Large Scale Microbial Fermentation Services for the «White Biotechnology Industry»

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Alexander J Oelke | 24 July 2017
Lonza at a Glance

“A trusted supplier to the pharmaceutical, biotech and specialty ingredients markets”

- > 40 Major manufacturing and R&D facilities worldwide
- ~4.1 bn Sales in 2016 in CHF
- ~10 000 Employees by the end of 2016
- 1 000 Trademarks globally
- > 5 000 trademark filings and more than one thousand brands
- 1897 founded
Target Markets and Technology Platforms

Pharma & Biotech
- Commercial Manufacturing, Clinical Development, Service Products (Consumables, Tests, Media, Equipment)

Consumer Care
- Personal Care, Homecare, Hygiene, Nutrition

Agro Ingredients
- Agro-chemical and Fermentation Active Ingredients, Fertilizers, Advanced Intermediates, Animal Nutrition Ingredients

Coatings & Composites
- Metal, Plastics, Carbon, Wood, Performance Ingredients

Water Treatment
- Recreational Industrial, Commercial, Municipal, Surface Water

Biological Technology
- Fine Chemistry
- Formulation & Application Technology
- Microbial Control Performance & Testing
- Regulatory
Fermentation Support for the White Biotech Industry

- Existing Fermenters in good shape
- Fermentation multi purpose set up
- Flexible DSP (down stream processing)
- Know how in contamination prevention
- For secondary metabolites: chemical capabilities in house available
- Experience in optimizing industrial fermentation processes
- Regulatory Support
- Formulation Support
Large Scale Fermentation Services @ Lonza
Microbial-Based Manufacturing

Major R&D and Production Sites
15 Employees

- Rochester, NY
- Williamsport, PA
- South Plainfield, NJ
- Allendale, NJ
- Mapleton, IL
- Walkersville, MD
- Rockland, ME
- Charleston, TN
- Alpharetta, GA
- Conley, GA
- Houston, TX
- Wayne, PA
- Rochester, NY
- North Plainfield, NJ
- Allendale, NJ
- Mapleton, IL
- Walkersville, MD
- Rockland, ME
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Bioprocess scale-up and manufacturing in Kouřim, Czech Republic

~ 200 people in all different functions at Kouřim and Visp

Bioprocess development and optimization in Visp, Switzerland
Bioprocess Development & Manufacturing

Visp R&T main competency
- Strain Improvement
- Fermentation Development
- DSP & Formulation
- Scale Up & Piloting
- Manufacturing & Regulatory

Kourim main competency
- Scale-down Studies Optimization
- Fermentation & Media Optimization
- Integration into a Multi-Steps Chemical Process
- DSP Development & Optimization
- Bioprocess Integration
- Formulation Development
- Pilot Validation Process
- Scale-up Criteria Definition for Industrial Tech Transfer
- Equipment Selection for best fit to Manufacturing
- Process Tech Transfer
- Engineering Batch
- Support Regulatory Registration
- Commercial Production

- All capabilities available to develop a fermentation derived product
- Full life cycle management from product launch to maturity
Fully Integrated Bioprocess Development and Manufacturing

Unique Combination with Chemical Manufacturing in Visp
R&T Team Visp

Core Competencies

- Focus on process development, scale-up and technology transfer to Kouřim
- Strong interaction with Lonza’s chemistry and process engineering teams
R&T Team Visp
Fermentation Development

Medium Design (DoE)
- Media cost optimization
- Raw material screening
- Nutrient screening
- C-source screening
- Media adaptation for manufacturing

Scale down studies
- Working cell cultures preparation
- Seed culture optimization
- Inoculation procedure (seed train)
- Process conditions (pH, temperature, aeration)
- Oxygen transfer rate

Fermentation Process Definition
- Process operation (batch, fed-batch, conti)
- Stirring speed
- Process control (pH, pO₂, T, etc.)
- Air flow rate
- Foam control
- Sterilisation
Offline process analysis

- all types of C-sources
- Product specific analytics (HPLC, UPLC, GC, etc.)
- Biomass (CDW, OD_{600nm}, PMV)
- Ion analysis (i.e. NH_4^+, PO_4^{3-}, organic acids, etc.)

Online process analysis & control

- pH, pO_2
- Temperature
- Feed (constant, exponential, pO_2 or pH based)
- Stirring
- Air flow rate

Off gas analysis

- O_2
- CO_2
- OUR (oxygen uptake rate)
- CPR (carbon production rate)
- RQ (respiratory coefficient)
Process take-over, Scale-up and Technology Transfer into production

Equipment available
- 10 x 20L, 2 x 75L lab scale fermenters
- Associated downstream processing to mirror original customer processes at lab scale and to propose alternative options

Continuous process support and optimization in close cooperation with our customers
- To account for any registration impact
- To consider impact on stability/formulation requirements
- 1:1 implementation in production scale, otherwise full lab/pilot support available

Achieving the most reliable and economical solution
State-of-the-Art Manufacturing Assets

Kouřim

- Kourim site and its infrastructure and operation mode dedicated to *non-cGMP* production since 2015

- 5 individually operated lines available for commercial scale production with *total capacity of 475 m³*
  - 2 x 15 m³
  - 3 x 15 m³
  - 2 x 50 m³
  - 3 x 50 m³
  - 2 x 75 m³

- Ex-Proof DSP facilities for *solvent handling*

- On-site *waste water treatment* plant

- 3’400 m² warehousing, storage conditions under ambient, 2 to 8 °C, and -20°C
State-of-the-Art Manufacturing Assets

Kouřim

- **Associated downstream process equipment**
  - Cross-flow filtration (MF, UF, NF, RO)
  - Evaporation
  - Electro dialysis
  - Centrifugation (Disc-stack, and Filter centrifuges)
  - Crystallization
  - Filling / Packaging lines
  - Dryer (Spray, double cone, tray, Lyophilization)
  - Homogenizers
  - Dry Mill

- **QC and Microbiology lab supporting production**
  - Physio-chemical assays (pH, OD, titrations, …)
  - Spectroscopy (UV, NIR, …)
  - Instrumental analysis (HPLC, UPLC, GC)
  - Microbiology testing
  - Biochemical assay (ELISA, enzyme activity assay, …)
  - Cell banking, strain release

- **Fermentation Processes and Microorganisms**
  - *Rhizobium*
  - *Pseudomonas*
  - *Bacillus (lentus, subtilis) (GMO)*
  - *Aspergillus sp*
  - *Burkholderia sp*
  - *E. Coli (K12, CMG 2576, (GMO)*
  - *Trichoderma*
  - *Pichia sp. (GMO)*

40 processes transferred to industrial scale within last 10 years
State-of-the-Art Manufacturing Assets

Kouřim

- Fermenter Line
- Down Stream Process Plant
- Ultra Filtration Unit
- Centrifugation Unit
- Spray Dryer (Upper part)
- Control room / Certification
Lonza Large Scale Fermentation Manufacturing

Service Offering

- Fermentation and DSP development starting with process package by our customer
- Technology transfer into Lonza’s assets based on any developmental stage
  - Customer lab process
  - Customer pilot trials
  - Large scale experience
- Process adjustments (process wise, and technology wise) to improve competitiveness
- Full life cycle management from initial market launch to large volumes at maturity
- Continuous process improvement in close cooperation with customer
Why Outsource with Lonza

- Proven track record in the custom manufacturing industry as reliable and trustworthy partner, and experience from more than 30 years of commercial fermentation
- Highest standards for process and worker safety, environment and quality assurance
- Unique combination of biotechnological and chemical platform
- Strong expertise in regulatory requirements for different industries
- Excellent know-how in prevention of cross contamination
- Excellent, state-of-the-art scientific know-how and outstanding customer focused project management
- Avoid large investments in your own capacity
- Speed to market, and high flexibility in your order volumes
- Full guarantee of your know-how and IP
Thank you!

Alexander J Oelke  |  24 July 2017