EQUIPNET

BRAND NEW MODULAR BIOPROCESSING FACIITY

PLANT DESCRIPTION

The objective of this plant is a flexible multi-product facility for commercial manufacturing of recombinant protein products produced by microbial fermentation.

The facility is designed for a single production line with one 2'000 L gross volume microbial production fermenter, equipped completely with the respective seed train and purification.

Basis of design are three different recombinant proteins and expressed in non-pathogenic E. coli.

The installations is however designed with suitable flexibility to allow for production of other products manufactured by means of microbial expression systems.

Microbial expression systems will be of Biosafety Level 1 (BSL 1)

This facility is exclusively dedicated to the production of low bioburden drug substance (API). None of the drug substances is a sterile drug substance and none will be pre-formulated, all will undergo subsequent formulation steps.

MANUFACTURING PROCESSES

The following standard process steps are implemented

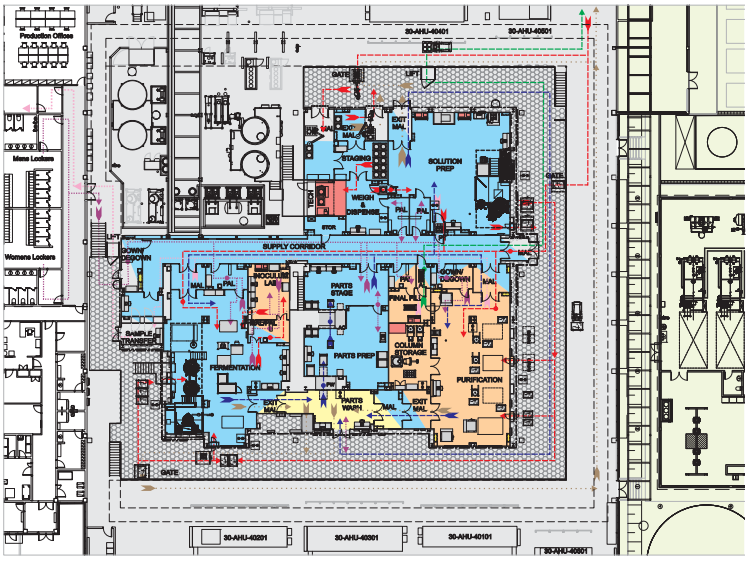
- Dispensing of raw materials
- Fermentation media and buffer preparation
- Inoculum (seed) preparation
- Fermentation, including addition of nutrients, base, antifoam or other
- Harvest by means of (depending on the product):
  - Centrifugation and filtration
  - Cell disruption by homogenization
- Buffer hold
- Chromatography
- Ultrafiltration/Diafiltration
- 0.2 mm filtration
- Filling of DS
- CIP/SIP of equipment, including mobile equipment where applicable
- Freezing of bulk DS
- Storage, packing, testing and unpacking of chromatography columns
- Online and offline filter testing

BASIC PRINCIPLES

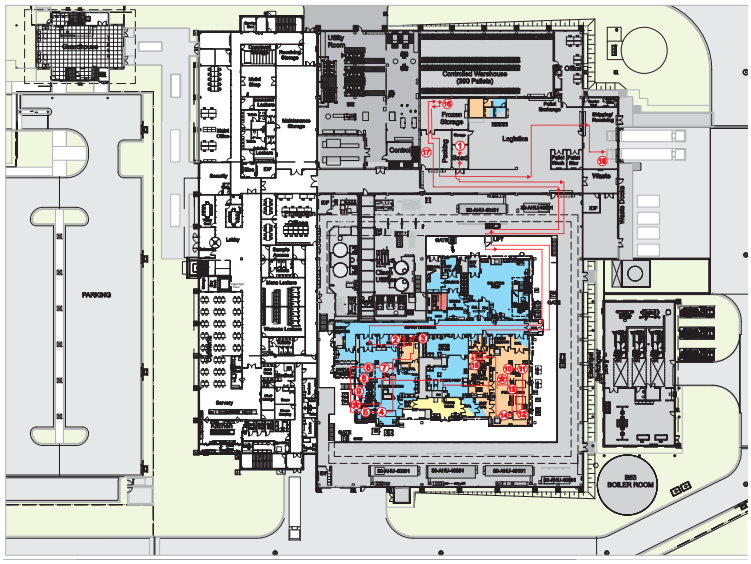
- Basic operational principles are:
- Minimal through-put time / process time ratio
- Maximal efficiency and utilization of the plant
- Production in closed systems in USP and DSP
- Adequate flexibility in production:
  - to allow fast and efficient change-over between products
  - to accommodate different types of processes and different process duration

5 Dan Road Canton, MA 02021 | 781.821.3482 | sales@EquipNet.com | www.EquipNet.com

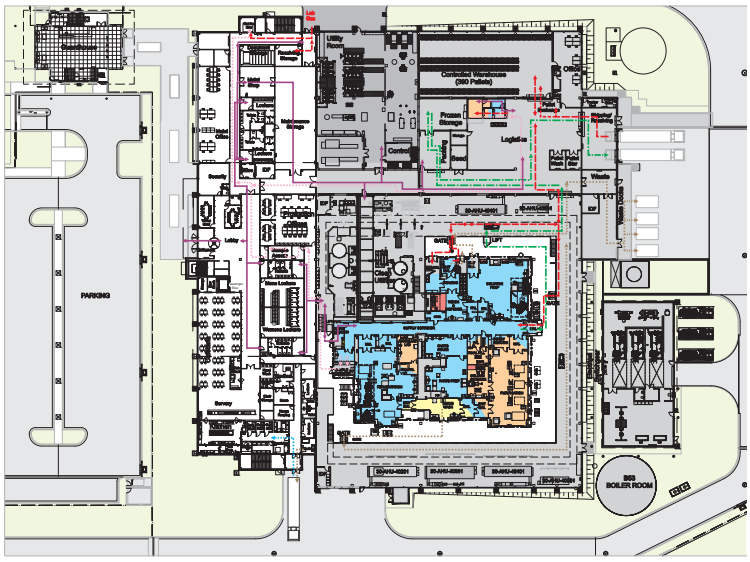
Production Area Flows



Ground Floor Plan Flows



Ground Floor Plan Process Flows



PRODUCTION AREA
Raw materials and disposables is distributed throughout the different areas of the manufacturing facility wherever required via material airlocks. The GMP area is around 1000 m2.

INOCULUM
The fermentation medium will be transported from the preparation room into the seed lab whenever needed. After completion of the expansion steps, the inoculum is prepared by pooling of different cultivation flasks, bottles or spinners. The inoculum should exit the seed lab via an air lock directly into the fermentation area where it will be transported to the seed fermenter for inoculation.

DISPOSABLES
Used disposables and any other solid waste have to be eliminated appropriately and it needs to be ensured that no living GMO from production activities leaves the site. Therefore, a decontamination autoclave is installed to adequately inactivate all solid waste from upstream areas.

PRODUCT (BULK DRUG SUBSTANCE)
The batch size depends upon titer and final bulk concentration and varies between 35 L and approximately 110 L. The DS will be frozen and stored in bottles.

The drug substance bottles will be transported to the cold room -20°C or freezers located in the warehouse area for freezing; once frozen at -20°C, the drug substance will be stored in the cold room.

WASTE
The main waste flow will be liquid and shall be handled by the waste water treatment plant. Liquid waste, which has been in contact with microbial cells or cell debris, has to be inactivated before being neutralized and directed towards the waste water treatment plant. The waste collecting system is designed to prevent any risk of back-contamination.

Liquid waste, which has not been in contact with cells or cell debris, does not need to be inactivated before being neutralized and directed towards the waste water treatment plant. The limit is all waste from the upstream area shall be treated for inactivation. The only exception is CIP, where only pre-rinse shall be directed to inactivation.

CONTACT
For more information please contact Sean Larkin at 617.407.9000 or slarkin@equipnet.com