Single-use and Sustainability

Core design philosophies for the new DSM Biologics facility

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PDA Australia Chapter Meeting:
Single-Use Systems for Pharmaceutical Applications
20th March 2012
Presentation Overview

- DSM Biologics
- New Brisbane Facility
- Design philosophies
  - Single-use
  - Sustainability
- Conclusions
DSM - A Global Presence

- To create brighter lives for people today and generations to come
  - Connecting unique competencies in life sciences and material sciences
    - Nutritional products, specialty chemical synthesis, polymers and pharmaceuticals
  - Annual net sales exceeding €9 billion
  - ~23,000 people employed
    - 49 countries, 5 continents

DSM Pharmaceutical Products:

Biopharmaceuticals:
- Groningen, Netherlands
- Delft, Netherlands (R&D)
- Capua, Italy
- Brisbane Australia (as of 2013)

Pharma Chemicals:
- Linz, Austria
- Venlo, Netherlands
- Regensburg, Germany
- Geleen, Netherlands (R&D)

Corporate Headquarters & Dosage Form Manufacturing:
- Parsippany, NJ
- Greenville, NC
Sustainability - from responsibility to business driver

- DSM manages its business with a focus on a triple bottom line: People, Planet and Profit
- Sustainability is DSM’s core value
  - Driving economic prosperity, environmental progress and social advances to create sustainable value for all stakeholders
DSM Biologics Services

• Contract development & cGMP manufacturing
  - Multi-product facility, bioreactor capacity to 1000L
  - Biological APIs - proteins, monoclonal Abs
  - 25 years experience, successful 2010 FDA and EMA audits

• Proprietary Technology development and licensing
  - Intensified platform processes:
    • XD® culture
    • RHOBUST® Direct Capture chromatography
    • The Kremer Method™

• Flexible manufacturing with Mammalian cell line expertise
  - Single-use technologies (SUT)
  - Suspension cell line focus

XD® and RHOBUST® are registered trademarks of DSM.
The Kremer Method™ is trademark of DSM.
New Brisbane Biologics Facility

• Construction underway for new cGMP manufacturing facility

• Partnership between DSM and BioPharmaceuticals Australia (BPA)
  - BPA established by Qld Government to construct a manufacturing facility and identify an experienced international CMO partner
  - DSMB selected to design and operate the facility
  - Facility funding provided by Commonwealth of Australia and Queensland government
DSM Biologics Facility Location

- Princess Alexandra Hospital Campus, Brisbane

(Image courtesy of Google Maps)
Facility - General

- Brownfield site
  - 24/7 manufacturing, 50 weeks/year

- 6 levels, (60x35m, 8000m² total space)
  - 285m² warehouse
  - 1200m² clean room (465m² CNC)
  - Future expansion to the west
    - Fit out of level 2/3 manufacturing

- Extending Groningen CMO capacity
  - USP: Fully Single-use Technology (SUT)
    - Up to 2000L fed batch
    - 50 - 500L XD®
  - DSP: Hybrid SUT/multiple use (10kg batch)
  - QA, QC, PD, Engineering, Sales/Admin

- Building Status
  - Shell currently to level 6 - (due to be complete April 2012)
    - Internal fit out & equipment procurement - 2012
    - Commissioning and validation - 1Q/2Q 2013
  - Open for GMP manufacture - Expected mid 2013
Level 1 - Warehouse and Plant Utilities

- Reduced WFI and overall energy footprint due to single-use systems
  - Significantly reduced stainless steel equipment scope
  - No SIP required
  - No CIP skids
Level 4 - Manufacturing Area

- “Ballroom” approach to clean room design - mobile equipment
  - Dedicated pre-culture rooms with multi-product upstream suites
  - Single downstream train and post viral clearance finishing suite
Single-Use Media/Buffer Approach

- Media and buffer supply and storage based on Bag-based technology
  - 500L bag-lined totes to be located outside of the clean room
  - Connected aseptically through the wall to process skids

(Images courtesy of Sartorius, Pall and Thermo)
Level 5 - Mezzanine

- Utilities supporting level 4 manufacturing
- Client viewing corridor
Level 5 - Client Viewing Corridor

- Example view into cell culture and Primary DSP suites
  - Less disturbance to operations
  - Reduced safety and environmental risk to production area cleanliness
Level 6

- Workshop, QC Laboratories, Office/Admin
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• Conclusions
Single-Use Technology Drivers

• Ideally suited to contract manufacturing operations
  - Reduced risk for cross contamination
  - Minimal cleaning / sterilisation validation
  - Focus operators on value-add activities
    • Very fast change-over (no cleaning or sterilising)
  - Enable flexible manufacture
    • Must be adaptable to suit the client’s needs/process
    • “Future proof” for new innovations (skids easy to replace)

• Facility design implications
  - Smaller footprint (clean room area)
    • Increased use of non classified areas
  - No SS transfer piping
    • Use of pass throughs and pre-sterilised tubing
  - Faster implementation and reduced Cap Ex
    • Standard equipment delivery in 2-3 months
    • Reduced qualification (IOQ at supplier)

(Image courtesy of Wyeth)
Single-Use Implementation - Upstream

- Fully single-use envisioned for upstream:
  - Dispensing operations through to buffer and media make-up
  - Solution filtering, storage and transfer
  - Cell culture vessels
  - Cell Harvest (depth filtration)

(Images courtesy of Thermo, Sartorius, Pall and Millipore)
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(Images courtesy of Corning, GE and Xcellerex)
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(Image courtesy of Millipore and 3M CUNO)
Single-Use Implementation - Downstream

- Hybrid single-use / multi-use equipment:
  - Looking to utilise single-use where possible
  - Often limited by sensors or requirements for in-line dilution

(Images courtesy of Sartorius, Millipore, PALL and GE)
Single-Use = Sustainability?

- While SU systems do produce additional solid waste, they can however provide a range of environmental benefits beyond traditional stainless steel (SS) systems:
  - Reduced WFI needs (no CIP/SIP)
  - Reduced CO₂ footprint and resource conservation
  - Reduction of hazardous cleaning chemicals sent to sewer
    - Safety hazard reduction for not exposing operators to cleaning agents
  - Reduced sterilisation autoclave needs

- Multiple studies have looked to evaluate the environmental cost of using single-use systems:
  - Most recently - a comprehensive Life Cycle Analysis by GE & BioPharm Services
    - “Cradle to grave” analysis of mAb process using entirely SUT at 100L, 500L and 2000L vs. a SS facility
    - All 18 environmental impacts studied returned measurably positive impacts with single use over SS!
Single-Use = Sustainability?

Environmental impact assessment

Single Use approach exhibits lower environmental impact in all 18 categories studied
The Future of Protein Manufacturing

Today

• Large stainless steel bioreactors
• DSP bottlenecks
• Large footprint/high CAPEX

Tomorrow

• Single-use systems
• Efficient processes
• Small footprint/low CAPEX
• Fast and flexible
• Meeting product quality demands
Conclusions

- DSM expecting to begin GMP operations for our new Brisbane cGMP manufacturing facility by mid 2013
  - Mammalian-produced API production, up to 2000L bioreactors
  - Open-plan, flexible design incorporating single-use technology

- DSM Biologics is excited to expand into the Australasian market and partner with BPA
  - We see excellent opportunities for collaboration with BPA and the Australian biotech industry, and are looking forward to providing high-quality manufacturing services
  - Look for the up-coming April DSM Roadshows (major centres)

- We are interested in hiring
  - Please contact or send CVs to ben.hughes@dsm.com