

## SUCCESS STORY

Dynamic crossflow  
filters have modernized  
insulin production in  
Kalundborg, Denmark



SEPARATION

# PROCESS KNOW-HOW AND INNOVATION

FULLY AUTOMATED AND ENCLOSED PROCESS WITH  
KRAUSS-MAFFEI DYNAMIC CROSSFLOW FILTERS

**ANDRITZ**

ENGINEERED SUCCESS



# The challenge

## Modernize the biotechnology-based insulin production

Topping several lists of the world's most sustainable enterprises, Novo Nordisk is a Danish pharmaceutical company and one of the largest manufacturers for diabetes medication in the world. For designing the production process, special care is needed as insulin is a peptide that is sensitive to chemical and physical treatment. Today, insulin is produced by means of biotechnology. At their plant in Kalundborg, on Denmark's largest island, Novo Nordisk uses the cells of yeast strain *saccharomyces cerevisiae* to produce its diabetes care products. The production is complex and consists of multiple steps: The yeast cells are cultivated in large-scale fermentation tanks, where they are given the optimal conditions to grow, reproduce and

express the desired peptide. Each of the large number of cells functions like a microscopic factory producing the pharmaceutical peptide. The downstream process consists of several different purification steps. Some of the purification steps require solid/liquid separation. Sometimes the liquid component is the value stream, sometimes the solid fraction contains the intermediate product. The production needs to comply with regulatory good manufacturing practice requirements and needs to take place in a controlled, contained production system. The new separation technology to be invested in is required to be a versatile type of solid/liquid separation technology so that the various process tasks can be performed.



**5,000 1/s**

SHEAR RATE TO KEEP  
THE FILTER CLEAN

**7,000 mPAS**

VISCOSITY OF THE  
RETENTATE

**50%**

LESS MECHANICAL FORCE  
AND STRESS ON THE  
PRODUCT

Krauss-Maffei dynamic crossflow filter DCF 312/16



# Our solution

## Fully automated Krauss-Maffei dynamic crossflow filters

The Krauss-Maffei dynamic crossflow filter, with overlapping ceramic membranes was the right solution. The hermetic design is ideal for pharmaceutical applications. Optimum separation and quality is ensured thanks to the single-pass filtration concept and minimum thermal and mechanical impact. The lower impact comes from the reduced feed pressure and the fact that the trans-membrane pressure is homogeneous across the entire surface as there are no inlet or outlet zones in the membranes. Since 2012, Novo Nordisk has purchased several lab-scale test units and pilot equipment to evaluate the technology before accepting delivery of GMP dynamic crossflow filters in 2019 with their respective sensors and actuators. They chose the DCF-technology due to its outstanding

process performance, for example filtration speed and solids concentration in multiple test samples. But the control system also played a major role. With one of the most innovative automation solutions on the market today, which is based on the Metris addIQ control system, ANDRITZ also provided the entire control system, incorporating all GMP-relevant software functions and enabling a fully automatic process. The measurements of the calibrated instruments are logged and quality reports are generated so compliance to specification of any batch produced can be verified at any given time. Every operator action is logged with user identification, and every modification of the operation recipes is also logged, and a very strict change control system is implemented.

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## Results

### Unrivalled consistency and efficiency

With the DCF, the efficiency of the separation process and yield of the compound are higher than with any other crossflow technology thanks to the high shear rate that prevents a clogging layer from forming (yield is at least 50% higher than with conventional crossflow technology). The technology is highly reliable as the open filtration area avoids any blockages, while the need for manual intervention is eliminated entirely. The filters work in a way that is completely enclosed and fully automatic – right down to the Cleaning-In-Place (CIP) and Sterilization-In-Place (SIP) features. Safety aside,

the high solids concentrations produced allow the process to be intensified at several steps, with favorable results for quality and a reduction in energy consumption of up to 80% compared to traditional crossflow filtration. What's more, the permeate is absolutely clear, outperforming traditional sedimenting technology or precoat filter technology. And the technology exerts 50% less mechanical force and stress on the product compared to other crossflow filters and disk stack separators. All of the equipment, including the machine itself and peripherals, conform to GMP requirements.

**"We are very happy with the collaboration and the results it has generated. ANDRITZ understood the highly detailed testing routines required by the pharmaceutical industry and complies with the high level of good manufacturing practice needed for pharmaceutical grade manufacturing."**

**MICHAEL HALLGREN**

Senior Vice President of Diabetes API manufacturing, Novo Nordisk





## WHAT'S YOUR SEPARATION CHALLENGE?

ANDRITZ Separation is the world's leading separation specialist with the broadest technology portfolio and more than 2,000 specialists in 40 countries. For more than 150 years, we have been a driving force in the evolution of separation solutions and services for industries ranging from environment to food, chemicals, and mining & minerals. As the OEM for many of the world's leading brands, we have the solutions and services to transform your business to meet tomorrow's changing demands – wherever you are and whatever your separation challenge. **Ask your separation specialist!**

### AFRICA

ANDRITZ Delkor (Pty) Ltd.  
p: +27 11 012 7300  
separation.za@andritz.com

### EUROPE

ANDRITZ Separation GmbH  
p: +49 8139 80 299 0  
separation.de@andritz.com

### ASIA

ANDRITZ Singapore Pte. Ltd.  
p: +65 6512 1800  
separation.sg@andritz.com

### NORTH AMERICA

ANDRITZ Separation Inc.  
p: +1 817 465 5611  
separation.us@andritz.com

### AUSTRALIA

ANDRITZ Pty. Ltd.  
p: +61 3 8773 4888  
separation.au@andritz.com

### SOUTH AMERICA

ANDRITZ Separation Ltda.  
p: +55 47 3387 9100  
separation.bra@andritz.com

### CHINA

ANDRITZ (China) Ltd.  
p: +86 757 8258 6802  
separation.cn@andritz.com

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