

# Production of the equine influenza vaccine using a baculovirus expression system in insect cell lines

## Part IV: Sustainability analysis and future improvements

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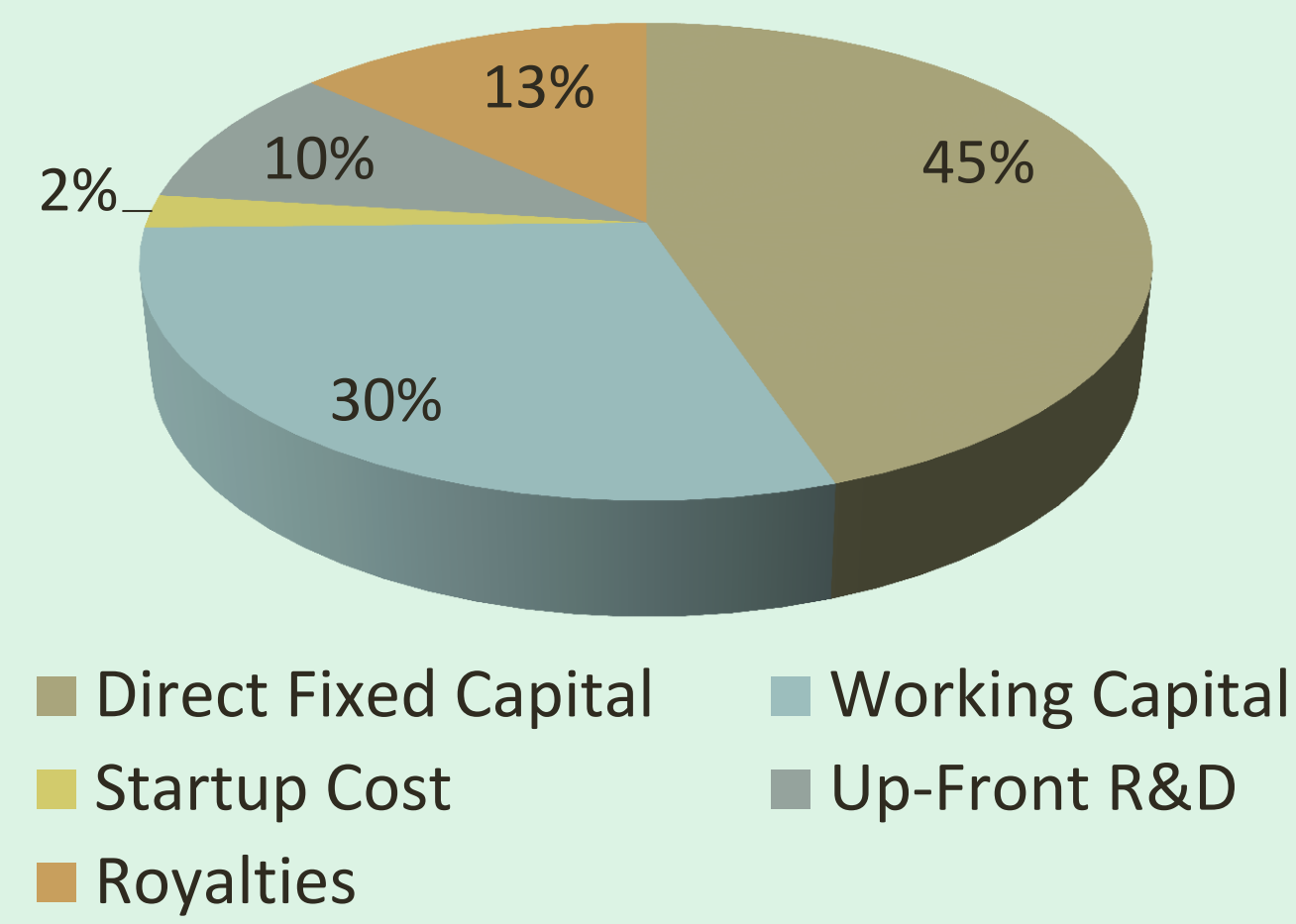
### GLOBAL OBJECTIVE

Design of an industrial bioprocess plant with the simulator SuperPro Designer for the production of the equine influenza vaccine using a baculovirus expression system in insect cell lines, and subsequent analysis of its sustainability.

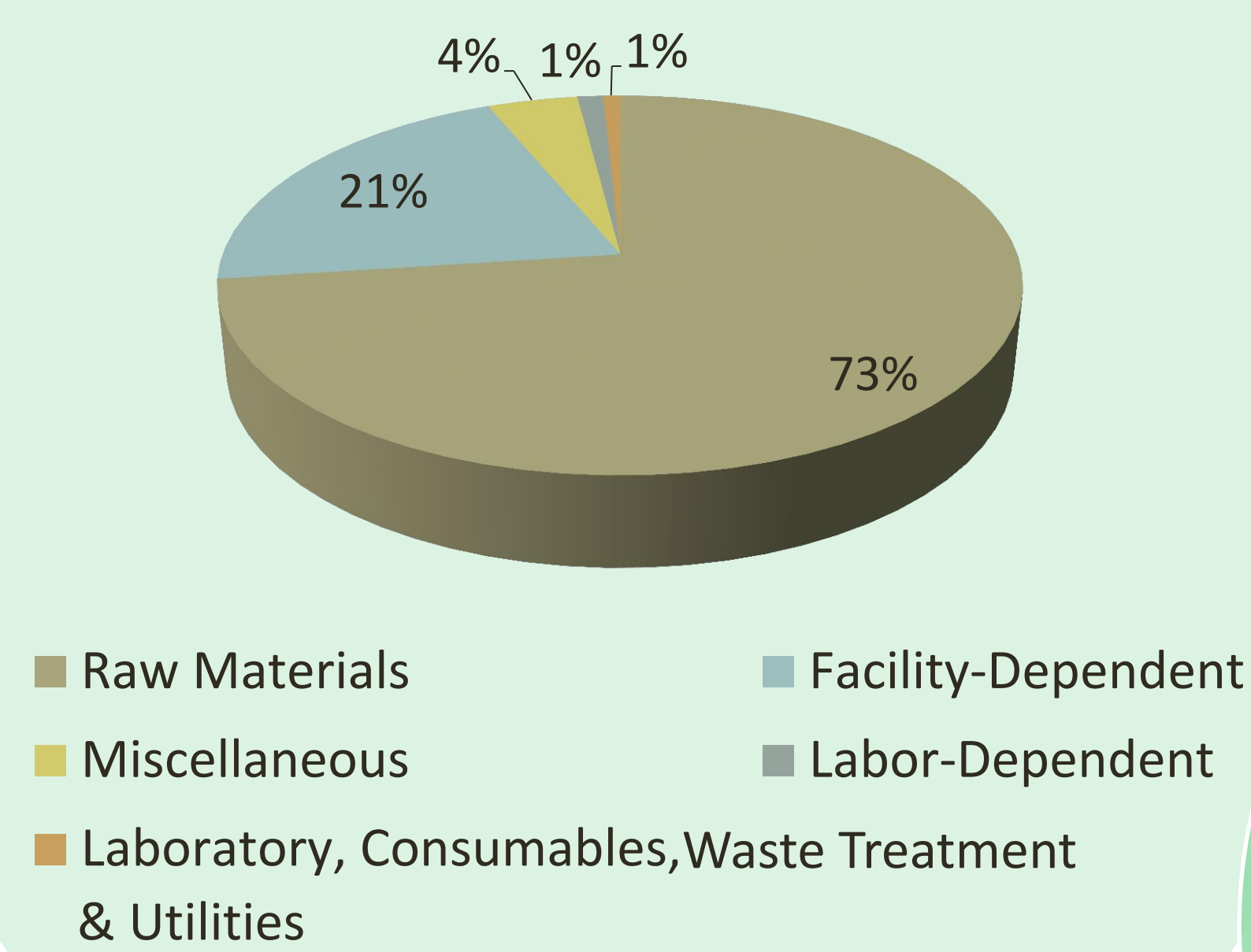
### Executive Summary

Total Capital Investment	\$ 92,377,000
Operating Costs	\$37,045,000
Revenues	\$ 80,495,000
Benefits	\$ 43,450,000
Unit Production Cost	4.60 \$/Entry
Unit Production Revenue	10 \$/Entry
Payback Time	3.08 years
IRR	27.58 %
NPV (7%)	\$ 138,762,000

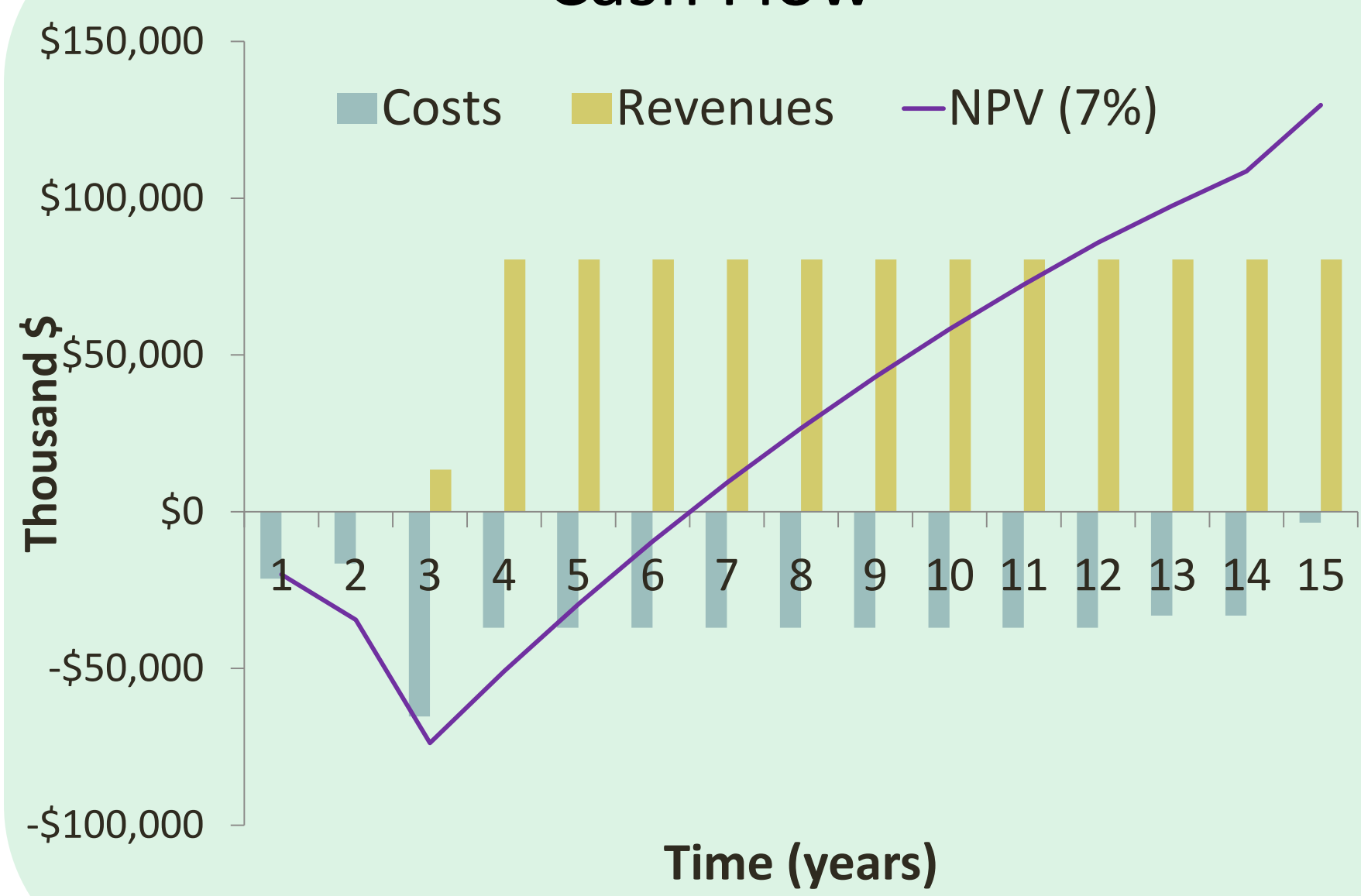
### Total Capital Investment



### Operating Costs



### Cash Flow



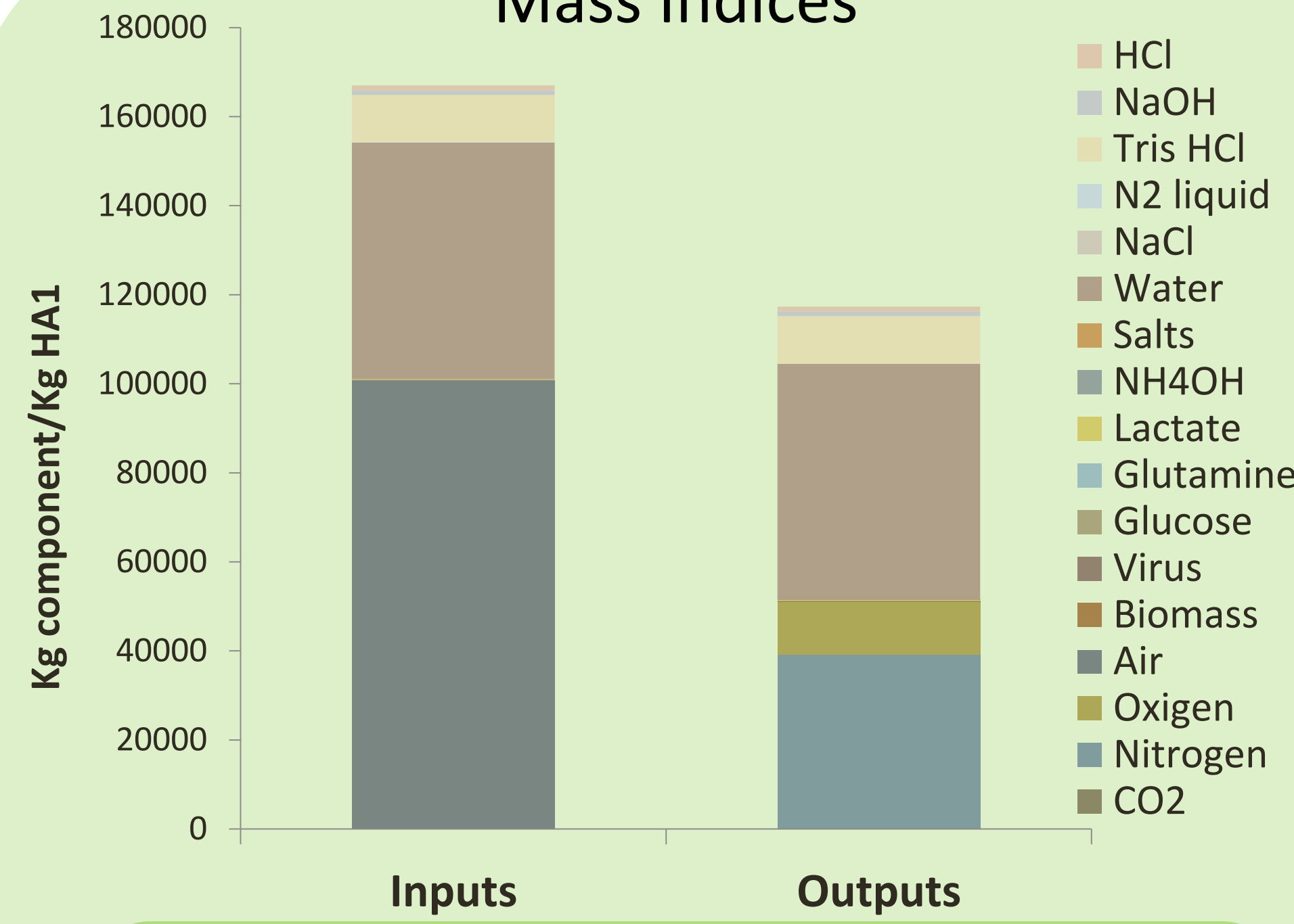
- High initial investment
- Short period recovery: 3.08 years from the production start time
- Adjustable market price

### COST-EFFECTIVE PROCESS

### Potentially dangerous streams:

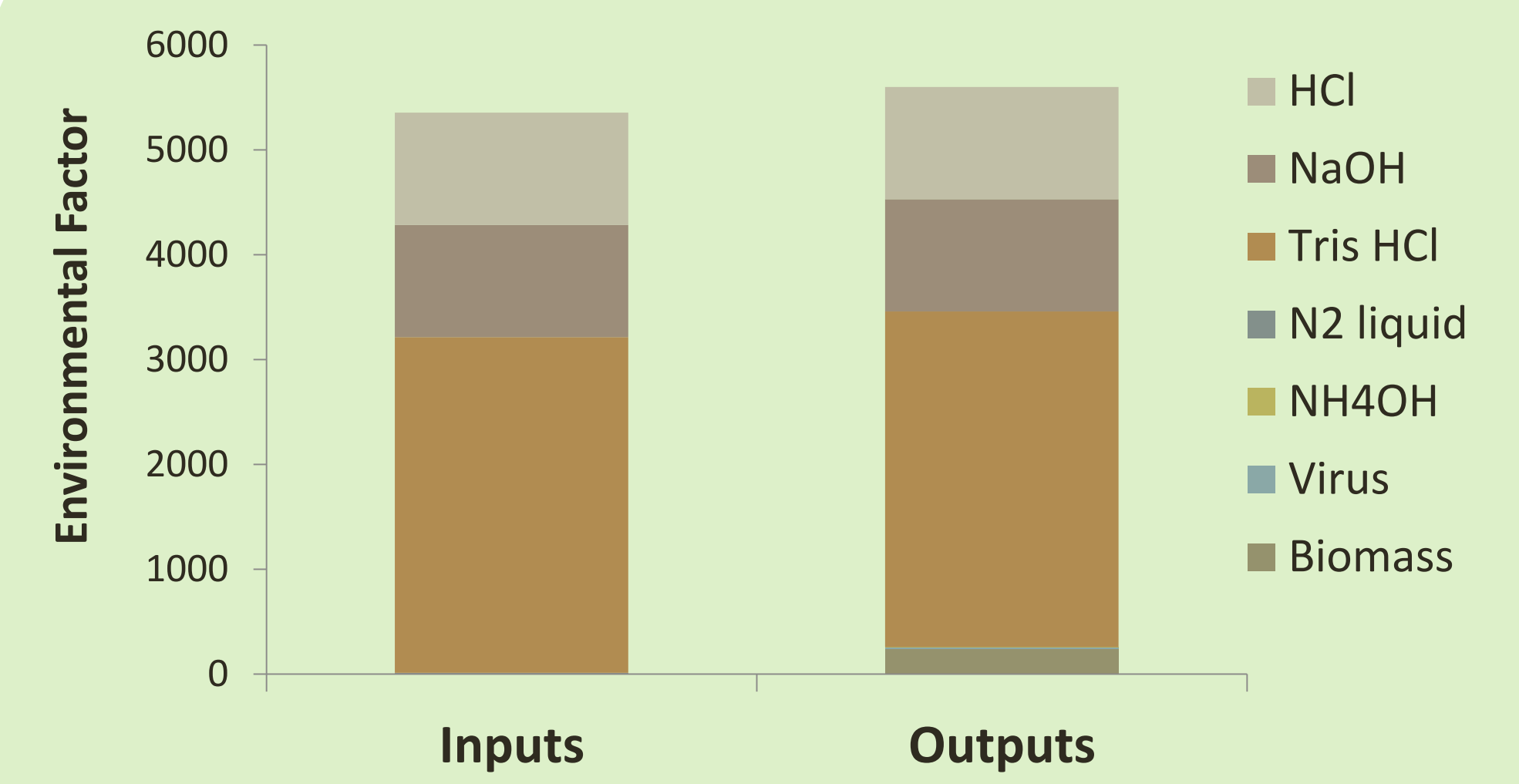
- Air inputs and outputs → HEPA filters
- Wastes from GMP process → NaOH inactivation and HCl neutralization

### Mass Indices



Air and Water are the major inputs required, while Emissions and Water are the major outputs obtained

### Environmental Factors



Tris HCl, NaOH and HCl are the most hazardous components for the environment; followed by N<sub>2</sub> liquid, Biomass and Viruses

### ENVIRONMENTALLY SUSTAINABLE PROCESS

### Environmental

### Economic

### Social

- Horses health improved
- Innovation in the existing production system
- Strong acceptance among the society
- Optimal security measures and process automation
- Quality work respecting international standards
- Active competition among operators and high salary
- GMP product

### SOCIALLY ACCEPTABLE PROCESS

### EVOLUTIONARY LINE AND FUTURE IMPROVEMENTS

#### Advantages BEVS

- ✓ Low-cost and rapid production of proteins
- ✓ Correctly folded and biologically active proteins
- ✓ GMP-qualified master virus banks and cell line
- ✓ Scalable to large volumes and high cell densities
- ✓ Platform for the development of a wide range of vaccines



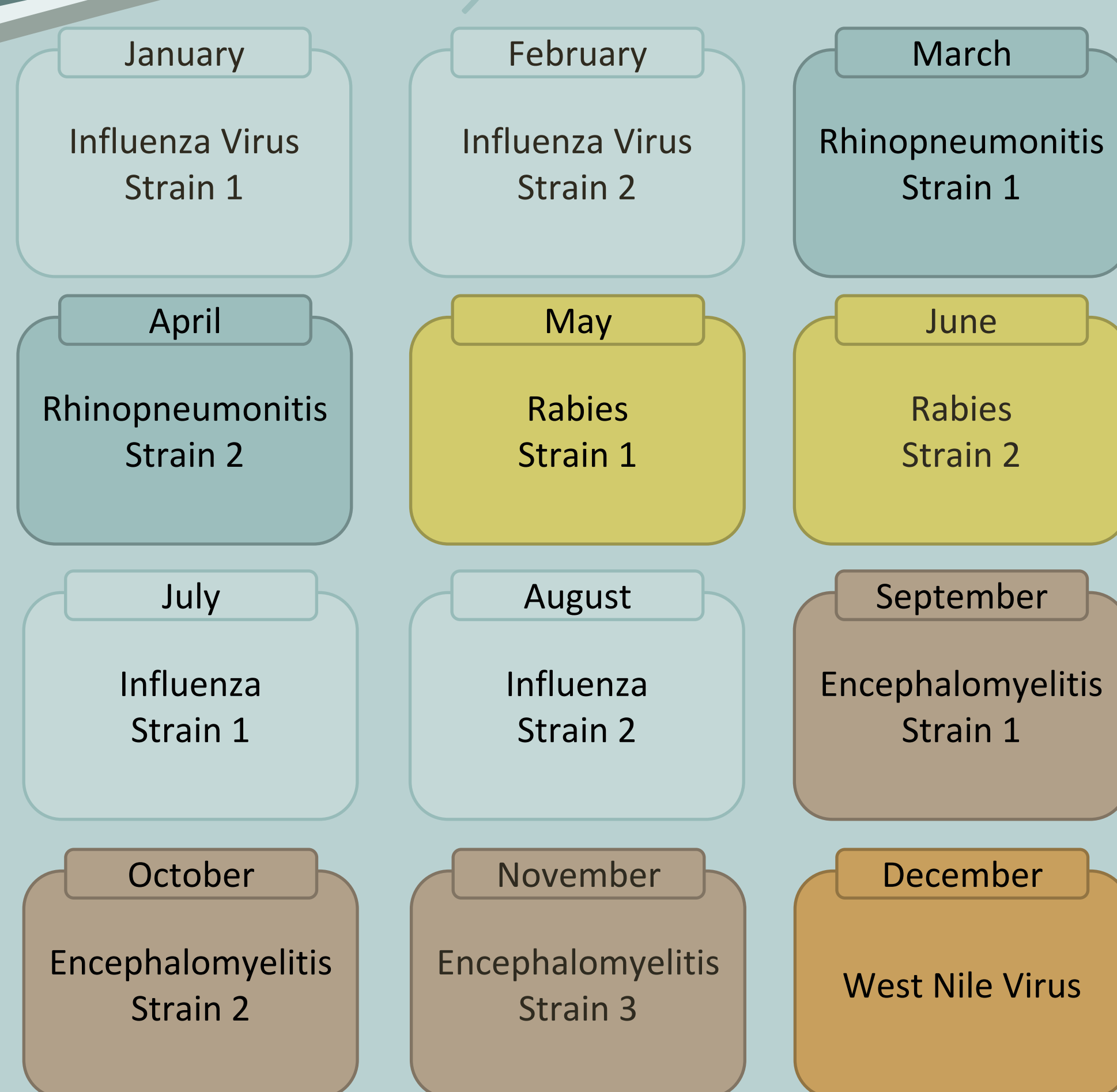
- ✓ Serum-free, low cost media
- ✓ High density growth
- ✓ Duplication time: 18-24h
- ✓ Viral production 48-72h post-infection

- ✓ High virus titres
- ✓ High production of recombinant proteins
- ✓ Scalable for GMP manufacturing
- ✓ No aggregation

New type of cells: **ExpresSF+**

Use of a **pFastBac™ Dual** expression vector

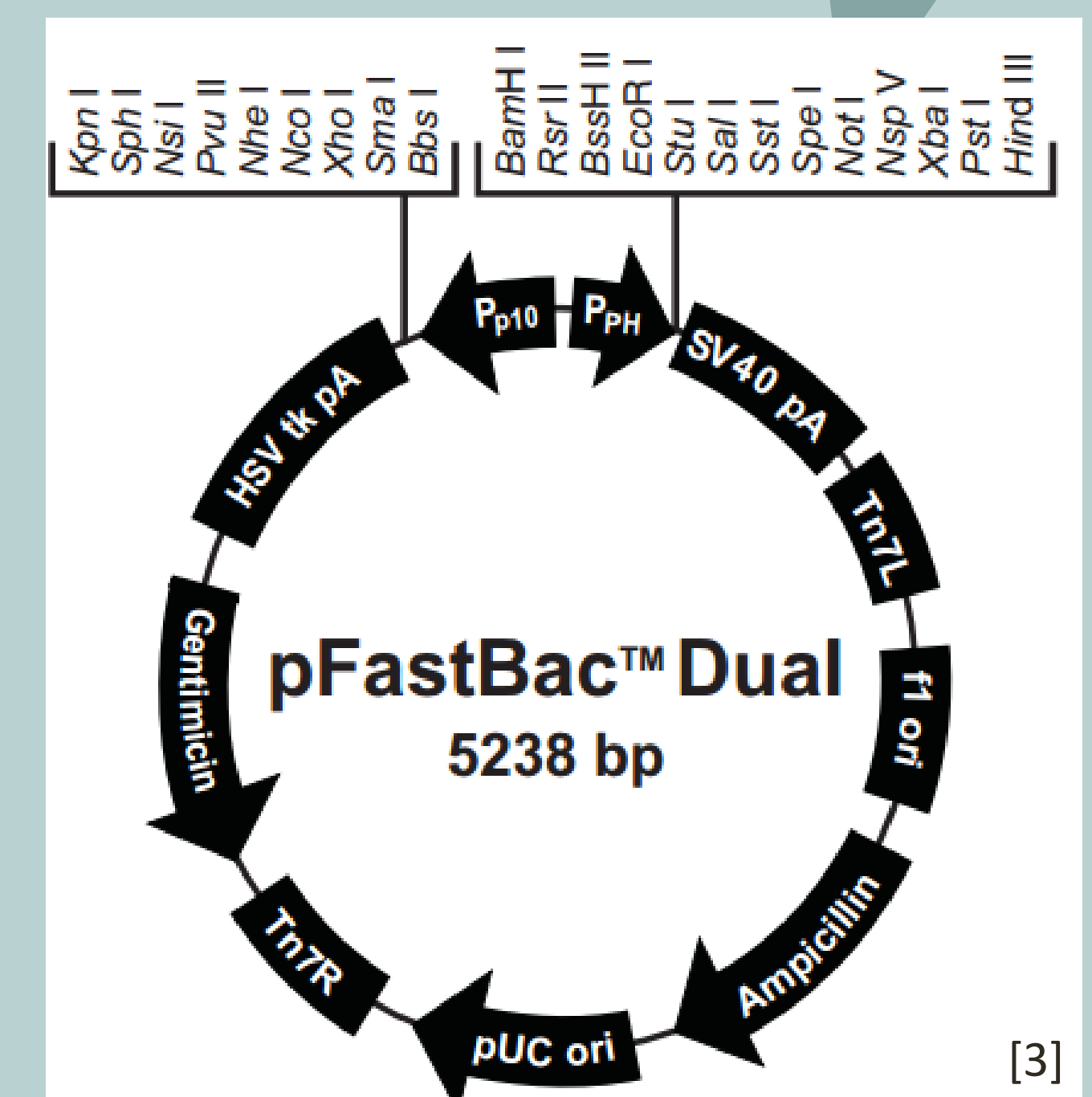
#### Multi-process industry



#### VACCINATION CAMPAIGN

Take advantage of the 8 months of inactivity to produce more vaccines for the equine sector

### PROCESS OPTIMIZATION

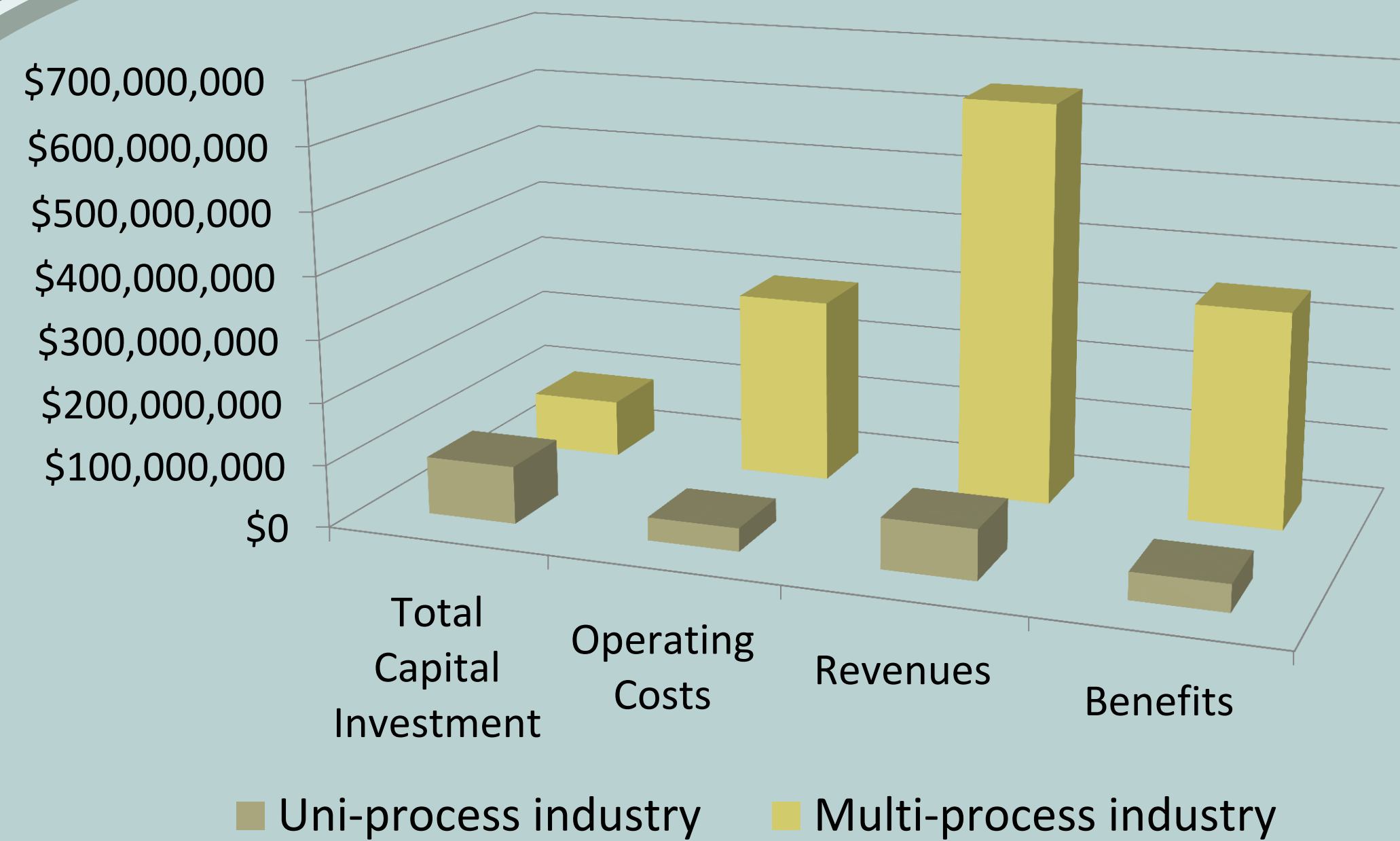


Simultaneous expression of 2 proteins of interest thanks to:

- 2 strong promoters in opposite direction (p10 and polyhedrin)
- 2 multiple cloning sites for large inserts

#### Egg-derived vaccines

- ✓ Reliable
- ✓ Effective
- ✓ Affordable
- X High production time
- X Heavily dependent on eggs
- X Possible allergic reactions



### ECONOMICS COMPARISON

Cost optimization and higher benefits

### REFERENCES

- [1] Published in : Strauss, S. (2010). BARDA funds vaccine makers aiming to phase out eggs. *Nature biotechnology*, 28 (12), 1227-1228.
- [2] Published in: *Genetic Engineering & Biotechnology News*. August 1, 2012, 32(14): 34-39. © Mary Ann Liebert, Inc.
- [3] Published in: Bac-toBac® Baculovirus Expression System. An efficient site-specific transposition system to generate baculovirus for high-level expression of recombinant proteins. Life Technologies, Carlsbad, CA, USA. Available online at: [http://tools.lifetechnologies.com/content/sfs/manuals/bactobac\\_man.pdf](http://tools.lifetechnologies.com/content/sfs/manuals/bactobac_man.pdf)
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- [5] Buggiarello, G. (Editor in Chief). Engineering and Vaccine Production for an Influenza Pandemic. (2006). *The Bridge* 36 (3).