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Post Graduate (P.G.), Monsoon semester

VMC 607: VACCINOLOGY

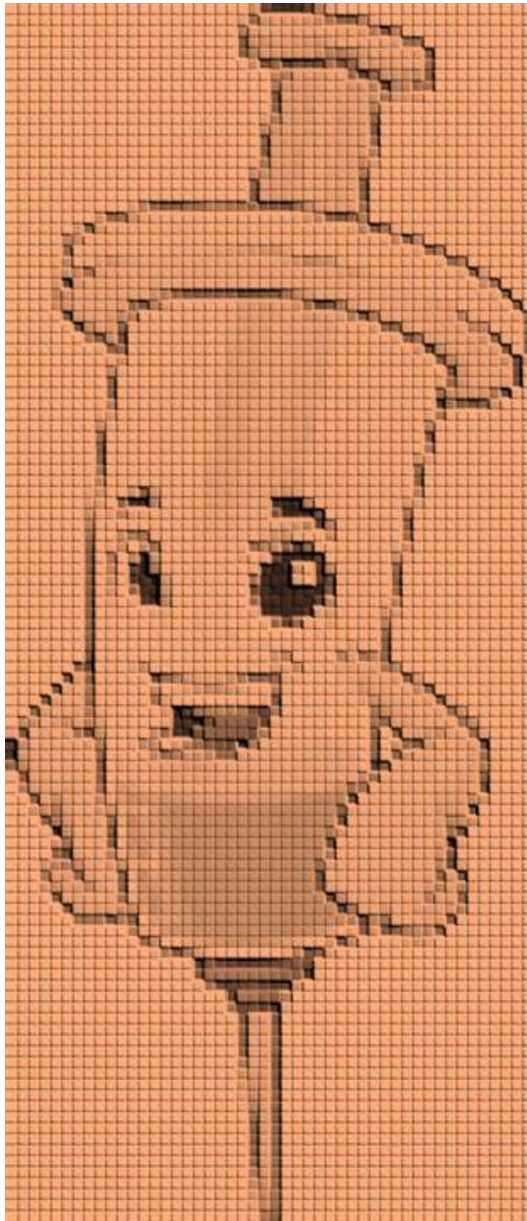
Topic: Methods of construction of traditional vaccines

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PROCESS OUTLOOK

- The vast majority of the over one billion doses of vaccines manufactured today
- The ability to manufacture these vaccines safely and consistently is built on 4 competencies
 1. The manufacturing process that defines how the product is made
 2. The compliance of the organization to successfully complete that process
 3. The testing of that product and supporting operations
 4. The regulatory authorization to release and distribute that product

REGULATORY PROCESS

- New vaccines are subjected to a well defined regulatory process for approval
- The approval process consists of 4 principal elements
- Preparation of pre clinical materials for proof of concept testing in animal models, manufacture of clinical materials according to current good manufacturing practices (cGMP) and toxicology analysis in an appropriate animal system
- Submission of investigational new drug application (IND) for submission to FDA for review
- Testing for safety and effectiveness through clinical and further non clinical studies
- Submission of all data to FDA in the form of a biologics license application (BLA) for final review and licensure

VACCINE PREPARATION BASICS

- Conventionally two classes of microbes are targeted for vaccine production:
 - Bacteria and
 - Viruses.
- Bacterial vaccines are comparatively easy to prepare, extract and formulate in comparison to viral vaccines.

Process for manufacturing a vaccine preparation

Upstream process

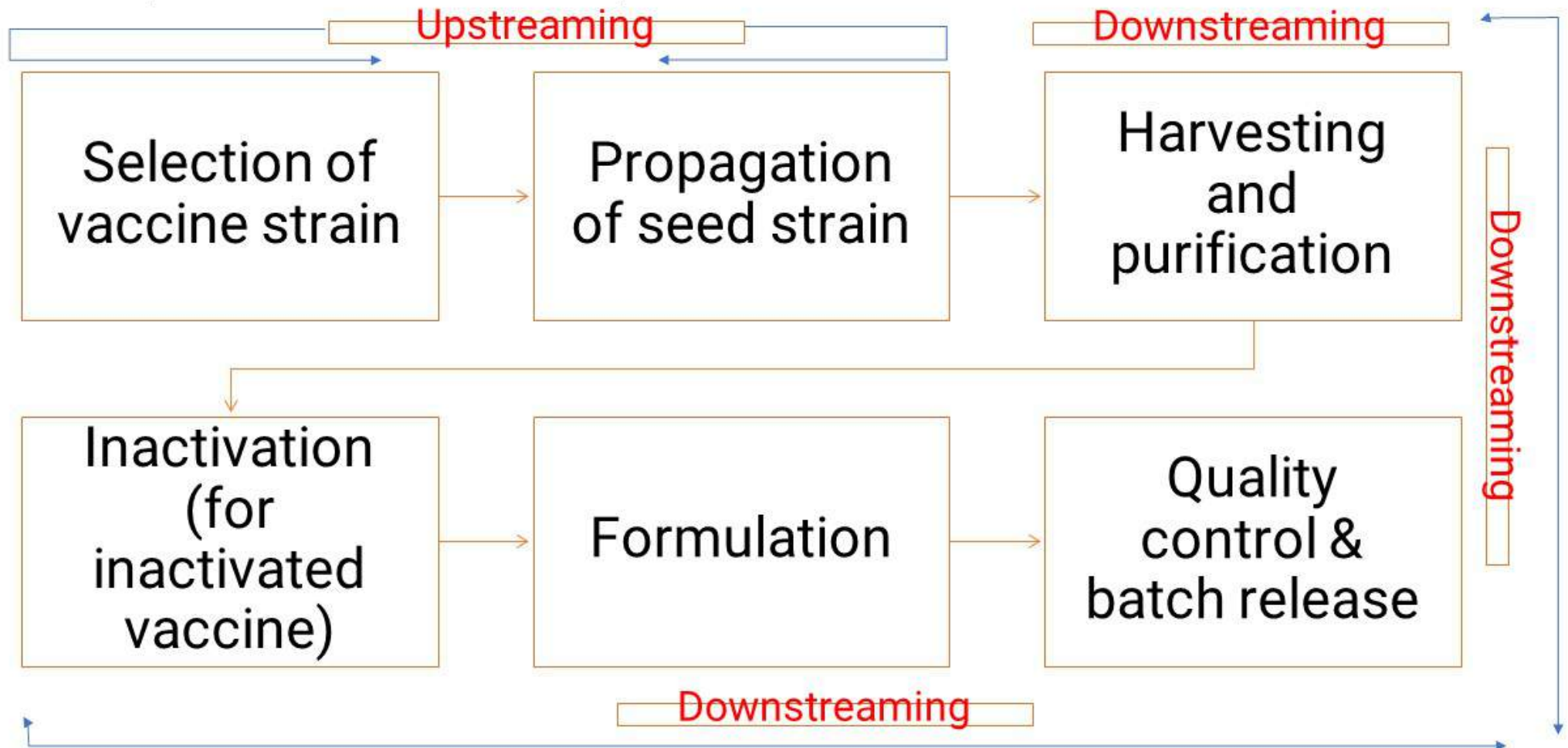
Downstream process



Different techniques and ways are employed to produce a vaccine agent based on

upstream and downstream processes

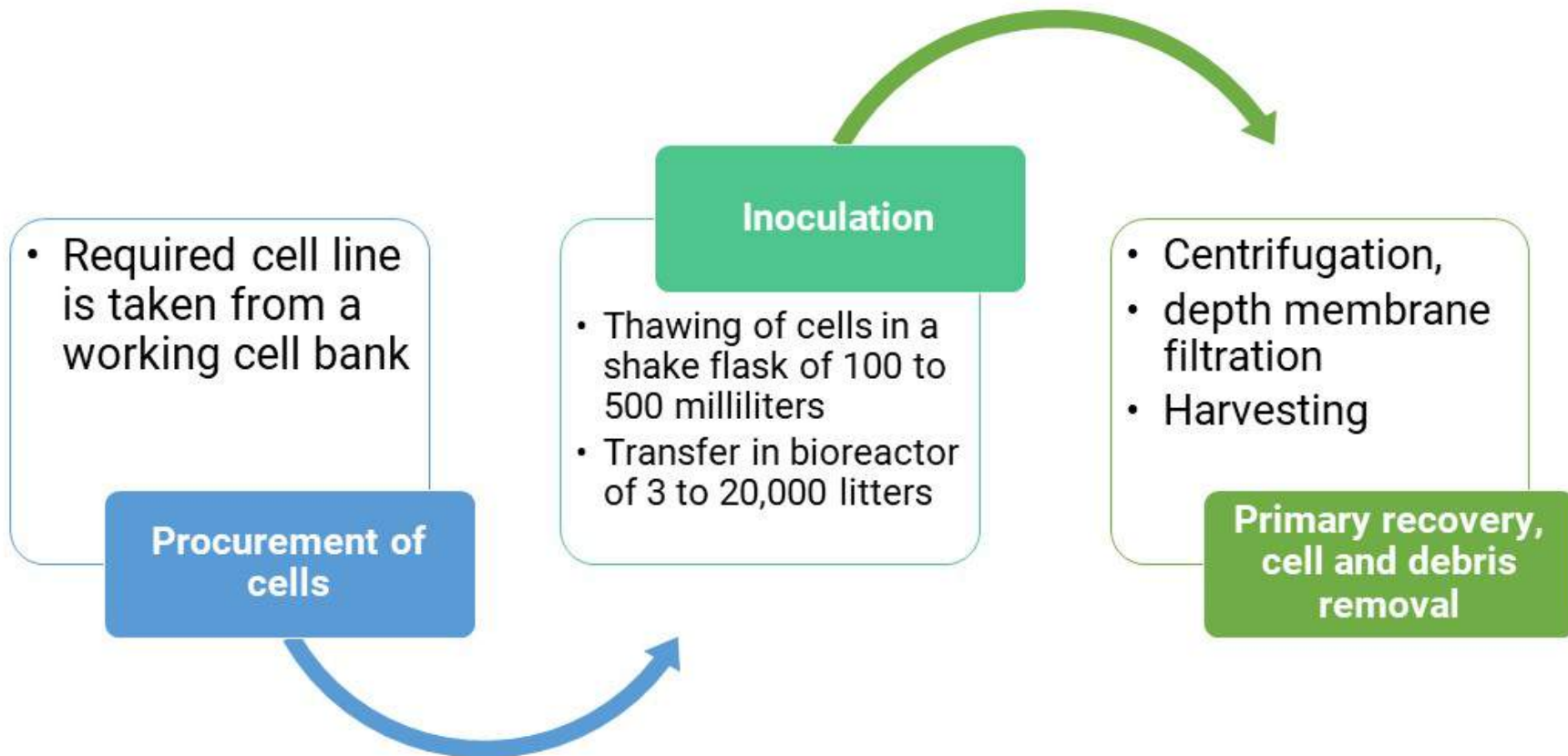
Steps of vaccine production



Upstream entire process from early cell isolation and cultivation

Cell bank storage

Culture expansion of the cells,
fermentation process and the final harvest



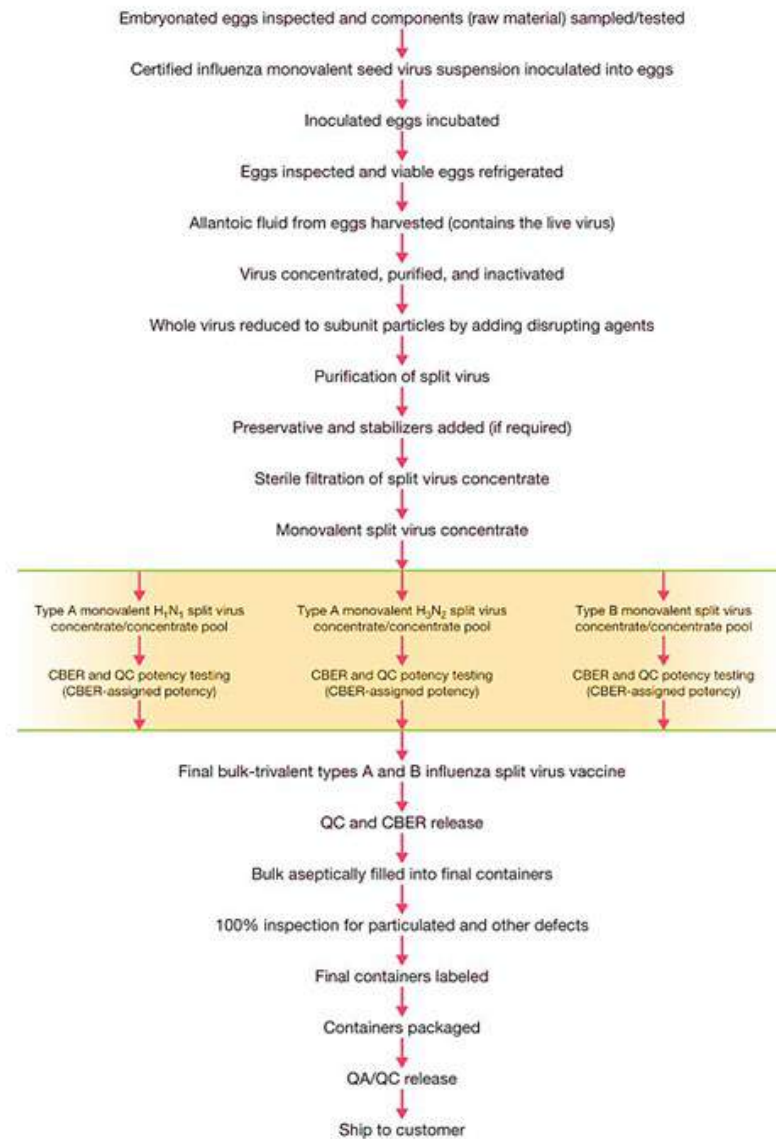
Egg-based
manufacturing
system

Embryonated Chickens' eggs to replicate the virus

Advantages- safe and effective

Limitation - needs constant supply of eggs. One or two
eggs yield one vaccine dose

Might leave some egg components that might cause an
allergic reaction



Egg-based vaccine manufacturing process flow

Source: Plotkin's Vaccines

Cell culture-
based
manufacturing

Uses mammalian cells to culture the virus for vaccine production

Production has also better process control, higher safety level and shorter production cycle

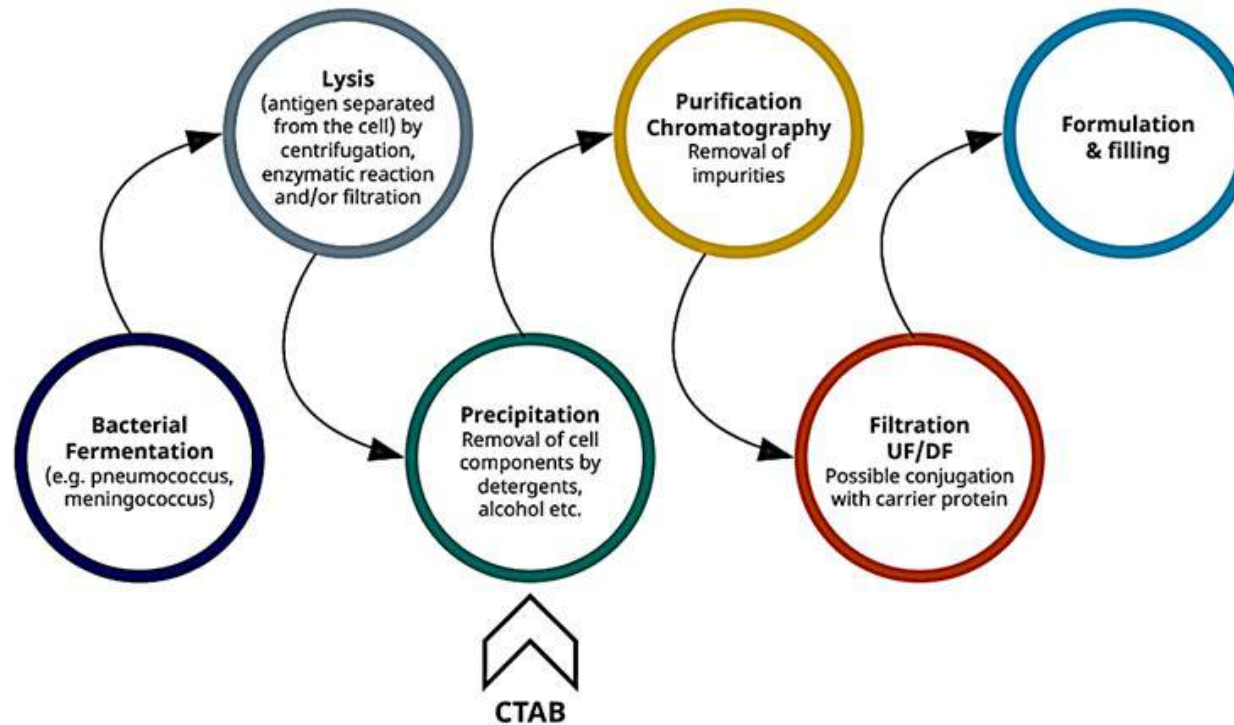
Higher quantities are made in a shorter period of time and pathogenic viruses can be produced safely

Reduces the possibility of mutation of the virus culture in the manufacturing process

Limitations: cell-based manufacturing are that the costs are relatively high and the cells should be free from another virus

Bacterial vaccine production

Polysaccharide-based vaccine manufacturing (simplified)



Bacteria are grown in bioreactors

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graph TD; A[Processing] --> B[Batch Processing]; B --> C[Continuous Processing];
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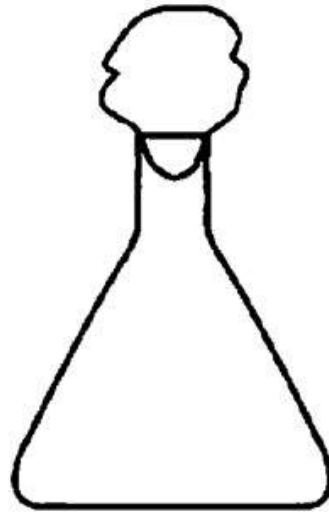
Processing

Batch Processing

Continuous Processing

Batch culture

Culture incubated
in a closed vessel
with a single batch
Of medium.



Flask culture
A batch culture



Batch
processing


Process has at least six steps and six pieces of equipment before it is completed

Production stops every time when the equipment is changed

Components of the vaccine are added on through the process and new batch cannot start before the previous one is completed.

Advantages of using a batch processing

Setting up is little bit less expensive and the process is easily modified.



Some products can be only made with batch processing.

Continuous process

| | |
|--------------------|------------------------------|
| Continuous process | Product is done continuously |
|--------------------|------------------------------|

| | |
|--|--------------------------------------------------------------------|
| | All the base ingredients are added at the beginning of the process |
|--|--------------------------------------------------------------------|

Continuous culture

Growth in an open system

- continual provision of nutrients
- continual removal of wastes

Continuous culture aims to keep a culture growing indefinitely. This can be done if:

- fresh nutrients are continually supplied
- Accumulated cells and waste products are removed at the same rate
- Conditions such as temperature and pH are kept at their optimum values.

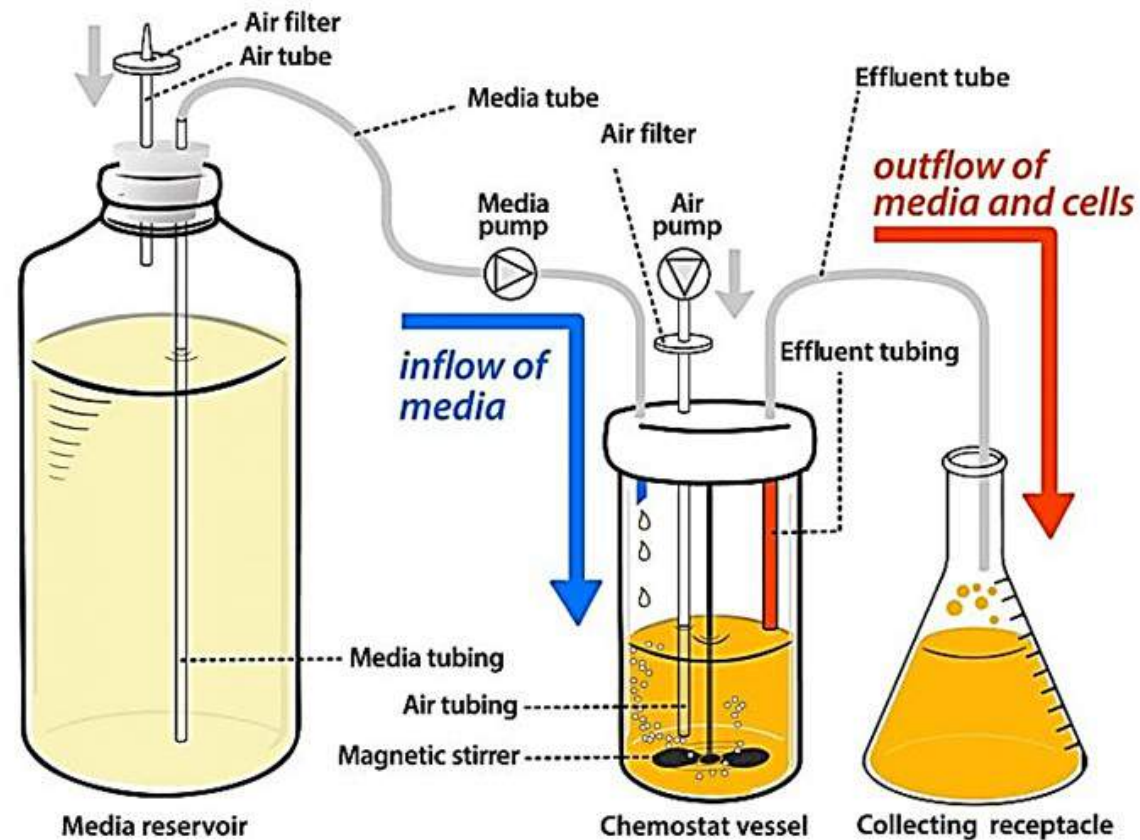
Raw materials are trickled in at the top of a column

- **Product flows out the bottom in a pure state.**
- **No need to be separated from the catalyst.**

Consisting of immobilised micro organisms .

- **Process can only be used for reactions that are fast**
 - **Culture vessel designed for continuous - chemostat.**
-

Continuous culture- chemostat



Source of image: microdok.com

Continuous process

Advantage

It can speed up the process significantly compared to batch processing

It can also be more environment friendly option



Process is continuous and fewer people are involved in the process

Risk of human error is reduced



Thank you

