

# Product Datasheet

# 4Cell® NutriVero™ Flex 10 Medium

Next Generation Chemically
Defined Medium Designed to
Support the Growth of Vero
Cells and Virus Production



#### **Product Information**

4Cell® NutriVero™ Flex 10 is a chemically defined, serum-free, animal component-free medium, newly developed to support Vero cell growth in 2D monolayers as well as in 3D microcarriers suspension culture systems and optimized for the production of viruses.

The chemically defined 4Cell® NutriVero™ Flex 10 is a robust medium which contains solely recombinant components and does not contain any plant extract (hydrolysates), therefore providing consistent results.

#### **Benefits**

Developed together with Intravacc, an R&D organization for translational vaccinology, this chemically defined, serum-free, animal component-free medium will give you consistent results and maximum control over your virus production process:

- Production efficacy: high cell growth and virus titer in a chemically defined format
- Operational efficiency: simplify your downstream purification and filtration processes while increasing virus productivity
- Safety and regulatory-friendly: reduced process variability and contamination risks for optimal safety

#### **Applications**

Isolated from the kidney of the African green monkey by Yasumura and Kawakita in Japan (1962), the Vero cell line is used for various purposes, most importantly for the production of cell culture-based viral vaccines. Reasons for the extensive use of the Vero cell line are the consistent high viral yields and relatively easy adaptation for growth in bioreactors on microcarriers, thus allowing greater vaccine purity as well as quantity.

#### Features of the Standard Product



## Technical Data

#### **Specifications**

Media Type	Chemically defined medium: does <b>not</b> contain serum or animal origin components		
Easy-to-use	Available in liquid or as powder with supplement		
Cell Line	Developed for adherent Vero cells in monolayers and microcarriers		
Storage Condition	Bottle: 2-8 °C, protect from direct light Bag: 2-8 °C, protect from direct light Powder: 2-8 °C, protect from direct light Frozen liquid supplement for powder: -20 °C, protect from direct light		

#### Features of the Standard Product

CD Chemically defined: the exact concentration and size of every component is known

Non-animal origin: the formulation is entirely made from non-animal-human origin components

Recombinant protein: the formulation contains very low concentration of recombinant factors

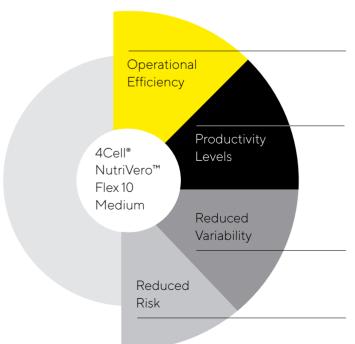
FFM For research or for further manufacturing use

Product available in liquid format

A Product available in powder format

Product available in bag format

#### Your Benefits at a Glance



One medium from seed to manufacturing with easy downstream processing due to serum-free composition

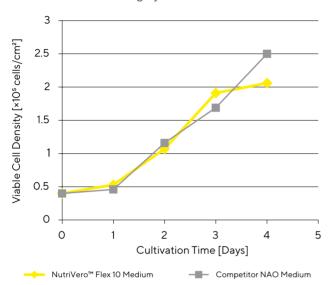
Excellent performances in supporting Vero grow and **high virus production** as 2D monolayers as well as 3D microcarriers **suspension cultures** 

**Absence of hydrolysates** significantly reduces the amount of process variability

**Fully chemically defined medium** reduces the possibility of contamination by animal-derived components and **facilitates regulatory compliance** 

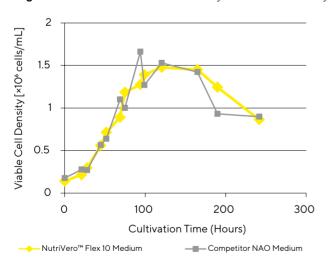
4Cell® NutriVero™ Flex 10 Medium performance have been evaluated on Vero cells' growth in adherent 2D monolayers (fig. 1A) and 3D microcarriers beads (fig. 1B). In both systems 4Cell® NutriVero™ Flex 10 Medium showed equivalent performance as reference medium containing undefined extracts (hydrolysates).

**Figure 1A**: 4Cell® NutriVero™ Flex 10 Performance in Vero Cell 2D Culturing System



Note. Vero cells were seeded in T25 flasks at a cell density of  $40,000 \text{ cells/cm}^2$  and incubated at  $37 \,^{\circ}\text{C}$  in a humidified atmosphere and  $5\% \, \text{CO}_2$  with  $4\text{Cell}^{\circ}$  NutriVero<sup>TM</sup> Flex 10 or reference medium.

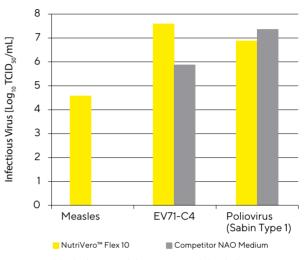
Figure 1B: Vero Cell Growth Density in a 3D Culture System



Note. Two parallel bioreactors were filled up to 2 L of working volume of chemically defined 4Cell® NutriVero $^{\rm TM}$  Flex 10 and undefined reference medium. Stirring speed was set between 70 and 130 rpm, temperature set to 37 °C and pH controlled to 7.2. The bioreactors were seeded with 0.15×109 cells/L and 3 g/L of microcarriers.

Virus quantification was performed by calculating the TCID<sub>50</sub> (50% Tissue Culture Infective Dose) index. 4Cell® NutriVero™ Flex 10 Medium showed high abilities in supporting Vero infection and virus productivity in 2D monolayers (fig. 2A) and suspension in microcarriers beads (fig. 2B) compared to reference medium containing undefined extracts (hydrolysates).

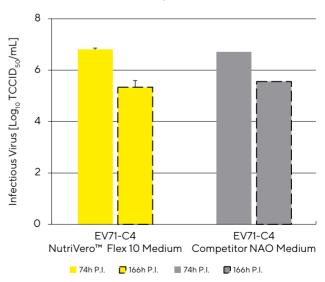
**Figure 2A**: Initial Assessment of Defined 4Cell® NutriVero™ Flex 10 Medium Viral Production Capacity



\*Measles (competitor) the virus titers was below the limit of quantification (LOQ =  $4 \times log_{10}TClD_{50}/mL$ ).

Note. Vero cells were seeded in 6-well plates at a cell density of  $30,000 \text{ cells/cm}^2$  of culture, the cultures were infected with various viruses: Measles, Sabin poliovirus type 1 and EV71-C4. Following 7 days the cultures showed a positive CPE and the supernatant was harvested and analyzed for the amount of infectious particles by means of a virus titration procedure.

**Figure 2B**: Enterovirus 71-C4 Virus Production in a 3D Microcarriers Culture System



Note. Vero cells were cultured in 1 L bioreactors at  $0.12\pm0.03\times10^{\circ}$  cells/mL for 3 days, up to a concentration of  $0.9\pm0.2\times10^{\circ}$  cells/mL. At 66 hours post seeding, the cells were infected with EV71-C4 at a titer of  $7.55\log_{10}$  TCID<sub>50</sub>/mL. Samples were taken at indicated time points post infection, and analyzed for virus titer.

# Ordering Information

Form	Package	Volume*	Order Code
Liquid	Bottle	0.5 L	CFV3FA4009
Liquid	Bottle	1 L	CFV3FA4010
Liquid	Bottle	0.5 L	CFV3FA4000
Liquid	Bottle	1 L	CFV3FA4001
Liquid	Bag	10 L	CFV3FA4013
Liquid	Bag	20 L	CFV3FA4014
Powder and frozen supplement	Bucket and bottle	10 L	CQV3FA5002
Powder and frozen supplement	Bucket and bottle	50 L	CQV3FA5003
Powder and frozen supplement	Bucket and bottle	100 L	CQV3FA5004
	Liquid Liquid Liquid Liquid Liquid Liquid Liquid Powder and frozen supplement Powder and frozen supplement	Liquid Bottle  Liquid Bottle  Liquid Bottle  Liquid Bottle  Liquid Bottle  Liquid Bag  Liquid Bag  Powder and frozen supplement Bucket and bottle  Powder and frozen supplement Bucket and bottle	Liquid Bottle 0.5 L  Liquid Bottle 1 L  Liquid Bottle 0.5 L  Liquid Bottle 1 L  Liquid Bottle 1 L  Liquid Bag 10 L  Liquid Bag 20 L  Powder and frozen supplement Bucket and bottle 10 L  Powder and frozen supplement Bucket and bottle 50 L

<sup>\*</sup> Other sizes are available on request

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<sup>\*\*</sup> Articles delivered in two parts: powder bucket and frozen liquid supplement