

Modern Challenges in Therapeutic Protein Production

The BioPark Hertfordshire, Welwyn Garden City, AL7 3AX: Friday, 11 June 2010 09:00 - 17:00

The purpose of this meeting is to look at the challenges facing therapeutic protein production and demystify some of the novel approaches and new technologies currently being developed. *Meeting chair - Dr Brendan Fish*, NPI-PT Director at GSK Barnard Castle

This event has CPD accreditation and will have a [troubleshooting panel session](#).

On registration you will be able to submit your questions to the panel that will be asked by the chair on the day of the event

- 9:00 – 9:45 **Registration**
- 9:45 – 9:55 **Introduction by the Chair:** *Dr Brendan Fish*, NPI-PT Director at GSK Barnard Castle
- 9:55 – 10:20 **Faster, cheaper, better: How novel approaches are helping develop biotherapeutics for tomorrow.**
Mrs Alison Mason, MedImmune, Cambridge, UK
Developing successful biotherapeutics takes many years and is a costly process. Time to the clinic can be reduced by improving efficiency of the processes used at each stage of the drug development cycle and cost of goods can be decreased by optimising manufacturing processes. This talk focuses on some strategies and new technologies which have been adopted at MedImmune to streamline and optimise our cell line development and upstream production processes.
- 10:20 – 10:45 **Slonomics Technology - Generation of Multiple Length Variants in Synthetic Antibody Libraries**
Dr. Thomas Waldmann, Sloning BioTechnology GmbH, Germany
Traditional research has focussed on process development to improve therapeutic protein yield and quality. Another more recent approach is to engineer the genes themselves to obtain the desired protein - a process known as directed evolution. The Slonomics® technology platform generates highly diverse and precise combinatorial libraries for such protein engineering. Unlike traditional mutagenesis methods that rely on single stranded oligo nucleotides, the process uses double stranded DNA triplets as universal building blocks for the synthesis of any gene sequence - 'one amino acid at a time'. For library production, a mixture of codons can be introduced at any desired sequence position, in any combination and at any ratio. The absence of functional bias and the sequence independent synthesis process result in exceptionally high quality libraries containing the complete set of desired mutants. Any sequence position can be mutated individually, in a stretch, or in multiple sequence combinations. In addition, individual mutation patterns can be uniquely combined with length diversifications or randomly mutated sequence regions.
- 10:45 – 10:55 **Speakers photo**
- 10:55 – 11:30 **Mid-morning break and poster viewing**
- 11:30 – 11:55 **Strategies to decrease cell line development - a review of the current technologies**
Dr Jenny Thirlway, Eden Biodesign, Liverpool, UK
One of the largest lead times in moving a biological drug candidate from the bench to a 'first in man' clinical trial is the development of a stable, high expressing production cell line. Here we present a strategic review of the key activities required to develop a cell line and discuss the pros and cons of the current proprietary technologies (including generation of cDNA, expression technologies and clone screening & selection) that are used to compress the timelines for cell line development.
- 11:55 – 12:20 **Talk to be confirmed**
Dr Gary Pettman, GSK, Harlow, UK
- 12:20 – 12:45 **Talk title to be confirmed**
Dr John Moys, Sartorius Stedim, UK
- 12:45–13:45 **Lunch and Poster Viewing**

- 13:45 - 14: 45 **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
- 14:45 – 15:10 **Forced degradation studies of proteins formulated by high-throughput techniques**
Dr. Paul Dalby, University College London
Microplate-based, and increasingly microfluidic platforms, enable very small quantities of proteins to be analysed under a wide range of formulation, stress and bioprocess conditions. A platform of automated high-throughput methods for pre-formulating protein conformational stability, solubility and tolerance to freeze-drying will first be introduced. Their application to pre-formulation, the design of bioprocesses and the early identification of problematic protein leads will be discussed. The benefits and current limitations of high-throughput approaches for gaining increased understanding of protein behaviour will also be discussed by comparison to forced degradation results and further detailed biophysical analyses of proteins in solution.
- 15:10 – 15:40 **Afternoon Tea/Coffee and Last Poster Viewing**
- 15:40 – 16:05 **Quality Issues, Guidelines and Requirements for Biological Products**
Charles Christy, Covance Laboratories Ltd, Harrogate, UK
The talk will cover the range and specific details of analytical testing that is currently required for biological products with specific reference to cell line release, process validation for contaminant clearance (virus, HCP, rDNA), and to characterise, ensure batch-to-batch consistency and appropriate product stability. This talk will cover the regulatory requirements and the relevant guidelines for both the EMEA and the FDA for biological therapies. Finally the talk will give guidance on the most appropriate analytical techniques required to demonstrate product consistency, purity, safety and potency.
- 16:05 – 16:30 **Regulatory aspects of therapeutic protein production**
Dr Stephen Thompson, *S-cubed Ltd*, Oxfordshire, UK
The evolution of regulation of biological products has resulted in the key concept of 'the process is the product, and the product is the process'. Biotech products are complex and diverse, resulting in a 'case by case' approach to assessment. While there is an absence of useful precedent in the regulatory requirements for biologicals, there is more scope for devising development programmes based on knowledge of the product and process. This presentation will cover the regulatory requirements and relevant guidelines for biological therapies, and the evidence require to meet regulator's expectations for a well-characterised product and well-characterised process.
- 16:30 - 17:00 **Chairman's summing up.**

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About the chair

Brendan Fish is Director of New Product Introduction and Process Technology for GSK at Barnard Castle. With a career spanning over 20 years, he was Director of Bioprocess Sciences at MedImmune Cambridge where he was responsible for all aspects of the development of purification methodologies, product characterisation, QC, formulation and delivery for MedImmune products in relation to their use in commercial pharmaceutical processes. This included initial design and optimisation, scale-up, process cost modelling, process integration and technology transfer to GMP Production for clinical trial supply. Brendan was also at Delta Biotechnology Limited as a Consulting Scientist. He played a key role in the development of their biotechnology-based products providing expert opinion and strategies for QA, QC, Production, Marketing, Operations, Regulatory Affairs and Engineering on all aspects of Process Development. Early in his career, he was a Post-doctoral fellowship at University of Toronto in Canada working in the School of Nutritional Sciences, studying the anti-nutritional effects of lectins in the diet.

About the speakers

Paul Dalby is a Reader in Biochemical Engineering and Biotechnology at University College London, where he has been a principle investigator since April 2000. His protein engineering and biophysics research aims to address key challenges in rapid bioprocess development using a combination of novel automated microscale and microfluidic methods, detailed biophysical analysis and both protein engineering and formulation to improve biopharmaceuticals. He graduated with a Natural Sciences degree from the University of Cambridge and received his PhD in 1998, also from the University of Cambridge, for work on protein engineering and protein folding under the guidance of Sir Prof Alan Fersht. He then undertook a Postdoctoral research fellowship at the University of Pennsylvania in the laboratory of Prof William DeGrado in collaboration with Ron Hoess at DuPont (Wilmington, Del.), to engineer WW domain proteins using phage display techniques. Since July 2008 Paul has been Chair of the Royal Society of Chemistry's Biotechnology Subject Group which aims to engage academia, industry and the public in debate and scientific discussion on advances in Biotechnology. He recently received the Evonik European Science-to-Business Award in November 2008 for his work on engineering enzyme routes for the production of chiral intermediates.

Alison Mason has over 11 years of experience of cell culture and bioreactor process development within the field of therapeutic protein production. After working at Lonza Biologics as a fermentation scientist, Alison moved to MedImmune Ltd (formerly Cambridge Antibody Technology) in 2000. At MedImmune, Alison has been responsible for developing cell culture media and feeds, optimising bioreactor processes and tech transfer of these processes for cGMP production at both an external CMO and at MedImmune's cGMP facility in Gaithersburg, Maryland. Alison holds a degree in industrial microbiology from the University of Manchester.

Charles Christy is the Associate Director of Biotechnology at **Covance Laboratories**. Covance is a global supplier of drug development services. The Biotechnology Division provides specialised support to biologics developers and manufacturers in the key areas of cell banking, cell line qualification, biosafety testing, process validation, GMP batch release, GMP protein characterisation, product stability and potency studies, and immunochemistry. Charles has a degree in Biochemical engineering from University College London, where he also followed research into the large-scale fermentation and isolation of a chloroperoxidase from a filamentous fungus. He then joined the engineering contracting company APV as a process engineer, and was mainly involved in the design of a state-of-the-art large-scale plasma fractionation facility for the Australian government. Charles then joined the leading specialist separations company Millipore Corporation and served in a variety of roles over 13 years, including system specialist, tangential flow product manager and finally as biotechnology market manager. In these roles Charles developed expertise in chromatography, filtration and process system scale-up, design and optimisation. During his time at Millipore Charles developed multiple training courses for the industry on topics such as separation technology, scale-up, and process design and optimisation. Charles has been widely published on downstream processing topics and holds a US patent regarding the design of a novel heat exchanger.

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Thomas Waldmann is Director Science & Technology Support at Sloning BioTechnology. Since 2006 he is responsible for technical customer liaison and support in Europe, USA and Japan. He joined Sloning BioTechnology as a scientific group leader in 2002 and contributed significantly to the development of the Slonomics[®] technology. Before, he has worked successfully in the field of automated screening technologies for several Munich-based biotech companies. Dr. Waldmann gained extensive scientific experience from his postdoctoral fellowships at the Memorial Sloan-Kettering Cancer Center in New York, USA. He holds a degree in biology from the Technical University in Munich, Germany and graduated at the Max Planck Institute of Biochemistry, Martinsried, Germany.

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Stephen Thompson has over twelve years' regulatory affairs experience in the pharmaceutical industry as a consultant, joining Origin Pharmaceutical Services (which then became Constella Group), before moving to S-cubed Ltd as Director of Regulatory Affairs in

March 2009. Stephen has provided regulatory support to many pharmaceutical and biotechnology companies in both Europe and the USA, and has worked with European regulatory agencies and the US FDA. His experience includes the preparation, submission and approval of clinical trial applications for clinical studies in the EU and USA, as well as marketing authorisation applications and subsequent maintenance, for both small molecules and biologicals.

*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. The event was hosted by **'BioPark** (www.biopark.co.uk), a research and development centre in Welwyn Garden City providing specialist facilities and support for bioscience and health technology businesses to grow, and to develop new products and technologies*

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