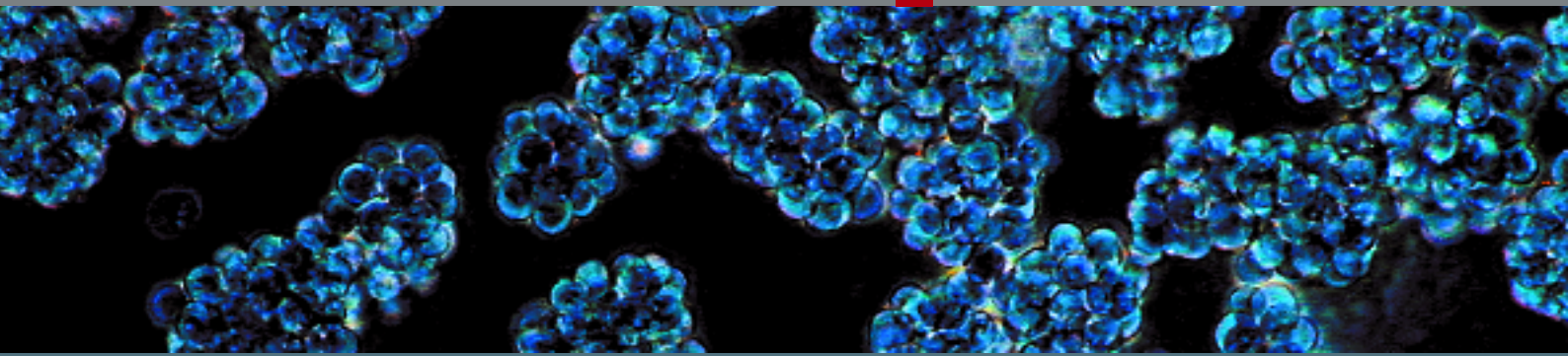


From cells to therapeutics **Vivalis**



and Forget eggs
accelerate your vaccine development with the EBx[®] cell line



Why rely on chicken eggs?

The EBx[®] platform: ... A breakthrough technology for the production of viral vaccines.

Background

Embryonated chicken eggs and primary chicken embryonic fibroblasts (CEF) have been used since decades for the manufacturing of human and veterinary viral vaccines, including traditional large volume vaccines such as human influenza or Newcastle disease vaccines, as well as more modern recombinant viral vectors (eg. poxviruses). But, such egg - and CEF - based production systems are however associated with serious limitations (risk of insufficient supply, time consuming process, concerns associated with using bovine sera, egg allergy, etc).

A proprietary and fully documented non genetically modified cell line displaying “industrial friendly” characteristics.

Building on the exceptional biological properties of avian embryonic stem cells, Vivalis has undertaken the development of a series of avian cell lines that fulfill current industrial specifications.

Vivalis has elected the EB66[®] cell line based on its remarkable features. EB66[®] cell line maintains desirable features of avian embryonic stem (ES) cells and display “industrial-friendly” characteristics:

- Genetic stability;
- Diploid karyotype;
- No adventitious agents (ALV, avian viruses);
- No RT activity;
- Indefinite cell proliferation;
- high cell densities as suspension cells (>20 millions cells/ml);
- Animal serum free culture conditions.

Cell-Based Production Technologies

A process compatible with most stringent regulations.

Benefits

- Higher initial purity;
- Closed system: improved quality;
- Fully qualified cell line: reduced sanitary hazard;
- Faster manufacturing process;
- Possibility of scale-up.



Highly susceptible to a large serie of human and animal viruses

More than 25 different vaccines could be produced in EB66® cell line. Vivalis provides a unique and revolutionary alternative platform for the cost-effective manufacturing of viral vaccines currently produced in eggs or in CEFs.

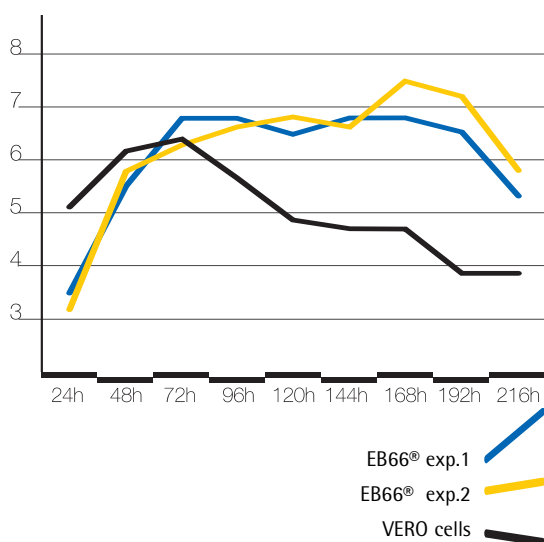
Human infectious diseases		Veterinary infectious diseases	
Traditional vaccines	Recombinant vaccines	Traditional vaccines	Recombinant vaccines
Influenza	Influenza (Alphavirus)	Influenza (avian, equine, porcine)	Rabies (Poxvirus)
Measles	CMV (Alphavirus)	Rabies	Feline leukemia (Poxvirus)
Mumps virus	AIDS (Poxvirus)	Poxvirus disease (chicken & canarypox)	Canine distemper (Poxvirus)
Smallpox	Pancreatic cancer (Poxvirus)	Newcastle Disease virus (avian)	West Nile (Poxvirus)
Rabies	Melanoma cancer (Poxvirus)	Herpes (falcon, pigeon, turkey, psittacine)	Equine influenza (Poxvirus)
Yellow fever	Prostate cancer (Poxvirus)	Infectious bursal disease (avian)	
Thick-borne encephalitis	Breast cancer (Poxvirus)	Infectious bronchitis (avian)	
	Cervical cancer (Poxvirus)	Marek's disease (avian)	
	Lung cancer (Poxvirus)	Reovirus (avian)	
	Kidney cancer (Poxvirus)	Chicken anemia	
	Colorectal cancer (Poxvirus)	Encephalomyelitis (avian, equine)	
	Japanese encephalitis (Poxvirus)	Polyomavirus type I & II (avian)	
		Avian adenovirus type I, II & III	
		Japanese encephalitis (swine)	
		Canine distemper	
		Canine parainfluenza	
		Bovine Ibaraki	
		Bovine parainfluenza	

Viruses that have been already propagated in EB66® cell line

Higher productivity obtained with a series of human and animal viruses

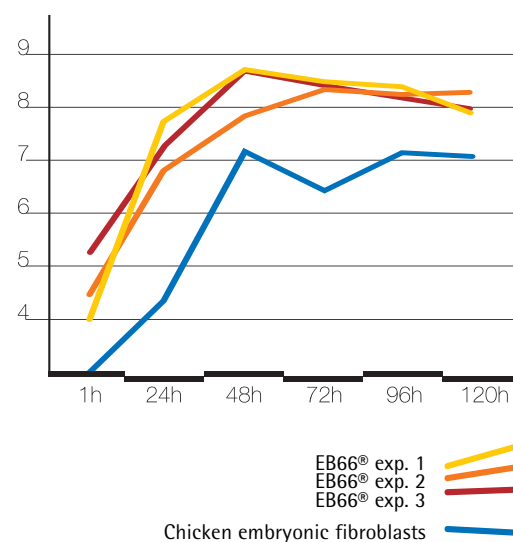
Measles

Concentration of Measles in LogTCID₅₀/ml.
Viral production in stirred-tank bioreactors (20L).



Poxviruses

Concentration of poxviruses in LogTCID₅₀/ml.
Viral production in stirred-tank bioreactors (20L).



From cells to therapeutics

Vivalis

Campus Bio-ouest – 6, rue Alain-Bombard
44821 Saint-Herblain cedex
Nantes – France

info@vivalis.com
www.vivalis.com

Tel **+33 (0) 228.07.37.10**
Fax **+33 (0) 228.07.37.11**

Types of collaboration

Research license agreement: the EB66® cell line is transferred to customers for a six to twelve months trial period during which the performance of EB66® cells are evaluated. Technical support is included.

R&D agreement: Vivalis offers to perform feasibility studies on contract basis in its own facility (eg. from virus susceptibility assays to production scale up in 20L bioreactors).

Commercial Licence: the EB66® cell line is available through a non-exclusive commercial license for the production of preclinical, clinical or commercial vaccines lots.

Commercial licenses include:

- Transfer of EB66® cell line derived from Vivalis fully characterized cGMP MCB;
- Rights to cross reference Vivalis EB66® cell line Biological Master File;
- Extensive know-how & technological transfer;
- Technical support from Vivalis;
- Access rights to Vivalis worldwide family of EBx® patents.

Contract manufacturing

Vivalis operates a state of the art cGMP production facility that includes three fully independent biosafety level-2 production suites, one pharmaceutical filing room and several quality control laboratories. This facility is dedicated to the production and purification of preclinical and clinical batches of viral vectors and recombinant proteins, using various production vessels that include stirred-tank (up to 100L) or disposable bioreactors (up to 200 liters).

