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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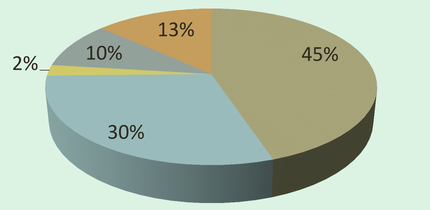
GLOBAL OBJECTIVE

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.

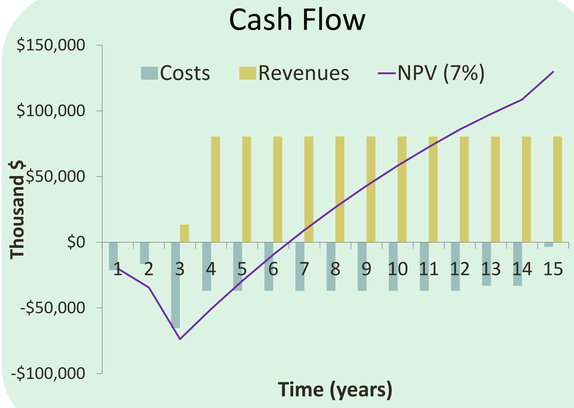
Executive Summary

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

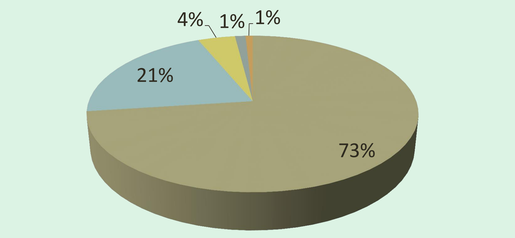
Total Capital Investment



Cash Flow



Operating Costs

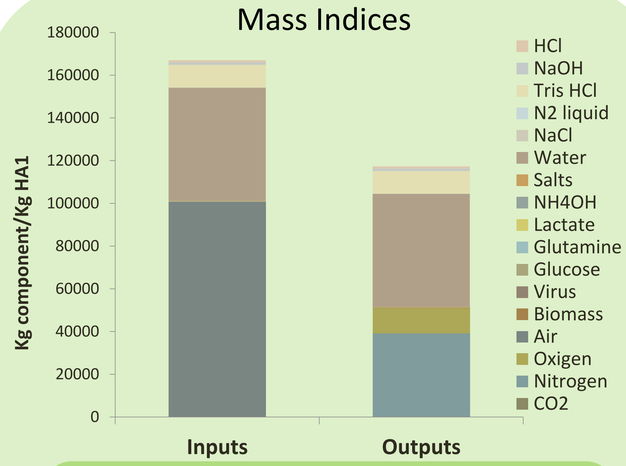


- High initial investment
- Short period recovery: 3.08 years from the production start time
- Adjustable market price

COST-EFFECTIVE PROCESS

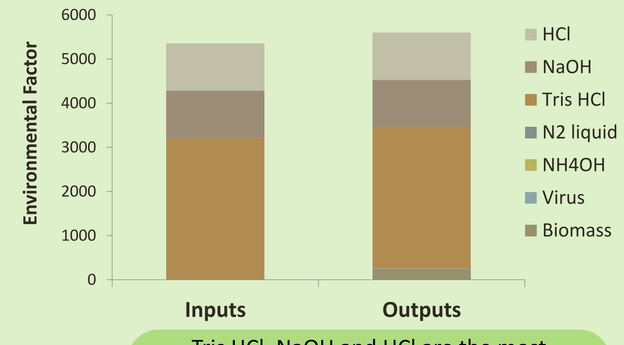
Potentially dangerous streams:
- Air inputs and outputs → HEPA filters
- Wastes from GMP process → NaOH inactivation and HCl neutralization

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_2 liquid, Biomass and Viruses

ENVIRONMENTALLY SUSTAINABLE PROCESS

- 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

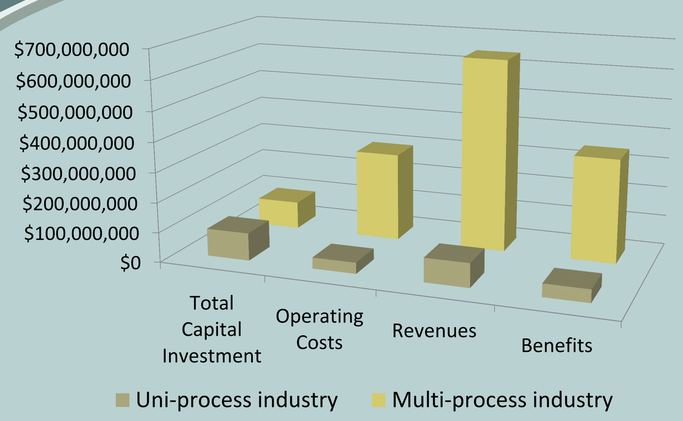
- ✓ Low-cost and rapid production of proteins
- ✓ Correctly folded and biologically active proteins
- ✓ GMP-qualified master virus banks and cell line
- ✓ Scalable to large volumes and high cell densities
- ✓ Platform for the development of a wide range of vaccines


[2]

Egg-derived vaccines

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


[1]



ECONOMICS COMPARISON
Cost optimization and higher benefits

- ✓ 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

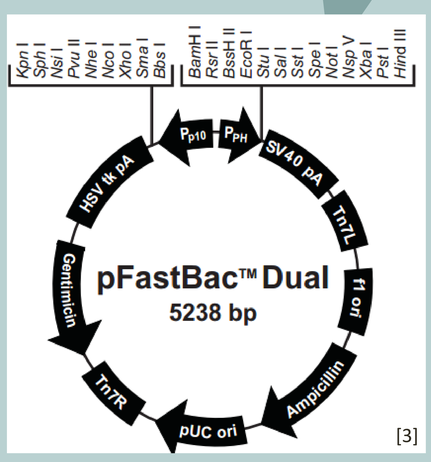
PROCESS OPTIMIZATION

Improvements

- New type of cells: **ExpresSF+**
- Use of a **pFastbac™ Dual expression vector**
- **Multi-process industry**

January	February	March
Influenza Virus Strain 1	Influenza Virus Strain 2	Rhinopneumonitis Strain 1
April	**May**	**June**
Rhinopneumonitis Strain 2	Rabies Strain 1	Rabies Strain 2
July	**August**	**September**
Influenza Strain 1	Influenza Strain 2	Encephalomyelitis Strain 1
October	**November**	**December**
Encephalomyelitis Strain 2	Encephalomyelitis Strain 3	West Nile Virus

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



[3]

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

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*
[4] Smith, G. E.; Foellmer, H. G.; Knell, J.; DeBartolomeis, J.; Voznesensky, A. I. (2000). "Spodoptera frugiperda single cell suspension cell line in serum-free media, methods of producing and using". US Patent 6103526 A.
[5] Buggliarello, G. (Editor in Chief). Engineering and Vaccine Production for an Influenza Pandemic. (2006). *The Bridge 36* (3).