

## Case Study

# End-to-end, GMP Production Platform for Synthon's Biologics Pipeline

"The engineering principles represented in the Sartorius bioreactor portfolio were essential in the smooth scale-up of cell culture from lab scale to a disposable 2000L reactor. Face-to-face meetings were instrumental in the design and quick implementation of all process equipment." – Synthon

### Key Achievements

#### An expanding biologics pipeline

Synthon started developing its pipeline of biopharmaceuticals in 2007. The company's biologics pipeline includes antibody-drug conjugates and other new molecular entities. It targets these medicines towards serious and complex medical conditions such as cancers and autoimmune diseases. In order to manufacture (pre-) clinical lots of the drug substances within the Synthon organization, the company needed to construct a GMP plant. The organization took the decision to build the new facility at the company's HQ in Nijmegen.

#### Scale-up from laboratory to commercial manufacturing

Synthon established a relationship with Sartorius Stedim Biotech (SSB) during the early stages of their venture into biopharmaceutical development and installed bench-scale equipment into their laboratories for process development activities. Having worked with the organization and upstream technologies within the laboratory setting, Synthon were already familiar and confident in Sartorius' upstream solutions and expertise.

#### GMP facility construction in collaboration with Sartorius

Synthon selected SSB as a supplier of single-use processing equipment for both upstream and downstream processing. They were able to leverage SSB's expertise to support the equipment design for the facility such that SSB provided detailed process flow diagrams, equipment layouts and designs for both systems and consumables.

Teams from the two organizations worked closely together to generate designs during workshops and meetings in Nijmegen. Engineers and operating personnel from Synthon made several trips to the SSB facility in Guxhagen, Germany, to meet with representatives of the Sartorius Integrated Solutions team. The high degree of technical expertise of the Integrated Solutions team allowed them to develop designs that were specific to their client's requirements. The engineering team was able to find solutions to engineering design problems and prove to Synthon that they would work. Working with SSB provided Synthon with additional engineering competencies that helped them to establish their new biologics manufacturing capabilities.

### Quick Info

#### ► Success criteria:

Multi-product facility to manufacture a pipeline of products

Flexible process design for performing either 500-L or 2000-L batch sizes

Entirely end-to-end, single-use process with integration of chromatography systems from a third party

#### ► Project duration:

Less than 12-months from kick-off to engineering batch #1

#### ► Provided solutions:

CERTOMAT® CT plus shaking incubator

BIOSTAT® RM (20 & 50 L)

BIOSTAT® STR (500 & 2000 L)

FlexAct® single-use systems for clarification, ultrafiltration, filtration, virus inactivation and virus removal

BioPAT® MFCS/win SCADA

Palletank® for Mixing

Palletank® for storage

BioSealer® & BioWelder TC®

Sartocheck® Filter and Bag Tester

Scales & Balances

#### Single-use processing solutions throughout the facility

Synthon decided at an early stage to install single-use technologies rather than stainless steel equipment. Dr. Thorsten Peuker, Managing Director, Sartorius Stedim Systems explains: "Single-use technology reduces upfront capital costs, shortens construction timelines and allows companies to make modifications to their production capacity as may be required for products emerging from the pipeline. The risk of product cross contaminations is reduced when using single-use technology. This is important in multi-product facilities such as Synthon was designing. We supported Synthon through the different phases of this project such as Equipment Design, Basic Engineering and Realization for a smooth fast track execution."

SSB BIOSTAT® STR single-use bioreactors were selected for the production cell culture operations. The team has designed into the facility the capability to harvest from either the 500-L or the 2000-L BIOSTAT® STR bioreactors to allow operations to modulate capacity easily.

Synthon staff performed hands-on testing on a FlexAct® system during the equipment selection process. SSB then incorporated their recommendations into the design of the FlexAct® systems Synthon purchased. SSB delivered three multifunctional systems with which Synthon perform seven separate operations during the purification process including ultrafiltration, virus filtration and virus inactivation steps.

Since the initial facility construction project, Synthon asked SSB to provide a solution that would automate their hitherto manual bioreactor harvest step. SSB designed a single-use cell harvest system based upon their FlexAct® CH technology. Automating what had been until then a manual bioprocessing step, improves data acquisition and process consistency while reducing the opportunity for errors.

Both upstream and downstream unit-operations are monitored and controlled with Sartorius' MFCS/win SCADA software.

### Facility Start-Up

The engineering kick-off meeting for the equipment was held in October 2014 and the project delivered, on time, by July 2015. The first medium hold batch was run a month later in August 2015. Since then a further two engineering batches have been run. Synthon has validated both the 500-L and 2000-L process equipment and, meanwhile, successfully conducted GMP production runs.

The process and engineering expertise of the Sartorius Integrated Solutions team has helped Synthon construct a biomanufacturing facility with an end-to-end single-use process for the production of the company's pipeline of biological products.

### Background Information

Synthon, with headquarters in Nijmegen, the Netherlands, is an international pharmaceutical company and a leader in the field of generic medicines. The company started its biopharmaceutical franchise in 2007 and is building a promising portfolio of next-generation medicines. Synthon is developing rapidly into a specialty pharmaceutical company, focusing on the therapeutic areas of oncology and auto-immune diseases. Synthon products are currently approved by regulatory agencies in over 90 countries worldwide and marketed through strategic partnerships and – in dedicated areas – through direct sales. Synthon employs about 1,900 staff worldwide, and in 2016 it recorded a turnover of EUR 258 million.



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