

MERCK

Invitation

Upstream Technical Symposium

October 11, 2018

8:45 – 16:00

Venue:

LFB Biomanufacturing

Impasse des Chênes Rouges
30100 Alès, France

www.LFBBiomanufacturing.com



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Merck and LFB Biomanufacturing invite you
to the Upstream Technical Symposium.

During this one day seminar you will:

- Learn from recent innovations to quickly achieve cell culture efficiency and consistency,
- Learn from a CDMO experience in driving process modification during clinical phase,
- Exchange with bioproduction subject matter experts during a tour of the GMP manufacturing area.

We look forward to meeting you.

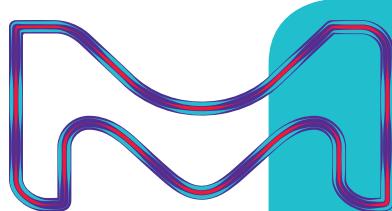
For more information, contact:

Sylvain Ribaud

Technical Manager, Upstream Process Solutions

sylvain.ribaud@merckgroup.com

**DISCOVER THE DETAILED AGENDA
OF THIS EVENT OVERLEAF, WITH KEY
INDUSTRY SPEAKERS INVOLVED.**



Attendance is free, though registration is required.

Space is limited, register now!

www.merckmillipore.com/upstream-symposium

Agenda*

8:45 – 9:00 **Welcome and introduction**

Cell culture media compaction: latest production technology to increase flowability, dissolution speed & bulk density

Dennis Binder, R&D Scientist
Advanced Cell Culture Technologies, Merck



Roller compaction is a granulation technology that works with compression force only, i.e.

no water or excipients are needed in order to form granules/compacted media. Homogeneously milled dry powder media is conveyed between two rolls that compress the powder to a plate, which is then crushed into the final compacted media. The main advantages of compacted cell culture media in comparison to its powder form is that the compacted material possesses increased flowability, which leads to better handling and less dust formation. Furthermore, compaction increases the bulk density, resulting in lower storage and transport costs. Lastly, compacted cell culture media show an increased dissolution speed of compacted material since the material sinks into the water instead of swimming on the water surface, thus decreasing the risk of contamination as well as overall processing time. Two parameters were shown to significantly influence the compactate quality, namely the media formulation itself as well as the compression force (pressure).

9:45 – 10:30 **New molecules to boost CHO productivity, simplify fed-batch processes and ensure batch-to-batch consistency**

Dennis Binder, R&D Scientist
Advanced Cell Culture Technologies, Merck



Main goal of pharmaceutical industries is the achievement of a reliable and robust production process with high titers and a defined quality of the recombinant product. This presentation will give an overview of molecules and technologies which improve bioprocesses. High quality raw materials ensuring batch-to-batch consistency and enhancing process efficiency will be presented. Molecules that are addressed enhance CHO productivity and simultaneously simplify fed batch processes. Furthermore, the possibility of influencing critical quality attributes of monoclonal antibodies with additives is shown.

10:30 – 11:00 **Break and networking**

11:00 – 11:20 **Ensuring lot-to-lot consistency with management of metal impurities in cell culture media - Electronic data sharing**

Sylvain Ribaud, Technical Manager Upstream, Merck

Rapid transfer of information between supplier and manufacturer is essential in securing a robust and consistent manufacturing platform. Merck are taking this to the next level with Electronic data sharing portals, where the client can access data on raw materials, N-1 information, C of A and release testing and process related data. This allows clients to identify and remove potential lot-to-lot process variability such as shifts in glycosylation.

11:20 – 12:15 **Single-use bioreactors: key engineering parameters for rapid scale-up from 2 to 2000 L**

Lénaïg Savary, MSAT Upstream Biomanufacturing Engineer, Merck

Single-use technologies at the 2000L scale have become the gold standard to deliver a fast, flexible and cost-effective solution for production of recombinant proteins in a cGMP environment. With the aim to deliver a faster, simpler and cheaper solution compared to conventional stainless steel equipment, the identification of a relevant single-use cell culture platform for a multi-product facility should rely on several considerations. One primary objective is to benefit from a platform with a clear definition of the key engineering parameters from bench to production scale, thus minimizing time during process development.

12:15 – 13:45 **Lunch and networking**

13:45 – 14:15 **Round table discussion**

Moderators: Abdel Zemmar, Head of BMG Process development and David Balbuena, Head of manufacturing, LFB Biomanufacturing

When developing new therapeutic molecules, investors expect to have a quick launch of the clinical studies. Time dedicated to Process development and scale-up to produce the first clinical Drug Substance is now reduced at the minimum applying platform approach. As soon as the process is implemented any process is then carefully reviewed to avoid any discrepancy or potential quality shift. However, after several years of clinical trials, investors, customers often would like to improve the process in order to reduce cost of good. The objective of the discussion is to discuss how to implement continuous process improvement throughout molecule development lifecycle without impacting Drug Substance quality and patient safety. In the frame of this topic, two case studies will be shared in the frame of the discussion:

Improving and change for media and feeds during clinical phase:

Media and feeds are the main drivers in the USP productivity and Quality. Any improvement in productivity can potentially lead to change in quality: Glycosylation Pattern, Isoform distribution; aggregation...

Biosimilar initiative clearly showed that targeting the suitable quality even changing the entire process from cell line to Process can be tried. The discussion will cover the different steps of the media and feeds optimization and the right time (Clinical phase's I/II/III) to be applied in order to stay within the timelines expectations.

Clarification optimization:

Platform approach is always targeting the right quality within the shorter timeframe. Optimization of the clarification is a good way to reduce the cost of goods reducing the number of consumables (Depth filtration cassettes) and also the buffer and solution required for the operations. An example will be discussed through the Merck Millipore clarification solution switching from the "old" platform technologies such as depth filtration including diatomaceous earth (COHC) to new depth filtration techniques up to the last ones (synthetic depth filtration).

14:15 – 14:45 **Case study: implementation of a new bioproduction unit**

Marc Vouillamoz, Chief Operating Officer, LFB Biomanufacturing

The LFB Group's strategy of development in 3 major areas (plasma derivatives, recombinant proteins and cell therapy) led it to a constant growth and investment approach aimed at supporting its R & D projects and the technological platforms developed. Since 2007, the LFB Group has chosen to acquire a small Biotech company specializing in the production of recombinant proteins expressed by mammalian cells: MAbgène (Alès), which has become LFB Biomanufacturing since 2012, a subsidiary of LFB Biotechnologies.

An investment strategy following a logical approach has allowed the Alès site to continue to grow in order to serve both the LFB Group pipeline and the growing needs of third-party customers in Service Delivery mode. A site in evolution must take into account many factors and constraints, and the industrial investment is the result of orientations, choices with a profitability approach. The strategy is to have clinical and commercial GMP Drug Substance production capacities that meet European and FDA standards, on a model open to third-party clients (CDMO). The site offers Cell Line Development activities to commercial batches with a capacity of up to 6x2000L of culture volume, hyperflexibility and multi-product with rapid changeover are key assets gained on using exclusively on Single-Use technologies. Choices, constraints, trade-offs, tips and things to consider will be covered in this presentation.

15:00 – 16:00 **Site tour (GMP Manufacturing Areas)**

* Agenda subject to change. Attendance to the Upstream Technical Symposium is limited and available to pharma or biopharma manufacturers and academics only. The offer does not extend to any company that provides pharma or biopharma products or services. Merck and LFB Biomanufacturing reserve the right to revoke or refuse participation at any time. The meeting is free of charge. Lunch and coffee breaks are provided compliments of LFB Biomanufacturing. Hotel accommodations and travel costs are at the expense of the attendees.



Our speakers

Dennis Binder, R&D scientist, Advanced Cell Culture Technologies

Dennis Binder studied biochemistry at the Heinrich-Heine-University in Düsseldorf. He obtained his Master degree in Biochemistry in 2013, which was followed by a PhD thesis in the field of microbial biotechnology. In 2017, he joined the Advanced Cell Culture Laboratory as a scientist and is currently working on new molecules and formulations to boost cell culture (media) performance. Main projects currently include lipid bioprocessing as well as the compaction of both raw materials and cell culture media.

Sylvain Ribaud, Technical Manager Upstream Process Solutions

Sylvain has 12 years of experience in process development, engineering and marketing in the biopharmaceutical industry and has led many industrial projects for design, implementation and validation of single-use technologies and critical raw materials within clients' biopharmaceutical production process. He started his career as a process engineer with Sanofi-Aventis, France. Then he joined Sartorius as a process engineer, followed by a position as global product manager for single-use systems in upstream processing. He is now responsible for the sales development activities in the Upstream Process Solutions group at Merck. Sylvain holds a Masters Degree from the "Ecole des Mines" of Albi, France, with a specialization in the pharmaceutical processes.

Lenaïg Savary, MSAT Upstream Biomanufacturing Engineer

Lenaig Savary, has more than 9 years of experience in the pharma and biotech industry. She started her career as a process engineer at Sanofi Pasteur in Swiftwater, US working on adjuvants for vaccines. She has been with Merck (previously Millipore) for 8 years. She provides technical support to EMEA customers on Single use bioreactors, as well as single-use and multi-use mixers. Lénaïg holds a Master Degree in Process Engineering from the Engineering School ENSIC in Nancy, France as well as a Master Degree in Marine Biotechnology from the University of Nantes, France.

Marc Vouillamoz, Chief Operating Officer, LFB Biomanufacturing

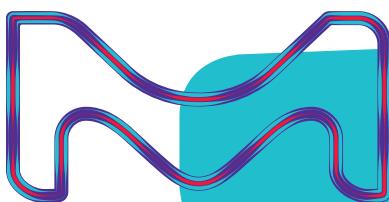
Marc has more than 20 years of experience in the field of Biotechnology, participating in 3 greenfield Biotech plant construction projects, including international Tech Transfer for manufacturing at industrial scale. He held different positions from Manufacturing to Quality Assurance acquired within Baxter BioScience (now Shire), B. Braun Medical and Merck Serono's companies. Since 2011 he joined the LFB Group as COO of LFB Biomanufacturing, an LFB Subsidiary acting as CDMO for third party project and for LFB Biotechnology own pipeline. He developed the Alès Site, in Southern France, to put together Cell Line Development capabilities, offering EMABling® Cell Line Development technology and prepared the site to pass successfully an FDA inspection while increasing site manufacturing capabilities. Marc holds an Engineering degree in Biotechnology and completed his education by a Master in Business and Administration (MBA).

David Balbuena, GMP Manufacturing Manager, LFB Biomanufacturing

Graduated in Biotechnology engineering and Microbiology (Agro Paris Tech), David has more than 22 years of experience in manufacturing, process development and scale up of recombinant medicinal proteins. David started his career at Sanofi in Process Development then in commercial Production in bacterial manufacturing (antibiotics and steroids). He developed his experience in recombinant protein manufacturing at Merck Serono following the development of more than 10 recombinant proteins and monoclonal antibodies. Moving as head of Process development within Merck Serono then Merck Millipore, he worked on Monoclonal manufacturing Platform, Technology transfer, Single Use Processes implementation and development of recombinant protein processes (Hormone, Mabs and Fc-Fusion). David joined LFB Biomanufacturing in 2014 as head of manufacturing to start the new manufacturing Unit (UP2) in 2016 and prepare the approval of the LFB biotechnology Manufacturing unit for ongoing FDA registration (commercial manufacturing).

Abdel Zemmar, Bioengineering Manager, LFB Biomanufacturing

Abdel, a MSc in Biochemical engineering & Molecular Biology, has more than 12 years of significant experience as bioprocess engineer, with relevant experiences on leading CMO technical projects of mammalian Bioprocess Development, Technology Transfer toward large scale Production of Mabs across 3 internationals major industrial sites. He also led project of industrialization of macromolecules, lentiviral gene vectors, Recombinant protein and Biosimilars for clinical trials phases I/II and late stage phase III, within world class biopharmaceutical leader such as Lonza Biologics UK and OxfordBiomedica. He joined LFB Biomanufacturing in 2016 as Bioengineering and MSAT Manager.



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