

ZETA
BEST
PRACTICE


EVOLUTION OF TECHNOLOGY



**PHARMACEUTICAL
MANUFACTURING**

- Extremely valuable product
- Hazardous substances
- Sensitive ingredients

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HIGHLY TOXIC COMPOUNDS
**DOWNSTREAM PROCESSING
AT THE HIGHEST SAFETY LEVEL**

Production of antibody-drug conjugates for targeting and killing of cancer cells

CHALLENGES ACHIEVED

Time to market is key ZETA's proven methods, like high parallelization of project phases, or the application of the Super Skid Concept (dividing the entire system into modules or skids) enabled fast track project execution within only 18 months.

Managing complexity in design and reduce 3D-modelling effort.

Basic design elements were created, copied and individually adapted. For example: in case of an ultrafiltration unit as basic element, the vessel size and pipe dimensioning were rearranged in its further copies, while conception and main parts remained the same.

User-friendly plant design.

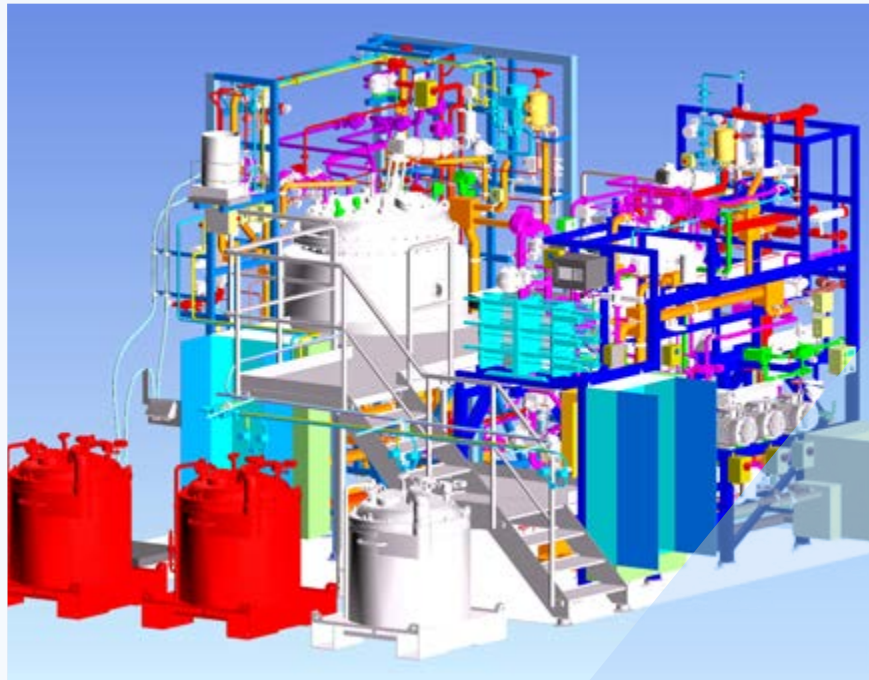
Process units are accessed easily and maintenance is carried out quickly thanks to special workshop platforms. With the help of a fully customized ladder rope crane, smaller media vessels are lifted for connection to the tanks.

Highly complex testing procedures to guarantee functional completeness at any level.

Extensive static and dynamic tests (FAT) of all units (process, TCUs, utilities, purified water, steam, air, ...) were performed. What's more, the time of four months until the building at the customer's site was ready for installation was used to perform and leverage tests for later qualification phases.

Ensure a secure and complete product transfer.

Very special, magnetically driven pumps were implemented to keep shear forces during transport low and the loss of valuable product to a minimum.



DOWNSTREAM TECHNOLOGY AT ITS BEST

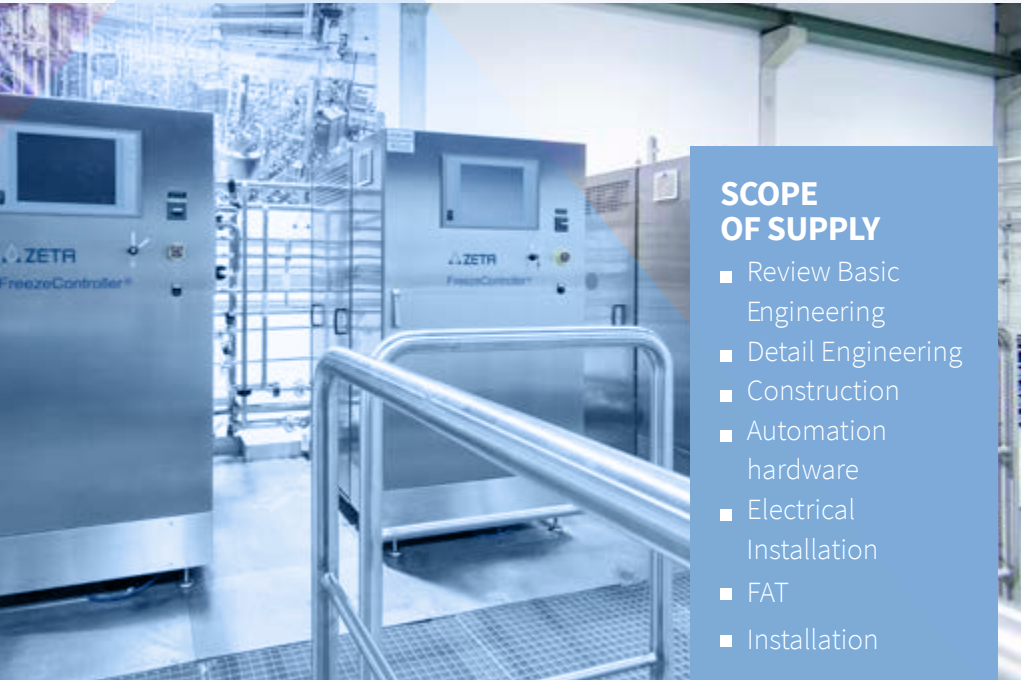
HIGH TECH PLANT FOR ANTIBODY-DRUG CONJUGATION

ZETA delivered a downstream system for the production of antibody-drug conjugates (ADCs) in the record-breaking time of only 18 months. The ZETA engineers provided complex technical solutions for handling sensitive as well as hazardous substances and ensured that the loss of the fairly sensitive and at the same time extremely valuable product was kept to a minimum.

ADCs are biopharmaceutical drugs designed as a targeted therapy for treating cancer. These complex molecules are composed of a monoclonal antibody linked to a cytotoxin. While the antibody specifically targets the cancer cells and the cytotoxin kills them, healthy cells are spared in this process. The production of ADCs must meet the most exacting demands on process technology – especially with regard to the critical conjugation step between antibody and toxin. In this project, the ZETA engineers faced a most challenging task: they had to develop the best production process for the delicate product. The plant includes two production lines, space for another line, a common buffer preparation and storage system, a common freeze and thaw area, plus all the required supporting functions. It is compliant with all safety regulations and GMP standards. Because of the special safety measures required for handling the toxic ingredient, the facility is separated into independent operation units. Carefully thought-out and highly customized solutions allow down-stream processing at supreme level.

Important steps in antibody-drug conjugation:

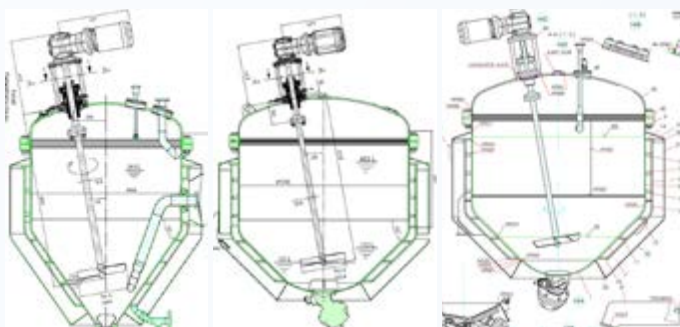
- Freezing and thawing of ingredients with help of freeze controller
- Ultrafiltration steps
- Safe transfer between operation units
- Addition of linker
- Addition of cytotoxin for conjugation with antibody
- Filling and freezing in customized and integrated freeze-and-thaw system



SCOPE OF SUPPLY

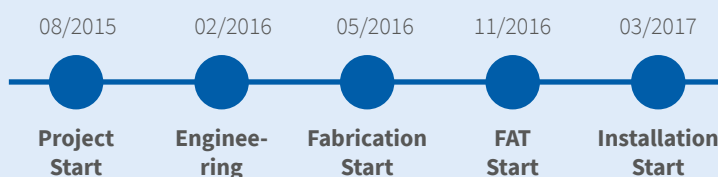
- Review Basic Engineering
- Detail Engineering
- Construction
- Automation hardware
- Electrical Installation
- FAT
- Installation

“The project was a perfect example of how a prefabrication and skid concept can be implemented even for complex monoclonal antibody and cytotoxin downstream processes” reports Matthias Goriupp, project manager at ZETA who emphasizes the close cooperation with the customer in Switzerland, especially throughout qualification: “During the functional FAT, the customer had the opportunity to perform comprehensive tests. We provided a perfect test environment at our workshop, where we had all the necessary media available. The result was the perfect optimization of software and functions.”



„Master-copy“ concept

PROJECT EXECUTION TIME



CHALLENGES ACHIEVED

Customized solution based on the ZETA Freeze & Thaw Systems.

Four freeze-and-thaw controllers are arranged on a platform, freeze containers can easily be connected underneath. The heating-cooling coils of the vessels are filled and emptied automatically. Controlled freezing, transport, storage and thawing of the sensitive substances is effectively accomplished.

Thorough process optimization.

The complete set-up of the facilities at the ZETA workshop was ideal for optimization: Circulating volumes were checked intensely, foam generation minimized, and a secure product transfer between operation units was ensured.

Vessel cleanability. A specific design of rotating spray balls and an evaluated cleaning procedure guaranteed complete removal of toxic substances from the vessels featuring unusual geometry.

Development of best-in-class vessel geometry for ultrafiltration.

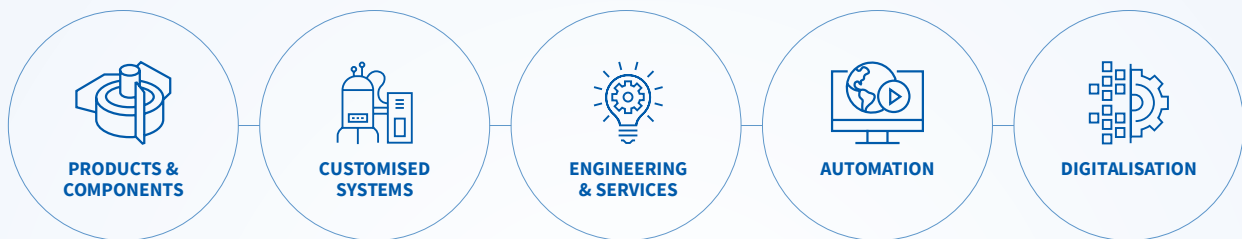
During ultrafiltration, the highly valuable product is concentrated in a decreasing volume. To avoid product losses, consistent cooling is mandatory. In computational fluid dynamics (CFD) studies, the ZETA engineers developed and tested specific vessel geometry solutions to ensure efficient cooling for all liquid levels.

RELEVANT KEY FIGURES

- 9 Process vessels (300-1500 L) with agitators
- 8x8 Filter holders
- 10 Floor scales
- 9 Dosing tanks (2.5 L)
- 34 Liquid and gas filters
- 1 Buffer preparation vessel (10,000L) with magnetic agitator
- 4 Buffer storage vessels (6,300-7,500L)
- >30 Pumps

INNOVATIVE SOLUTIONS FOR OUR CUSTOMERS

EVOLUTION OF TECHNOLOGY



ZETA Business Activities

EPCM contractor
Plant engineering
HVAC, cleanroom & BMS/EMS design
Decarbonization
Automation
Digitalisation
Qualification
Maintenance & Upgrades
Research & Development

Customer Benefits

Ultra-fast projects & faster time to market
End-to-end solutions from a single source
Customized solutions
GMP-/FDA-Compliance
Deep process understanding
Experience in complex biologics
High process reliability
Scale-up capabilities
Own innolab ZETA TechCenter

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