

Non-Antibody Protein Production

Brand
New
Event for
2011

Dedicated forum on regulatory and industry hurdles during production of recombinant and non-antibody proteins using microbial expression systems

Wednesday 8 - Thursday 9 June 2011 • Maritim Hotel, Berlin, Germany

Benefits of Attending:

- ✓ Learn how to improve non-antibody protein production using microbial and mammalian expression systems with **BioMarin**, **Lonza** and the **University of Delaware**
- ✓ Essential feedback from the **MHRA** on how to effectively implement **QbD** for recombinant proteins
- ✓ **Optimise upstream processes**, scale down experiments and media development for recombinant proteins with **Genzyme** and **BioMarin**
- ✓ **Learn valuable lessons** on how two small Biotech companies, **Syntaxin** and **Immunocore**, are developing their non-antibody proteins
- ✓ Conduct efficient downstream processing including protein refolding, small scale manufacturing and the use of disposables with case studies from **Merck Serono**, **MSD**, **Centocor** and the **Indian Institute of Immunology**
- ✓ **Overcome analytical, stability and formulation challenges** with feedback from **Pfizer**, **Areco** and the **Universities of Massachusetts and Manchester**

Key Speakers Include:

- **Dr Keith Chidwick**, Pharmaceutical Assessor, **MHRA**, UK
- **Subinay Ganguly**, Director, CMC Team Lead, **Centocor Research & Development**, USA
- **Dr Stephen Taylor**, Commercial Director, **MSD BioManufacturing Network**, UK
- **Dr Tom Crowley**, BioTherapeutics Pharmaceutical Sciences, **Pfizer**, USA
- **Dr Laenen Lada**, Managing Principal Scientist, Cell Culture Science Technology, **Genzyme**, Belgium
- **Peter Horrocks**, Group Leader BioProcess Development, **Syntaxin**, UK
- **Dr Diego Schmidhalter**, Head of Manufacturing Science and Technology, **Lonza**, Switzerland
- **Dr Bruno Antonsson**, Principal Scientist, Head Protein Biochemistry, **Merck Serono**, Switzerland
- **Andy Johnson**, Head of Analytical Development/ Formulation, **Immunocore Ltd**, UK
- **Dr Xing Wang**, Group Leader, Analytical Research and Development, **Pfizer**, USA
- **Dr Javier Femenia**, Senior Scientist 1, **BioMarin Pharmaceutical**, USA
- **Dr Kit Erlebach**, Head of Technical Operations, **MSD Biologics**, UK

Plus don't miss

Pre-Conference Workshop Tuesday 7 June 2011

Critical Analytical CMC Studies for Non-Antibody and Biosimilar Products: Why, When, and How?

Led by: **Dr Nadine Ritter**, Senior CMC Consultant, **Biologics Consulting Group**, USA

Evening Seminar Wednesday 8 June 2011

Regulatory Evening Surgery

Led by: **Dr Keith Chidwick**, Pharmaceutical Assessor, **MHRA**, UK
Keith Watson, CMC Principal Consultant, **PAREXEL**, UK
Dr Robin Thorpe, Head - Biotherapeutics, **NIBSC**, UK

Post-Conference Workshop Friday 10 June 2011

Delivering Cost Effective Processes for Biologics

Led by: **Andrew Sinclair**, President, **Miriam Monge**, VP Marketing & Bioprocess Applications, **Biopharm Services**, France

Register online: www.informa-ls.com/nonantibody

Critical Analytical CMC Studies for Non-Antibody and Biosimilar Products: Why, When, and How?

Registration 09.30 • Start 10.00 • End 16.00 • Lunch, morning and afternoon refreshments provided

Introduction

Biotechnology products have very specific expectations for characterisation and comparability studies, as well as ICH-defined parameters for QC release and stability testing. In addition, the emergence of Quality by Design, Risk Management, and Lifecycle Quality Systems have entered the discussions. The ultimate goal of product development CMC activities is to generate meaningful, reliable product specifications, and establish a rich technical database that can be mined throughout the product lifecycle.

What will be covered

This workshop will clearly outline the international regulatory requirements and key technical strategies for biotechnological/biological products for CMC analytical and stability studies needed to generate the data necessary to accomplish these objectives.

Specific attention will be given to the comparability study plans necessary for biosimilar products, which have greater safety concerns that generic forms of chemical pharmaceutical products. While sponsors of biosimilar products typically obtain regulatory relief from large scale clinical efficacy trials, greater regulatory attention is placed on the CMC elements.

This workshop will present the product characterisation and comparability study designs with increased focus on product and process impurities, as well as the challenges of incorporating the reference licensed product in comparability studies. The staged implementation of these studies by innovator, biosimilar, and contract organisations during each phase of product development will be discussed, as well as the quality practices that should be applied in the labs that generate critical data for product regulatory dossiers.

Led by: **Dr Nadine Ritter**, Senior CMC Consultant, **Biologics Consulting Group**, USA

DAY ONE: WEDNESDAY 8 JUNE 2011

08.15 Registration and coffee

08.50 Opening remarks from the Chairperson

09.00 KEYNOTE PRESENTATION**Next generation biologics and the new manufacturing challenge**

This talk will explore the new types of biologics entering the market, such as antibody fragments, recombinant vaccines and potent fusion proteins. It will also examine the role that novel expression technologies have to play in improving delivery, together with advances in engineering and disposables required to deal with rapid product changeovers and small volume products and how these are aligned with regulatory demands. Finally it will review the challenges of training and developing staff to deal with change and flexibility in multi-product facilities.

Dr Stephen Taylor, Commercial Director, MSD BioManufacturing Network, UK

Regulatory Feedback on Quality by Design for Recombinant Proteins09.35 **Group hysteria or sensible idea - A regulatory view of Quality by Design (QbD) for recombinant proteins**

This presentation will consider the practical aspects when considering a QbD application for recombinant proteins. The first important and neglected strategic decision "QbD is it worth the bother?" and the advantages and disadvantages will be discussed. The QbD jargon will be explained and a practical guide to pharmaceutical development provided.

The following for QbD applications will be considered:

- Risk assessment of process
- Definition of quality attributes and critical process parameters
- Proven acceptable ranges versus design space
- Quality systems and inspections

Dr Keith Chidwick, Pharmaceutical Assessor, MHRA, UK

10.10 Morning coffee break

Experience with Microbial & Mammalian Expression Systems10.40 **Membrane protein expression and characterisation: Can we build a better yeast expression host through understanding protein-protein interactions?**

Proteins that reside in the cell membrane represent the most difficult challenges for expression and isolation, because they are partially hydrophobic, flexible and unstable in isolation. However, they are among the most important of all proteins, as they play key roles in almost every cellular process and represent over a third of all proteins. This talk will highlight expression of G-protein coupled receptors (GPCRs) and trafficking in the heterologous host, *S. cerevisiae*.

Dr Anne Skaja Robinson, Professor of Chemical Engineering, Associate Chair for Biochemical Engineering, College of Engineering, University of Delaware, USA

11.15 **Evaluation of UCOE and GS™ expression systems for improving protein production for difficult to express lysosomal enzymes**

We evaluated two mammalian expression systems, UCOE (Ubiquitous Chromatin Opening Element) by Millipore and GS™ (Glutamine Synthetase) by Lonza with BioMarin's lysosomal enzyme pipeline molecules. Using an in-house serum-free cell line generation process, both systems can deliver high producers in a reasonable period of time. However, there still are challenges when producing lysosomal enzymes besides the expression, secretion, or product quality. This talk will summarize our evaluations and share some thoughts on their applications.

Dr Javier Femenia, Senior Scientist 1, BioMarin Pharmaceutical, USA

11.50 **Recombinant bacterial expression technology – A system SWAT analysis**

Microbial expression technology is widely used for the manufacture of therapeutic and non-therapeutic proteins, peptides and nucleotide based compounds. Why is there no such thing like a gold standard in the microbial field? What titre can be expected in bacterial fermentations? What triggers the choice of the microbial system?

Dr Diego Schmidhalter, Head of Manufacturing Science and Technology, Lonza, Switzerland

12.25 **SPOTLIGHT PRESENTATION**

These presentations are hosted by leading companies who aid in the manufacturing and testing of non-antibody and recombinant proteins and offer an opportunity to learn about the latest developments and technological advancements in the industry. If you would like to host a spotlight presentation, please contact james.miguel@informa.com or Tel: +44 (0) 207 017 5011

12.55 Lunch

Upstream & Downstream Production: Increasing Productivity and Reducing Timelines14.10 **Development of scale-down experiments and simulation models**

Please visit www.informa-ls.com/nonantibody to view abstract

Dr Laenen Lada, Managing Principal Scientist, Cell Culture Science Technology, Genzyme, Belgium

14.45 **A novel methodology for chemically defined production media development**

A statistically-driven methodology was implemented to quickly optimise an in-house custom media for recombinant protein production. This approach using response surface mapping (Bayesian D-Optimal design) allows large number of components to be screened simultaneously. It also provides an in-depth understanding of component interactions and their impact on cell behaviour and process performance. This talk will review the approach, the challenges and a case study.

Dr Maria Ng, Scientist 1, BioMarin Pharmaceutical, USA

15.20 **CaptureSelect; Introducing one-step selectivity in the primary recovery of biological products**

Affinity chromatography is one of the most effective methods for purifying protein therapeutics. For standard MAb purification, Protein A is a well established affinity ligand providing the benefits of a highly selective primary capture step. However, for non antibody based therapeutics and novel Ab based formats, it becomes a challenge to find a Protein A equivalent. The CaptureSelect technology addresses these challenges and provides a "plug-and-play" platform approach by introducing a generic capture step for the primary recovery of virtually any biological product, showing excellent contaminant clearance and enabling elution conditions that preserve product structure and activity.

Pim Hermans, Director of Ligand Discovery, BAC BV, The Netherlands

15.55 Afternoon coffee break

Join us for **HIGH SPEED NETWORKING**

16.30 **A design of experiments supported high-throughput protein refolding screen in 96-well format**

A limiting step in the production of active recombinant proteins from *Escherichia coli* is frequently the refolding of proteins expressed in inclusion bodies. We have developed a 2 step refolding screening process in 96-well format supported by design of experiments (DOE) for identification of optimal refolding conditions. This procedure identified refolding conditions for all proteins tested.

Dr Bruno Antonsson, Principal Scientist, Head Protein Biochemistry, Geneva Research Centre, Merck Serono, Switzerland

Evening Seminar & Dinner • Wednesday 8 June 2011**Regulatory Evening Surgery**

Registration 18.15 • Start 18.30 • End 20.30 • Dinner and refreshments will follow

This evening seminar will provide an opportunity for attendees to discuss regulatory challenges encountered specifically when working with non-antibody proteins and biosimilars. The leaders of this seminar will provide initial feedback on commonly encountered regulatory hurdles, before inviting the group to share individual issues. Solutions and guidance on how to overcome the issues that arise will be given

Key areas that this seminar will focus on include:

- Biosimilars: how similar is similar? What is likely to be accepted by the regulator?
- Comparability: regulatory guidance on how to practically carry out comparability studies and get it right first time
- QbD: how applicable is QbD to non-antibody proteins? How can you ensure it is done correctly?
- Immunogenicity: how can key concerns and risks be measured and addressed? Can you predict this?

The above themes will constitute the main focus of the seminar, however there will also be an opportunity to discuss other issues that attendees wish to specifically mention:

What attendees will gain:

Attendees will benefit from the unique chance to gain direct feedback on regulatory problems, both commonly encountered and those that are more specific, when working with biosimilars and/or non-antibody products. Take part in an intimate discussion with industry peers and leaders to share, evaluate and learn from others experiences in this field.

Led by:

Dr Keith Chidwick, Pharmaceutical Assessor, MHRA, UK
Keith Watson, CMC Principal Consultant, PAREXEL, UK
Dr Robin Thorpe, Head - Biotherapeutics Group, NIBSC, UK

17.05 High-throughput recovery of bioactive protein from inclusion bodies
There are only four ways to solubilise inclusion bodies: use of chaotropes (8 M urea or 6 M GdmCl), use of extreme of pH (pH below 3 or above 12), use of detergents and use of mechanical force in combination with low concentration of denaturant (high pressure). To date, organic solvents have not been used for solubilisation of inclusion body proteins. We tried different primary alcohols, diols and mercapto-alcohols to solubilise inclusion body proteins. We discovered that 6 M β -mercaptoethanol could solubilise many inclusion body proteins and the solubilised proteins could be refolded into bioactive form (*US Patent 7189811, March, 2007*). The proof of principle was established by using human growth hormone as model proteins and more than 50% of the inclusion body protein could be refolded into bioactive form. Such a novel solubilisation process can be used for the recovery of protein from inclusion bodies of *E. coli*.
Dr Amulya Panda, Product Development Cell, National Institute of Immunology, India

17.40 End of day one Q&A and closing remarks from the Chairperson

DAY TWO: THURSDAY 9 JUNE 2011

08.50 Opening remarks from the Chairperson

Downstream Production: Process Development & Use of Disposables

09.00 Case study: Process development and small-scale manufacturing of recombinant Targeted Secretion Inhibitors (TSIs)
Syntaxin have developed an innovative Targeted Secretion Inhibitor (TSI) technology platform to generate a new class of protein biopharmaceuticals for therapeutic treatment of neurological, endocrine and proliferative (oncology) secretion disorders. These novel recombinant proteins act through selective inhibition of cell secretory processes. This presentation will focus on the technical challenges in the process development and small-scale manufacturing of TSIs produced by microbial cell culture.
Peter Horrocks, Group Leader BioProcess Development, Syntaxin, UK

09.35 Single use technology and therapeutic protein manufacturing
Single use technologies are becoming increasing prevalent in biopharmaceutical manufacturing. A brief overview of the technologies available from a user's perspective will be given. There are some particular challenges and benefits for the therapeutic protein area around the bioreactors and diversity of purification technologies. Case studies of single use technologies will conclude the presentation.
Dr Kit Erlebach, Head of Technical Operations, MSD Billingham, UK

10.10 Key considerations for process development to manufacture alternate scaffolds
Alternate scaffolds such as DARPins (designed ankyrin repeat proteins) are considered to be the next generation protein therapeutics. They share many of the properties of therapeutic monoclonal antibodies (e.g. high affinity, selectivity etc), while also offering potential benefits such as increased stability, ease of manufacturing and alternate routes of delivery. The presentation will highlight the key considerations for developing the manufacturing process for a bi-specific DARPins to support preclinical and clinical studies.
Dr Subinay Ganguly, Associate Director, CMC Team Lead, Centocor Research & Development, USA

10.45 Morning coffee break

Analytical Challenges with Recombinant and Non-Antibody Proteins

11.15 Host Cell Protein and residual DNA analysis: Current approaches and novel technologies
This talk gives an overview of Host Cell Proteins in biologics development; the guidelines from regulatory agencies and ICH will be reviewed. The risk of Host Cell Proteins and residual DNA will also be discussed. Several case studies will be provided to demonstrate the importance of HCP analysis and the impact to the biologics development. Current technologies for both HCP and residual DNA analysis and some novel technologies on the horizon will be discussed.
Dr Xing Wang, Group Leader, Analytical Research and Development, Pfizer Worldwide Research and Development, USA

11.50 Emerging mass spectrometry-based methods for characterisation of recombinant proteins
Mass spectrometry (MS) has already become an indispensable tool in the analytical armamentarium of the biopharmaceutical industry, although its current uses are limited to characterisation of covalent structure of recombinant protein drugs. However, the scope of applications of MS-based methods is beginning to expand to include characterisation of the higher order structure and dynamics of biopharmaceutical products, a development which is catalysed by the recent progress in MS-based methods to study higher order protein structure. The two particularly promising methods that are likely to have the most significant and lasting impact in many areas of biopharmaceutical analysis, direct ESI MS and hydrogen/deuterium exchange, will be the focus of this presentation.
Dr Igor Kaltashov, Associate Professor, Chemistry Department, University of Massachusetts, USA

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12.55 Lunch

Formulation & Stability Studies for Recombinant & Non-Antibody Proteins

14.00 Case studies: Utilising Arrhenius Kinetics to predict stability of recombinant proteins
This talk will focus on the relationship between temperature and reaction rates for a number of common degradation pathways observed in recombinant proteins and its utility in predicting stability at refrigerated storage conditions.
Dr Thomas Crowley, BioTherapeutics Pharmaceutical Sciences, Pfizer, USA

14.35 The development of a non-antibody protein (a small Biotech's experience)
This talk will give an overview of the development of a recombinant T Cell Receptor (TCR) fusion protein, from the pre-clinical to clinical phase. The talk will cover strategies taken on protein design, formulation, analytical support and stability to ensure success in reaching the clinic within the usual heavy time constraints.
Andy Johnson, Head of Analytical Development/ Formulation, Immunocore, UK

15.10 Afternoon coffee break

15.40 Stability challenges and stability solutions for recombinant proteins
Stability of recombinant proteins is key to their successful commercial development. This talk will summarise major degradation pathways affecting recombinant proteins and ways of improving their stability through formulation. Conventional approaches to formulation optimisation will be described together with unique innovative methods to produce protein therapeutics with superior stability. The stabilising principles will be illustrated on several case studies.
Dr Jan Jezek, Chief Scientific Officer, Arecor, UK

16.15 Bioinformatics tools for predicting protein solubility and aggregation
This presentation will review the chemical and physical properties of proteins that affect the propensity for aggregation. Developing computer algorithms to quantify aggregative properties will be presented along with the application for algorithms to high throughput datasets, and performance of a predictive tool.
Dr Jim Warwicker, Senior Lecturer, Faculty of Life Sciences, University of Manchester, UK

17.00 End of conference Q&A and closing remarks from the Chairperson

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Conference Sponsor



MSD BioManufacturing Network is one of the world's leading third-party contract process development and manufacturing companies for biologics. Through its predecessor companies Avecia Biologics and Diosynth Biotechnology, the BioManufacturing Network has particular expertise in recombinant proteins with a proven track record in delivering successful programmes at all stages of the development pipeline
MSD is a trade name of Merck & Co Inc, with headquarters in Whitehouse Station, NJ, USA.



Post Conference Workshop • Friday 10 June 2011

Delivering Cost Effective Processes for Biologics

Registration 09.30 • Start 10.00 • End 16.00 • Lunch, morning and afternoon refreshments provided

A workshop to explore the challenges and opportunities

A combination of rising manufacturing costs and pressure on pharmaceutical companies to reduce the cost of new biopharmaceutical proteins is raising the profile of cost of manufacture within the sector. The focus in the industry is to look at ways to develop cost effective processes for making non-MAb based proteins that fit easily into a manufacturing environment. Recognising that process economics are set early on in development, this workshop will focus on how to assess choices regarding process (expression systems, purification matrices etc) and technologies (continuous, disposables, etc) on outcomes. Secondly, it will look at how to build the linkages between manufacturing and process development that ensures that there is a good fit between the process and the facility.

Led by: **Andrew Sinclair, President, Miriam Monge, VP Marketing & Bioprocess Applications, Biopharm Services, France**

The objectives of this workshop are to:

- Provide an overview of the cost structure of typical non MAb processes
- Provide insights into the cost drivers
- Review the methodology and approaches taken to economic analysis of bioprocesses
- Examine the opportunities to address cost effectiveness in process development and manufacturing
- Look at the impact of new developments and their potential to deliver more cost effective processes, looking in particular at advances in high cell density cell culture, continuous processing and advances in disposable technologies

