INTRODUCTION: The main objective of this project is to design a biotechnological industrial plant to produce recombinant tissue plasminogen activator (r-tPA), known commercially as Tenecteplase (TNK). With the goal of covering 5% of the r-tPA sales in China, the production will be of 30 kg TNK/year. The use of simulators to create different diagrams will help in defining the units of the process.

PROCESS
- Product: Tenecteplase
- Operation mode: Perfusion with immobilized cells
- Cell line: Chinese Hamster Ovarian cells (CHOs) DUKxB11
- Production: 30 kg TNK/year

The process is constituted by three essential parts:
- In the upstream section, cells are cultured in order to achieve the required concentration for the TNK production.
- In the reaction step, cells synthesize TNK and release it to the medium.
- In the downstream section, TNK will be isolated with a minimum purity of 99.5% for its further use in the pharmaceutical industry.

REACTORS
- Bioreactor
- Fed-batch reactor

LIVER OF IMMUNE SELECTIVITY
- CHO cell culture
- CHO SFM-II medium (defined and without FBS) and air

The reaction takes place in perfusion with the cells immobilized on a matrix and in a 650L packed reactor.

The following figure shows the piping and instrumentation diagram of the reactor, in which controllers and sensors of different parameters are indicated.

PARAMETER OF THE REACTOR VALUE
- Temperature: 33.5°C
- pH: 7.2-7.4
- Pressure: 1 bar
- Aeration rate: 0.5vvm
- Volumetric entry flow (medium): 500 L/h
- Glucose concentration: 0.5-1.5 mg/L
- Working volume: 598 L
- Residence time: 1.2 hours

REFERENCES
- Catalá, INVITROGEN. Available at: https://products.invitrogen.com/hsg/product/RT3807/ID=sreach-product. Visited on 20/04/2013

AUXILIARY EQUIPMENT
- Other equipment, apart from the one represented in the process flow diagram, will be necessary in our plant to allow the desired production of TNK:
  - Pumps to make liquids flow at the correct rate and pressure
  - Compressors to allow the correct air circulation
  - Filters to guarantee an exit of dust-free air
  - Filters to sterilize the medium
  - CIP and SIP processes. Integrated in the equipment