number of European territories.

Event Web Site: www.regonline.co.uk/biosimilar2013

This meeting was organised by Euroscicon (www.euroscicon.com), a team of dedicated professionals working for the continuous improvement of technical knowledge transfer to all scientists. Euroscicon believe that they can make a positive difference to the quality of science by providing cutting edge information on new technological advancements to the scientific community. This is provided via our exceptional services to individual scientists, research institutions and industry.

**NOTES ABOUT THIS EUROSCICON EVENT**

For your convenience we would like to bring your attention to the following

- You will be issued with a FULL delegate list within 14 days of the event, which will include the email addresses of the delegates (we are sorry that there is this delay in emailing the list, but we need to make sure that it takes into account any late arrivals). You will not be included in this list if you have opted out and you can do this by logging into your registration details. This list will not be sold or ever give out to third parties. Only people attending or sponsoring the event have access to the list
- There may be an independent meeting report published within a few months of this event. If this is published we will send you an email to let you know the reference details
- Notepads and pens are available from the Euroscicon reception desk
- We cannot give out the slides from our speaker's presentations as they are deleted immediately after each event. If you require a particular set of slides please approach the speaker
- Please remember that EuroSciCon is a small independent company with no subsidies from society memberships or academic rates for venues. We try to be as reasonably priced as possible and our delegate rates are substantially lower than comparable commercial meeting organisations
- To keep updated on our events and other Life Science News, please sign up for our newsletter at www.eurosciconnews.com
- We may take pictures during the meeting. These pictures will be used to promote our events and placed on our various websites and the closed Euroscicon group on Facebook. If you do not want your photograph distributed please let one of the Euroscicon staff know.

**POSTERS**

**Rational Design of Biobetters**

MA Carballo-Amador, J Warwicker and AJ Dickson
*Faculty of Life Sciences, University of Manchester, Michael Smith Building, Oxford Road, M13 9PT, UK.*
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Protein design is a potent approach for improving protein physicochemical properties with potential consequences for stability, activity, and solubility of proteins. Protein solubility plays an important role for recombinant therapeutic proteins during protein expression, purification, long-term storage and drug administration. Based on protein structure, Chan and Warwicker developed an algorithm to predict protein solubility, defining polar and non-polar patches on the protein surface. Using this algorithm, we predicted amino acid changes that would facilitate expression of forms of human erythropoietin (HuEPO) of directed solubility in *E. coli*. We found that a single point mutation (changing a single amino acid from positive to negative charge) verified the predicted effect on HuEPO solubility (the distribution between soluble and inclusion body fractions) in three different *E. coli* strains (Bl21 (DE3), CodonPlus and SHuffle). Further application of this algorithm will provide a powerful tool for the design of biobetters, with enhanced solubility and stability.

**Molecular Characterization of Biotherapeutics: Possibilities and Practicalities**

EW Chang, D Knight, KG Cook, and AJ Dickson
*Faculty of Life Sciences, University of Manchester, Michael Smith Building, Oxford Road, M13 9PT, UK.*
eric.chang@postgrad.manchester.ac.uk

The molecular characterization of protein therapeutics is very difficult due to the presence of a wide variety of post-translational modifications. Two of the main tools available for biopharmaceutical analytics are chromatography and mass spectrometry. In this presentation, we describe our work applying these approaches, especially with a view to the investigation of modifications such as phosphorylation, methylation, methionine oxidation, glycosylation and other charge variants.