BIOPROCESS FOR THE PRODUCTION OF GENE THERAPY FOR HAEMOPHILIA A:

Bioprocess design part I

I. BACKGROUND

Why is Haemophilia type A an attractive candidate for gene therapy?

Haemophilia type A is a life threatening X-linked genetic disease. Patients have a defective form of the gene that codes for Factor VIII in the coagulation cascade, causing recurrent hemorrhages and inflammation of tissues.

II. BASES OF DESIGN

Objective: 48,000 doses in 3 years (EU Market)
Product Critical/Quality Attributes:
- Cell source: 10^7 AAV
- SOX Full AAV capsids
- Purity and sterility

III. ALTERNATIVES

- Biocatalyst: HEK vs. Sf9
- Operational: Fed Batch vs. Batch
- Gradient: CsCl vs. Iodixanol

IV. MOLECULAR BASES

Sf9/Baculovirus system of production of AAV

ACKNOWLEDGEMENTS

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V. BLOCK FLOW DIAGRAM (BFD)

The process starts with the scale-up of a viral culture in a 50 L bioreactor, followed by aseptically transfer to a 300 L bioreactor, which is then followed by the addition of cells to the bioreactor. After a period of growth, the cells are harvested and the virus is purified, followed by a scale-up of the virus to the final product.

VI. PROCESS FLOW DIAGRAM (PFD)

The process flow diagram illustrates the steps involved in the production of the viral vector, from the initial culture to the final product.

REFERENCES


