

# PER.C6

**A Human Designer cell Line**

**Providing a Pandemic Proof Platform for the  
Manufacturing of Safe Influenza Vaccines**



**FONS**

**MARCH 26,**



# 1918-1919 FLU PANDEMIC



**~ 30 MILLION DEATHS**

# THE DEVIL IN

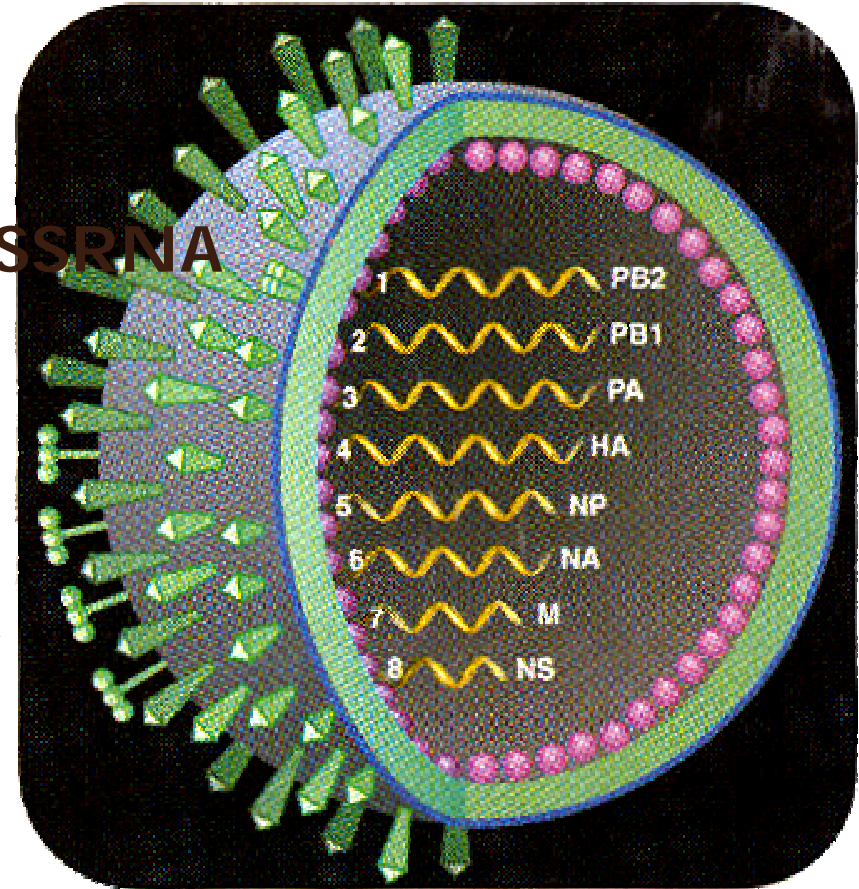
✓ ENVELOPED VIRIONS

✓ LINEAR NEGATIVE-SENSE SSRNA

✓ SURFACE

- HAEMAGGLUTINI

- NEURAMINIDASE (NA)

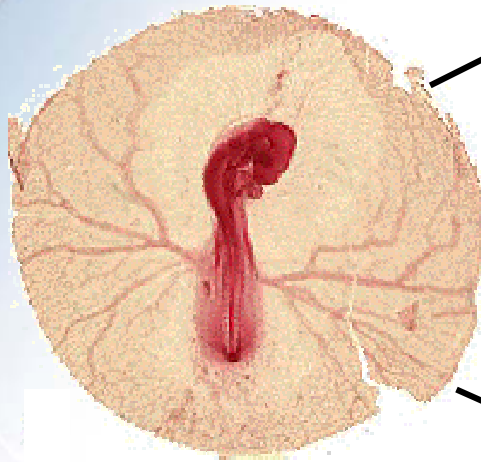


***“... NO INDIVIDUAL VACCINE PRODUCING  
HAVE THE CAPACITY TO PRODUCE ONE  
PANDEMIC VACCINE FOR EACH OF ITS***

***ESWI, Ferney Voltaire-June 10-11, 2001***



# PRODUCTION ON CHICKEN EMBRYONATED EGGS



REASSORTANTS REQUIRED  
FAILURE TO GROW

CUMBERSOME

LIMITED  
LACKS FLEXIBILITY

## NOT PANDEMIC

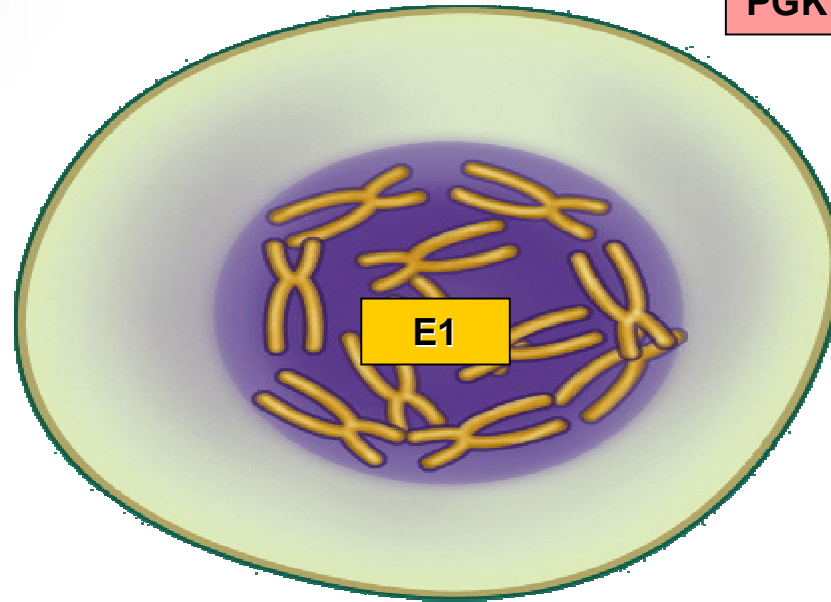
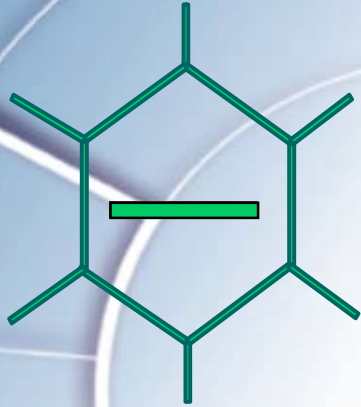
# WHO

## AN IMPROVED INFLUENZA VACCINE

*"... URGENT NEED FOR THE  
CELL CULTURE SYSTEMS WHICH WOULD  
UP OF PRODUCTION IN THE EVENT OF A*



# PER.C6: A HUMAN DESIGNER



PER.C6

# CHARACTERISTICS OF PER.C6

- IMMORTALIZED CELLS (NON TUMOR) ADENOVIRUS E1
- HUMAN CELLS – RETINA DERIVED- DOCUMENTED HISTORY
- MASTER & WORKING CELL BANKS QUALIFIED

**PER.C6<sup>TM</sup> = PGK-E1 RETINA.CLONE 6**



# PER.C6

# VACCINE MANUFACTURING

- **SAFE TECHNOLOGY**
- **SCALABLE TECHNOLOGY**
- **HIGH YIELD FOR ALL INFLUENZA STRAINS**

# PER.C6

## VACCINE MANUFACTURING

- **SAFETECHNOLOGY**
- SCALABLE TECHNOLOGY
- HIGH YIELD FOR ALL INFLUENZA STRAINS

# SAFE DESIGNER CELL

## PER.C6 DETAILED SAFETY HISTORY

### Viral/Bacterial Testing

- STERILITY
- MYCOPLASMA
- INVITRO AND INVIVO ADVENTITIOUS VIRUSES

### Species Specific Viruses

- HIV TYPE 1 & 2
- HUMAN T-LYMPHOTROPIC VIRUS 1 & 2
- HUMAN CYTOMEGALOVIRUS
- HUMAN HERPES VIRUS
- HUMAN HEPATITIS B & C
- SIMIAN VIRUS 40
- ADENO ASSOCIATED VIRUS
- EPSTEIN-BARR VIRUS

**NEGATIVE  
FOR ALL**

### Bovine/porcine viruses

- BOVINE DIARRHEA VIRUS
- INFECTIOUS BOVINE RHINORACHETITIS VIRUS
- PARA-INFLUENZA VIRUS
- PORCINE PARVOVIRUS

### Retrovirus assays

- REVERSE TRANSCRIPTASE
- TRANSMISSION ELECTRON MICROSCOPY
- S+L- AND XC PLAQUE

### Prions

- PRPCSC (NEGATIVE)
- NO MUTATIONS
- 129 V/M (HETEROGENICITY)

# SAFE DESIGNER CELL

**PER.C6**  
Detailed safety  
history

- **BEST DOCUMENTED CELL LINE TO DATE**
- **FULL SAFETY PROFILE**
- **Animal component free culture medium**
- **BMF AT FDA, UPDATED BY MERCK & CO.**

**PER.C6**  
Products in  
clinical trials

- **VACCINES : PHASE I/II MERCK HIV VACCINE,  
WITH HEALTHY VOLUNTEERS & PATIENTS**
- **GENE THERAPY : MULTIPLE PHASE I-II TRIALS**

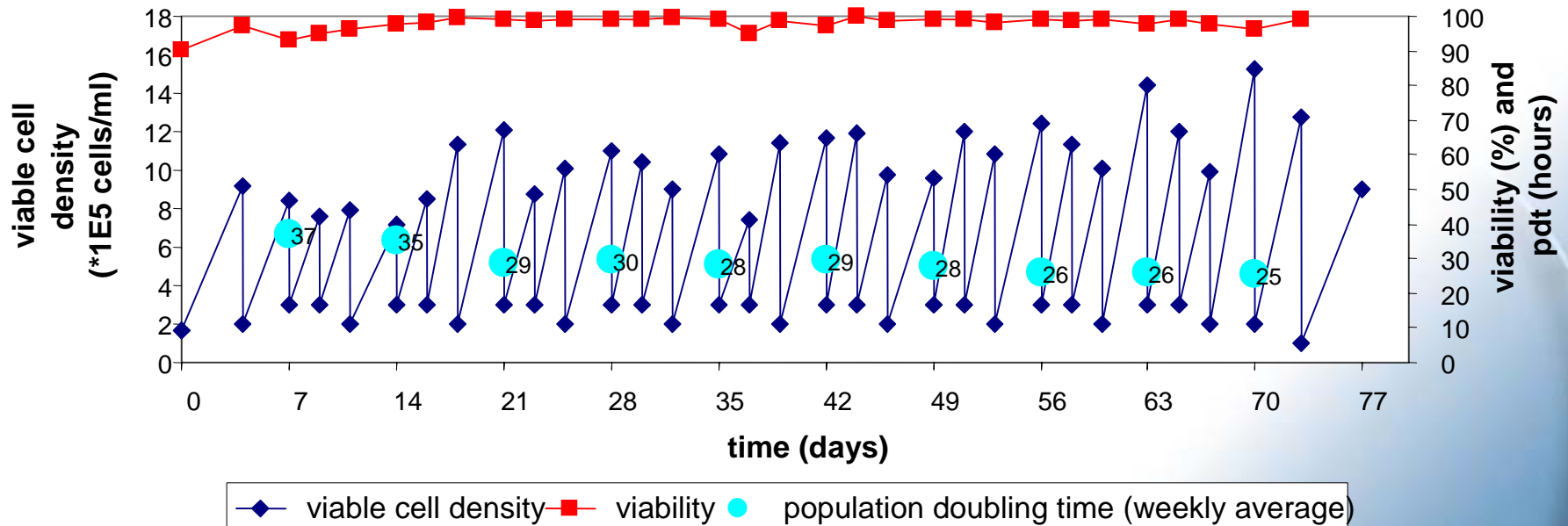
# PER.C6

## VACCINE MANUFACTURING

- SAFETECHNOLOGY
- **SCALABLE TECHNOLOGY**
- HIGH YIELD FOR ALL INFLUENZA STRAINS

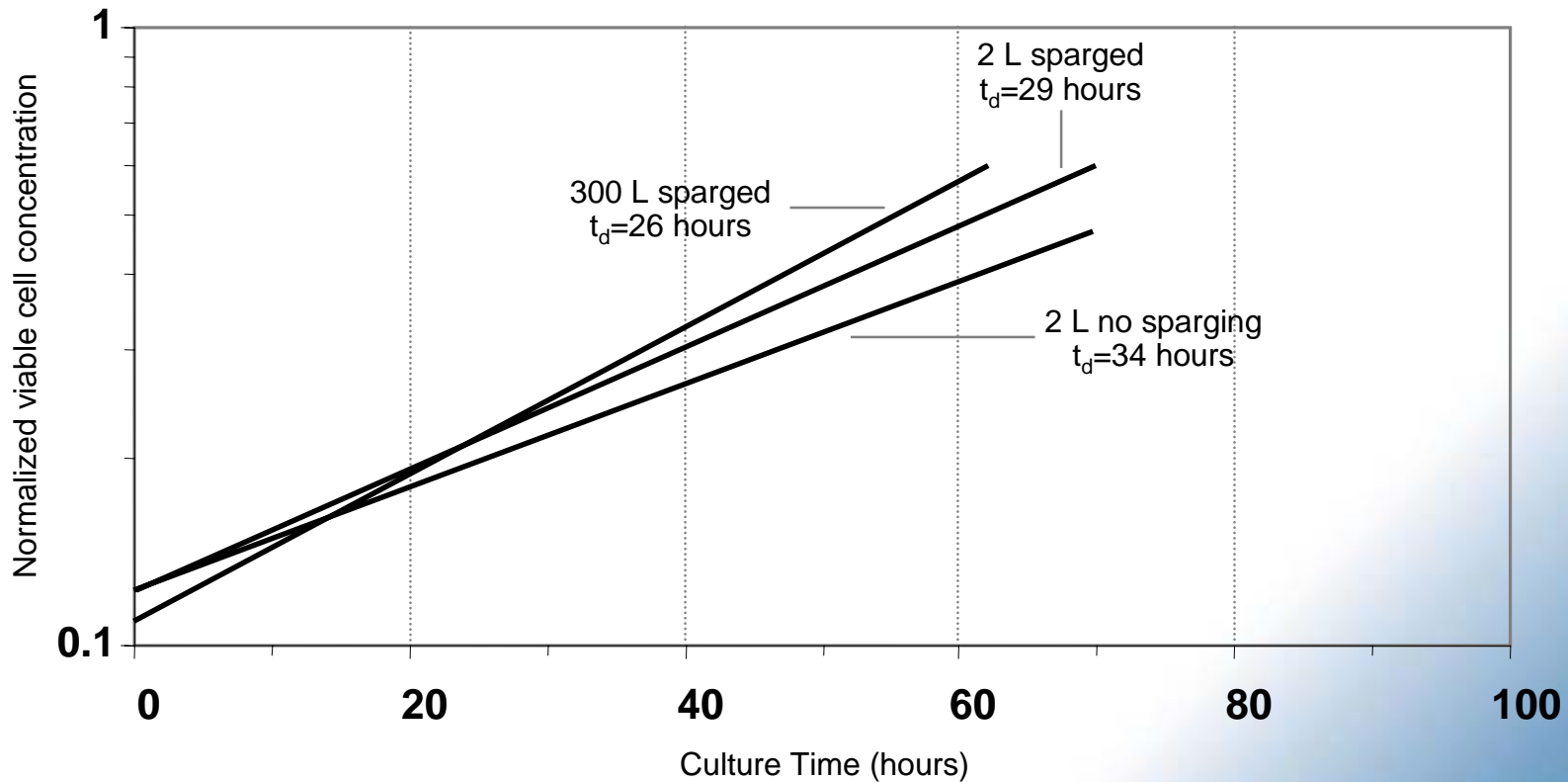
# SCALABLE DESIGNER CELL

## STABILITY OF PER.C6 SUSPENSION CULTURE



# SCALABLE DESIGNER CELL

## SUCCESSFUL SCALING FROM 2L TO 300L BIOREACTORS



Weichang Zhou, 2001 Merck & Co at Williamsburg Viral Vaccines Meeting

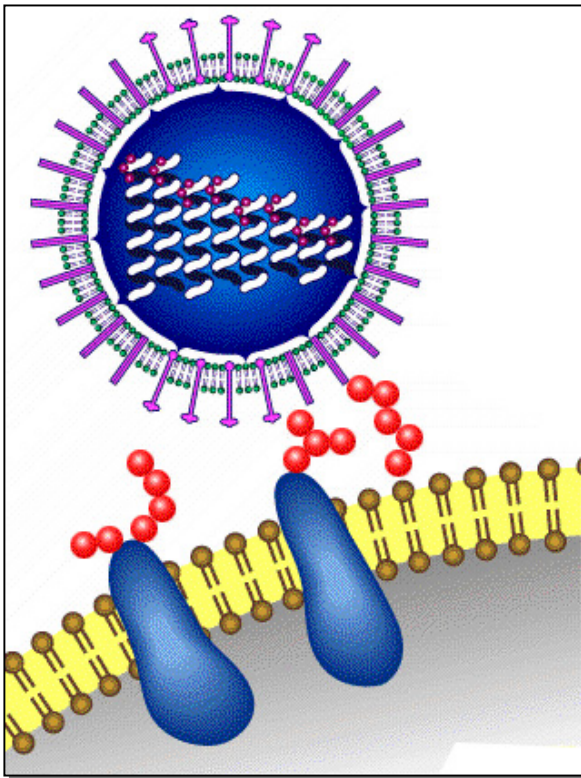
# PER.C6

# VACCINE MANUFACTURING

- SAFETECHNOLOGY
- SCALABLE TECHNOLOGY
- **HIGH YIELD FOR ALL INFLUENZA STRAINS**



# HOST CELL SPECIFICITY

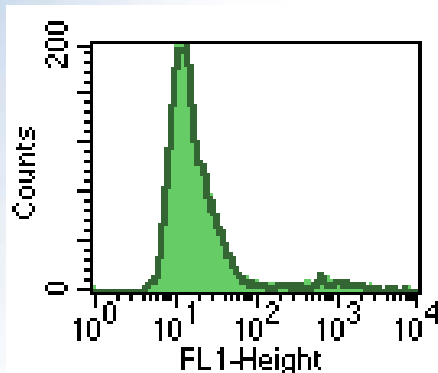


- Hemagglutinin (HA) binds to sialic acid (SA) on glycoproteins and proteoglycans on the cell surface
- Human influenza HA: SA $\alpha$ 2,6Gal (human respiratory tract)
- Avian influenza HA: SA $\alpha$ 2,3Gal (avian intestine and egg chorioallantoic sac)

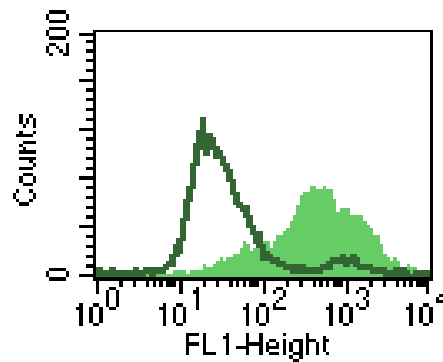
# INFLUENZA HA CELL SURFACE

Sia 2-6 Gal

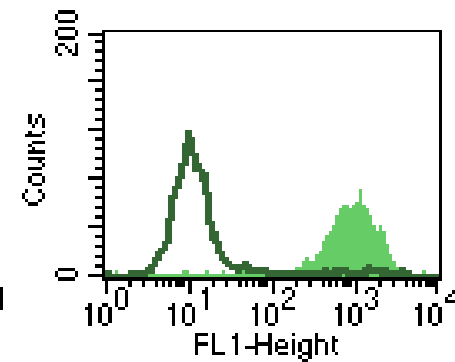
CHO



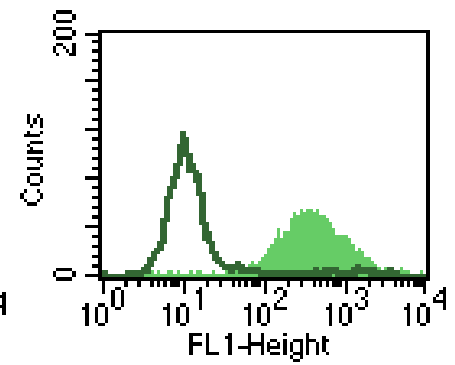
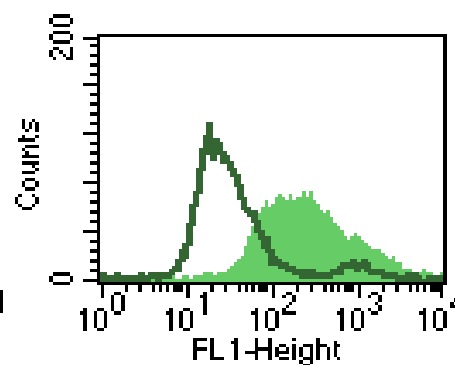
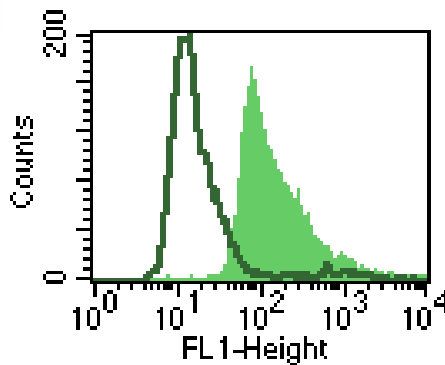
PER.C6



MDCK



Sia 2-3 Gal



# INFLUENZA VACCINE REPLICATING STRAINS

- H3N2 strains

A/Sydney/5/97

A/Johannesburg/33/94

A/Nanchang/933/95

A/Wuhan/359/95

A/Moscow/10/99

A/Panama/2007/99

Resvir 17 A/Panama reass.

- H1N1 strains

A/Beijing/262/95

X-127 A/Beijing reassortant

A/New Caledonia/20/99

IVR-116 A/New Caledonia reass.

A/Johannesburg/282/96

A/Texas/36/91

- B strains

B/Harbin/7/94

B/Yamanashi/166/98

B/Beijing/184/93

B/Shandong/7/97

B/Victoria/504/2000

B/Johannesburg/5/99

B/Sichuan/379/99

B/Guandong/120/2000

B/Canada/16188/2000

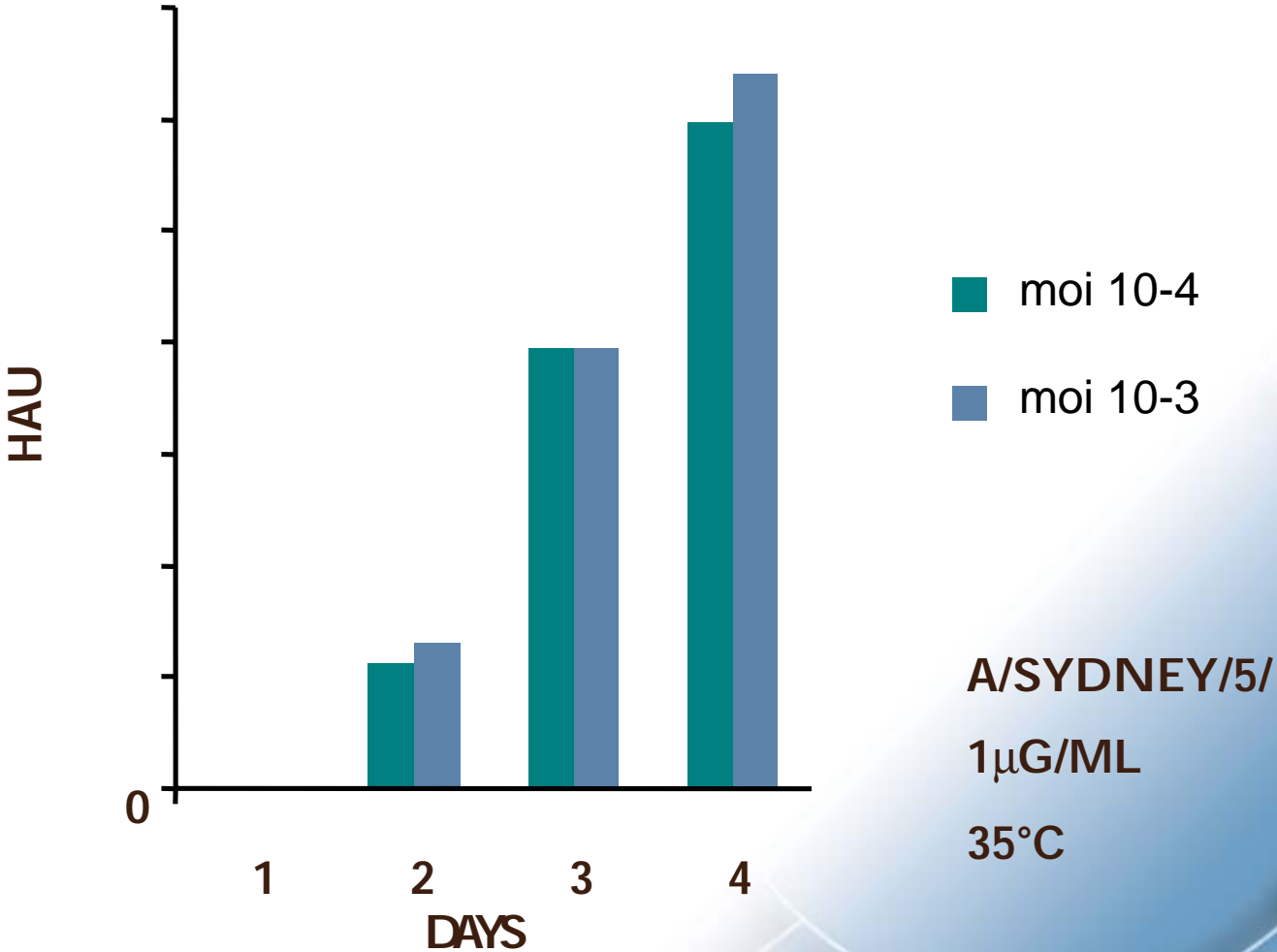
- Avian strains

A/Duck/Singapore

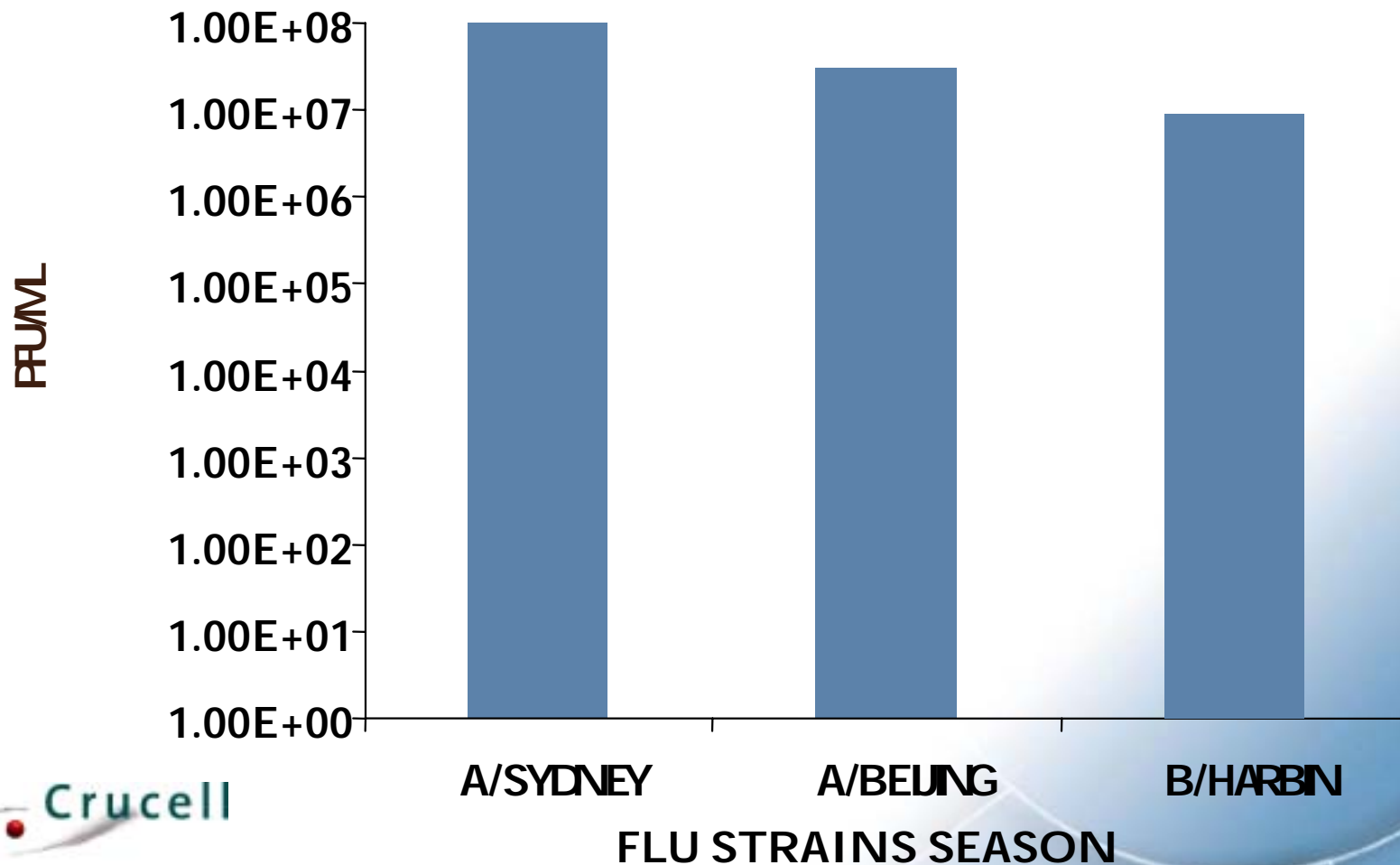
Q/F119-3/97

# INFLUENZA VACCINE

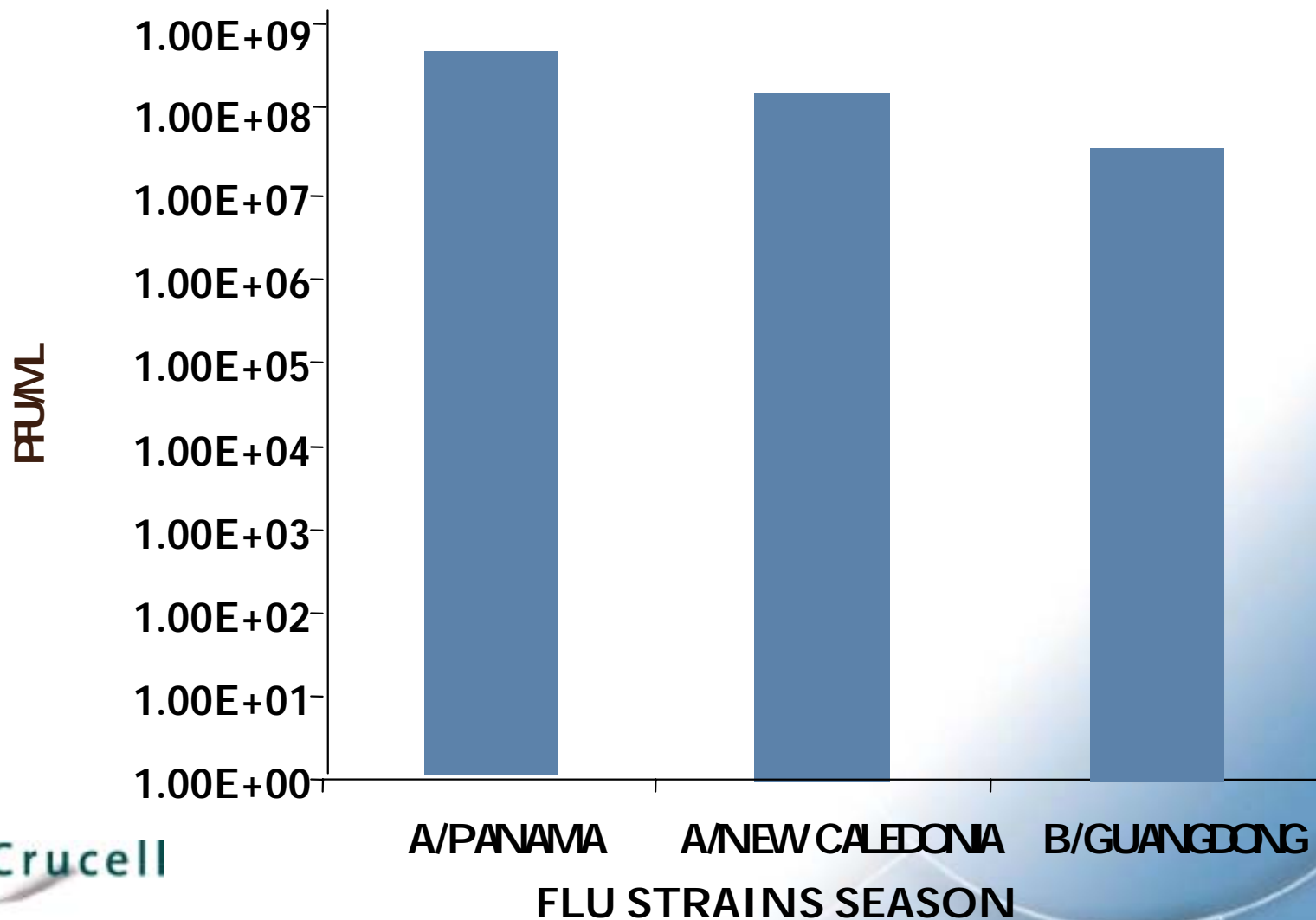
## FAST KINETICS



# INFLUENZA VACCINE HIGH TITERS

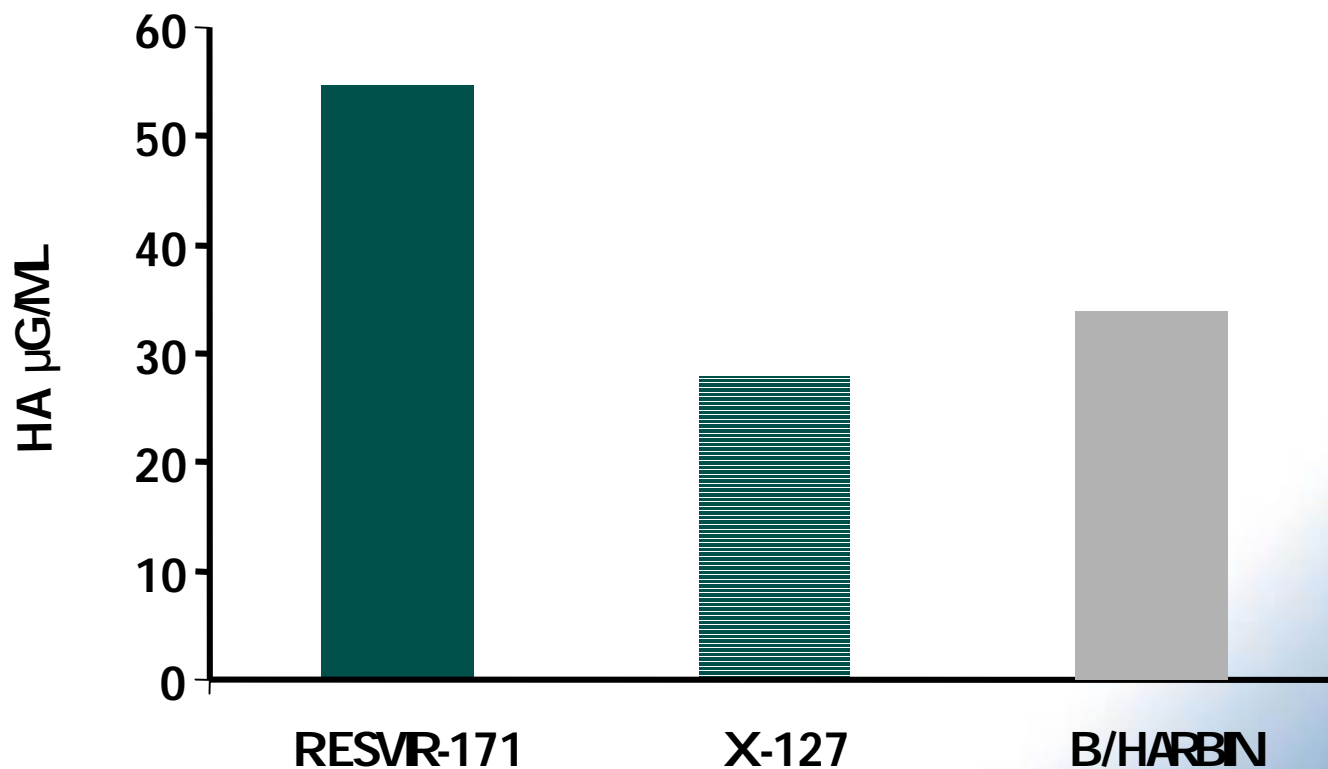


# INFLUENZA VACCINE HIGH TITERS



# INFLUENZA VACCINE

## HIGH HA YIELDS



*Responding to the Challenge of Pandemic Influenza*



**1997 THE HONG-KONG**

- **GROWTH OF WITH HIGH HA**
- **100 M MONOVALENT DOSES (15 UG HA/ML)**
- **TIME TO 3 MONTHS**



# CREDEN

**MARIA GRAZIA  
GUISEPPE  
JUTTA PASMAN  
MARCO  
RICHARD  
ANDRE VOOYS  
CARLA OPHORST  
JAAP GOUDSMIT**

