

# SARTORIUS

## Customer Case Study

# Safer and Faster Conjugation and Purification of Antibody-Drug Conjugates (ADCs) at 1-20 L Scale



### Customer Profile

Company Name:  
Piramal Pharma Solutions

Company Location:  
Grangemouth, UK

Company Type:  
CDMO, part of Piramal Enterprises Ltd.

Industry:  
Health Care

Specialty:  
Bio-conjugates

Company Profile:  
[www.piramalpharmasolutions.com/  
our-facilities/grangemouth](http://www.piramalpharmasolutions.com/our-facilities/grangemouth)

## Customer Challenge

Piramal Pharma Solutions aimed to reduce the complexity of antibody-drug conjugates (ADC) processes. To achieve this goal, they sought to replace the multiple skids required for conjugation, filtration, and Con-Di-Con, which take up significant floor space and pose connectivity challenges. The setup, connection, and sanitization of these systems is time-consuming. Additionally, because the steps are usually conducted on individual multi-use systems which are dedicated to an individual product, multiple operators are needed for their preparation and execution and various automation platforms may also be involved. Such complex setups also require additional resource-intensive safety precautions.

To streamline and scale up their ADC manufacturing process, Piramal Pharma Solutions tested the Sartoflow® Expert single-use tangential flow filtration (SUTFF) system, a fully-automated and closed system designed for ADC applications.



# Background Information

Manufacturing ADCs is complex and process requirements change frequently. As highly toxic substances are being processed and batch values are very high, the assurance of operator safety and product integrity is a critical prerequisite. Meanwhile, the transition and scale-up to commercial manufacturing creates additional challenges of investment cost and training efforts.

Piramal Pharma Solutions sought to optimize and streamline scale-up during ADC process development. To meet this need, Sartorius provided the Sartoflow® Expert SU system on-site for two weeks for training and evaluation, including installation, recipe writing, and mixing tests.

## Provided Solution

To streamline parts of their ADC process steps, Piramal Pharma Solutions tested the Sartoflow® Expert SU TFF system with integrated mixing for conjugation. Their goal was to reduce the number of skids needed and therefore minimize the number of connections, limiting the complexity and time associated with set-up and sanitization. This decreases the number of operator hours and automation solutions required. Piramal Pharma Solutions also offers GMP services; the automation and documentation capabilities had the potential to simplify their GMP records.

The system was set up to run a 42 g test batch of ADC, automating the antibody reduction, payload addition, conjugation, precipitate removal, ultrafiltration, and diafiltration, on a single skid.

## Results

A 42 g test batch of ADC was prepared, running the following steps on the system at 3.7 L process scale:

- Payload conjugation
- Precipitate removal
- Tangential flow filtration (TFF)

Size-exclusion chromatography (SEC), drug-to-antibody ratio (DAR), and purification analysis were performed, and the data was compared to small-scale experiments.

Piramal Pharma Solutions reported substantial time savings compared to running three separate unit operations (Table 1, Figure 1). Additionally, due to the highly toxic substances that were processed, the system was required to go behind a shield (comparable to an isolator), which was easily feasible due to the system's compactness and small footprint. This helped to facilitate risk management for these critical processes.

In terms of performance, the customer's target DAR of 4.0 was achieved (DAR was 4.1 in Sartoflow® Expert SU). The final yield was 91.2% which was satisfactory and will be improved in future optimization runs.

## Project Key Indicators

Keywords:

- ADC manufacturing streamlined and simplified
- Conjugation, precipitate removal, and subsequent TFF on one skid
- Operator safety and product integrity

Molecule Type:

Antibody-drug conjugates (ADCs)

Process steps:

- Conjugation
- Precipitate removal (transfer)
- Con-Di-Con

Project Duration:

2 weeks

Success Criteria:

- Increased speed
- Product quality maintained
- Fewer resources required

Provided Solution:

- Sartoflow® Expert SU fully automated single-use TFF system optimized for ADC synthesis
- Flexsafe® Sartoflow® Expert SU 20 L 3D Mixing Bags for recirculation and conjugation
- Sartocon® Self-Contained TFF Cassette



*"Piramal has nearly 20 years experience in developing and scaling up safe and robust ADC processes. The Sartoflow® Expert SU will be one of the the SU option in our portfolio offered in addition to standard glass or stainless steel equipment. The key differentiators are fewer resources and less time required with the Sartoflow® Expert SU compared to a traditional set-up."*

**Xavier Despinoy**

Process Technology Lead at Piramal

**Table 1:** Comparison Between Conventional Pilot Scale mAb Conjugation and Sartoflow® Expert SU Process

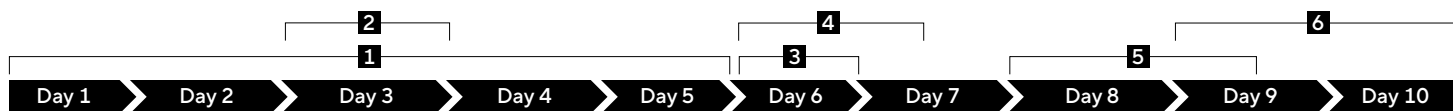
	Traditional Setup With Multi-Use Equipment (Incl. Set-up And Sanitization )	Intensified Process With Sartoflow® Expert SU
No. of skids to facilitate 8 process steps (mAb charge, dilution, pH adjust, reduction, conjugation, quench, NFF Filtration, TFF)	2	1
Transfer steps between skids	1	0
<b>Total process time frame</b>	<b>10 days</b>	<b>3 days</b>
Operator hours for preparation	~40 h	~8 h
Operator hours for sanitization	~24 h	0 h / ~12 h with MU cassettes
Operator hours to run process	~45 h	~26 h (incl. 4 h post-TFF filtration)
Operator hours for formulation and filling	~16 h	~16 h
Operator time for clean out and break down	~32 h	~40 min**
<b>Total operator time</b>	<b>~157 h</b>	<b>~50 h (64 h with open cassettes)</b>
Volume NaOH needed for sanitization	40 L	0 L (~5 L with open cassettes)
No. of manual addition steps	6	2 (payload + reducing agent)*

All times include general process handling i.e. handling of peripheral equipment and safety measures.

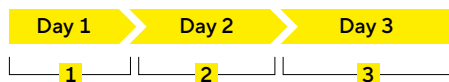
\*addition system of choice was peristaltic pump. \*\*take down time for Sartoflow® Expert SU consumable = 5 min.

**Figure 1:** Timeline Comparison Between Conventional Pilot Scale mAb Conjugation and Process on Sartoflow® Expert SU

#### Traditional Setup With Dedicated Multi-Use Equipment



#### Intensified Process With Sartoflow® Expert SU



##### 1 SU Flow Kit Installation

(4 hrs × 2 Operators)

SU kit installed day before batch (including bag-to-bag filter) and both bags integrity checked before use.

- Installation (flow kits etc.)
- Sensor & valve calibration
- Integrity test of bags

##### 2 Equilibration & Calibration

(1–2 hrs × 2 Operators)

- TFF lines equilibrated with ~20 L TFF buffer before use
- Flow meter tare
- Flushing cassettes

##### Process Execution

(10–12 hrs × 2 Operators)

- Reagent preparation
- mAb charge
- Dilution
- pH adjust
- Reduction
- Conjugation
- Quench
- NFF Filtration
- TFF
- Harvest out of Sartoflow®

##### 3 Final Filtration & Filling

(8–10 hrs × 2 Operators)

Operation performed outside of the Sartoflow® Expert SU skid

- Pre-formulation filtration
- Dilution & formulation
- Final filtration & filling

##### Take Down

(20 min. × 2 Operators)

- Take down of flow kit & bags

##### 1 Equipment Preparation

(30–32 hrs × 2 Operators)

1 × 10 L vessels (1 × TFF, 1 × conjugation glass vessel)

- Installation
- Pump calibration
- Stirring checks
- Sensors pre-calibrated
- Other equipment parts preparation & sanitisation

##### 2 Sanitisation

(12 hrs × 2 Operators)

- Dedicated TFF flow path and vessel sanitisation

##### 3 Process Execution

(16–20 hrs × 2.5 Operators)

- Transfer as extra step (discharge–recharge) or vessel to vessel transfer
- Manual process operation (usually in fume cupboard)
- mAb charge
- Dilution
- pH adjust
- Reduction
- Conjugation
- Quench
- NFF Filtration
- TFF
- Post TFF filtration

##### 4 Formulation & Filling

(6–8 hrs × 2 Operators)

- Dilution & formulation, filling
- Separate setup

##### 5 Decontamination

(8 hrs × 2 Operators)

- Decontamination of vessel and TFF

##### 6 Take Down

(8 hrs × 2 Operators)

- Dismantling of equipment

# Conclusion

ADC manufacturing is typically carried out in multi-use setups because of the presence of solvents and high pressures, creating safety concerns surrounding the ability of plastic containers to withstand these harsh conditions. As such, transferring an ADC process to SU setups is a challenge. The data presented here demonstrates that the Sartoflow® Expert SU was successfully engineered for ADC processes with the required solvent-resistance, safety concept, and automation solution in mind. Therefore, ADC manufacturers can benefit from all the ease of use that comes with SU applications, including eliminating time-consuming sanitization, flushes, and validations, while retaining the high performance associated with multi-use unit operations.

## At a Glance

Employee **hours reduced** by **3x**

Process **timeline shortened** from  
**10 to 3 days**

**91.2% yield\*** and  
**4.0 DAR** achieved

Purpose-built for **ADC**



### Before: Conventional Pilot Scale mAb Conjugation

- Complex, time-consuming process
- Multi-use set up



### After: Sartoflow® Expert SU Process

- Streamlined, faster process
- Single-use set up

\*For future runs the yield will be improved by further process optimization.

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