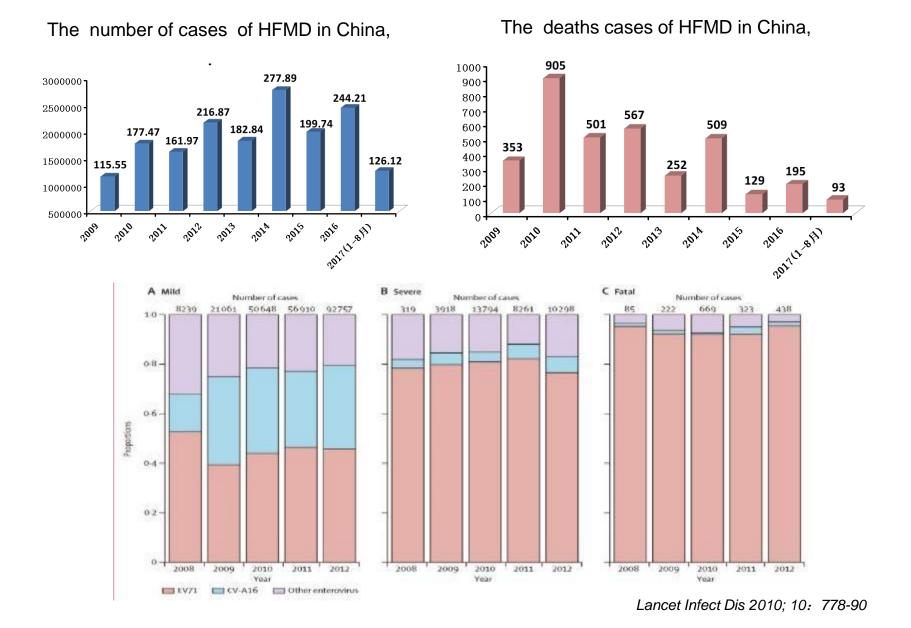


Inactivated Enterovirus 71 vaccine(Human diploid cell)

-Development, purification and clinical evaluation

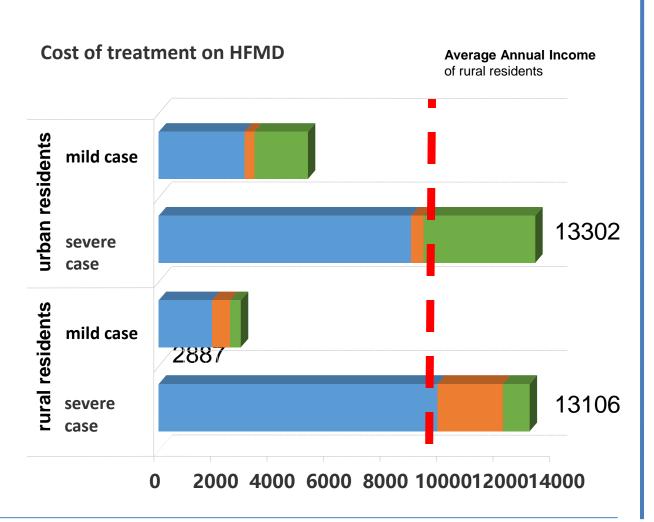
Longding Liu, PhD, Professor Institute of medical Biology, CAMS, PUMC.

EV71 infection and its risk in China



Economic analysis of HFMD

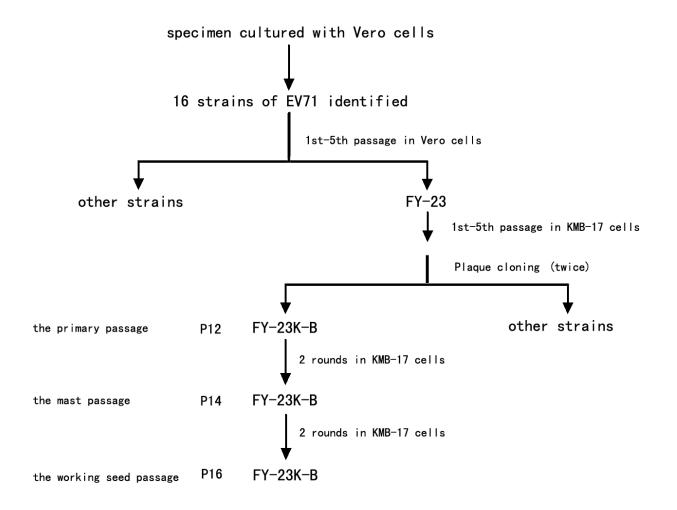




Good news: 20,000 doses
EV71 vaccine had been used
in areas with population of
12.43 million, incidences of
HFMD and its severe case
decreased 41% and 68%
respectively.

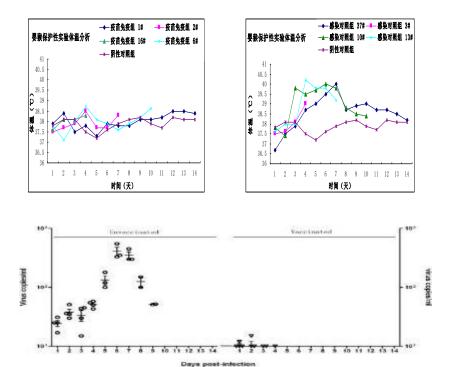


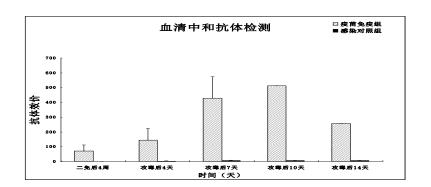
Zheng-kai Gan, Hui Jin, Jing-xin Li,(2015) Disease burden of enterovirus 71 in rural central China: A community-based survey, Human Vaccines & Immunotherapeutics, 11:10, 2400-2405

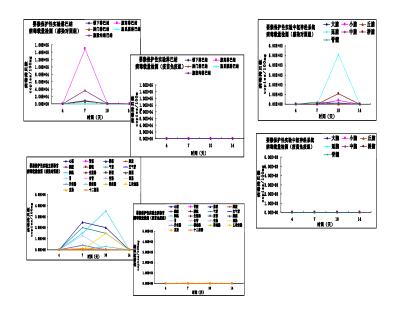


By adaptation in KMB-17 cell substance, the primary, mast and working seed-lot were set up at 12th, 14th, and 16th passage, respectively.

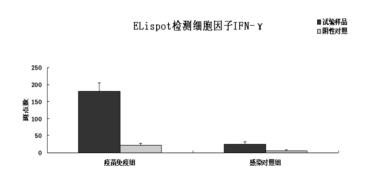
Protective effect of EV inactivated vaccine in monkey







Viral loads detection of various organs of immunized animal at viral challenge



Clinical trial of EV71 inactivated vaccine (human diploid cell)

Approved by China FDA Registered number NCT01569581 in Clinicaltrials.gov,

Phase I: safety;

Phase II: safety; immunogenicity;

effective dose and immunization program

Phase III: safety; effect and clinical

protective efficacy.

图家食品蒸品數督管導局 药物临床试验批件

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	に関係するのであった。 物理を表現である。 MAIN ARTERNATION	提供的如果的 中	PAR TYTE HE KNUMB SIEK PRVC ROSWKI
4.46	に関係を認める場合とは 特別を提供を提供をは 動によるとは は人でのないのはは	權信的關於以為中位計算 世紀2一次,在李貞高別也 今至正是也為此。 無經濟	PAN, 1775 HI KOLAMI SIDER PANG ROSWA
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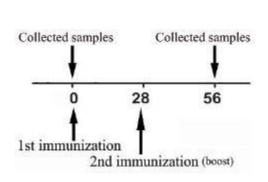
Phase III

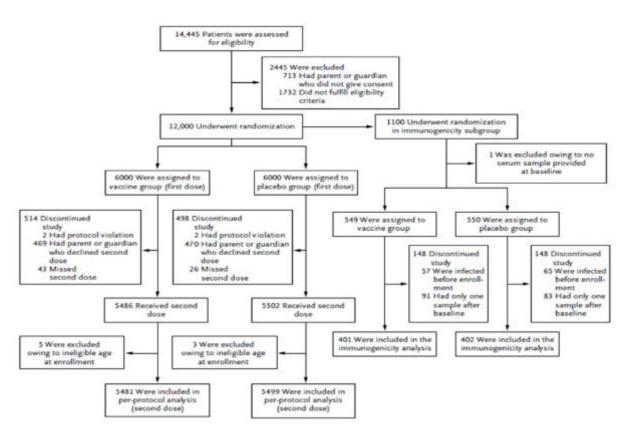
Subjects: 12000 Children (6 – 71 month old)

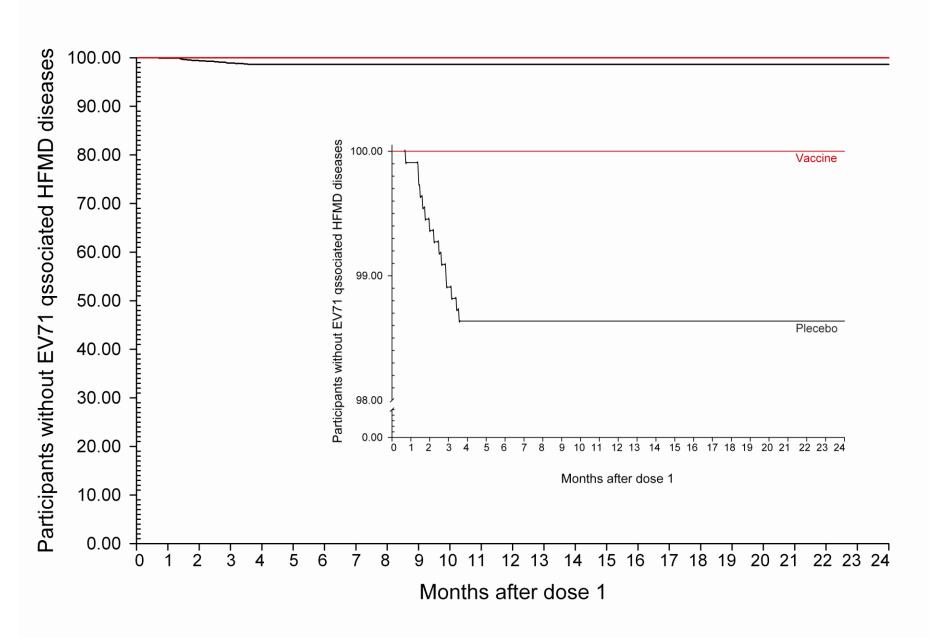
Principle: random, double-blind and placebo control

Dose: 100U (320EU)

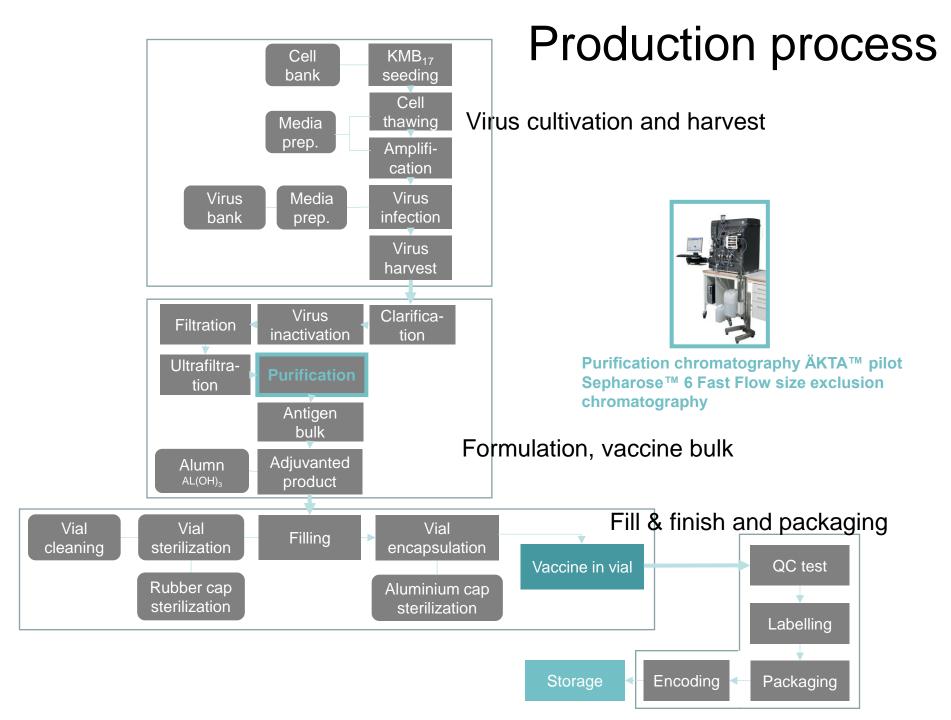
Program: 0, 28 days





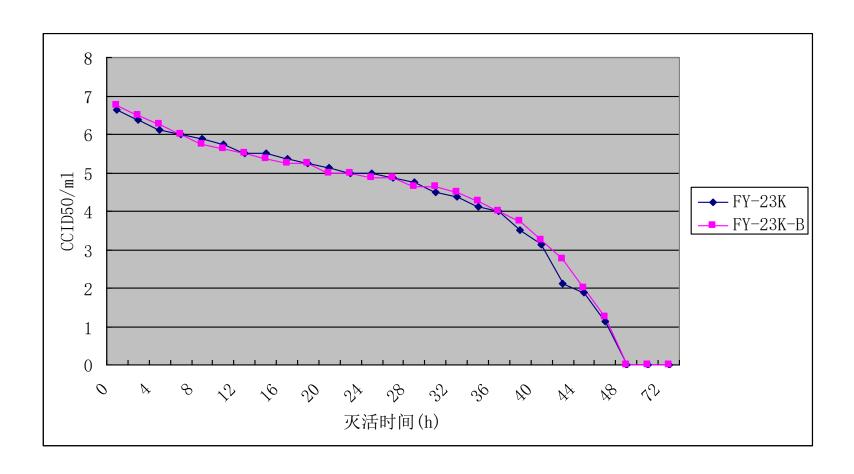


Production process



Inactivation Validation

evaluation of the efficiency of viral inactivation and vaccine antigenicity



VALIDATION OF THE PROCESS

Purification of the bulk

- exclusion of extraneous agents from the product
- adequate removal of culture medium and reagent-derived contaminants from the product
- Omaintenance within stated limits of the yield of product from the culture

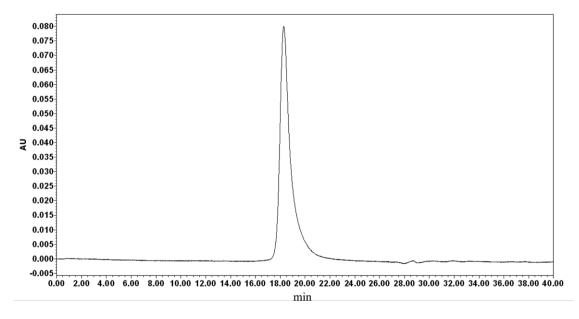


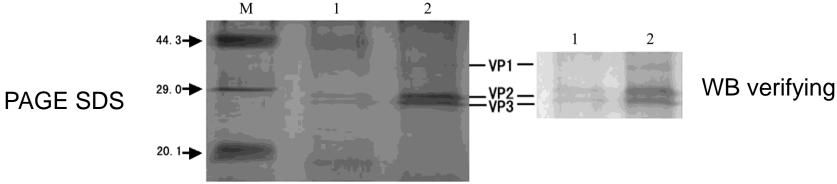
ÄKTA™ pilot



Identity Confirmation

Purity detection by HPLC





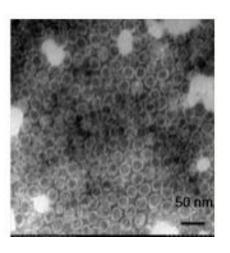


Purification of EV71 VLP

Dr. Mats Lundgren October 10, 2017

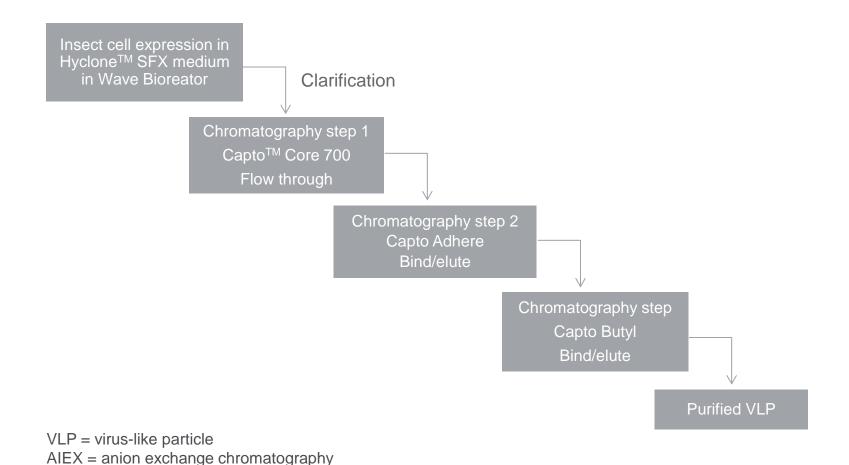
Key facts of EV71 VLP

- VLP as an alternative to inactivated virus based vaccines
- ~30nm size VLP particle
- Baculovirus based expression in insect cells (Sf9) grown in WAVE bioreactor
- Serum-free bioreactor process using Hyclone (GE) SFX medium
- Chromatography based purification as an alternative to density ultracentrifugation
- 3 step chromatography process
- Over 95% purity



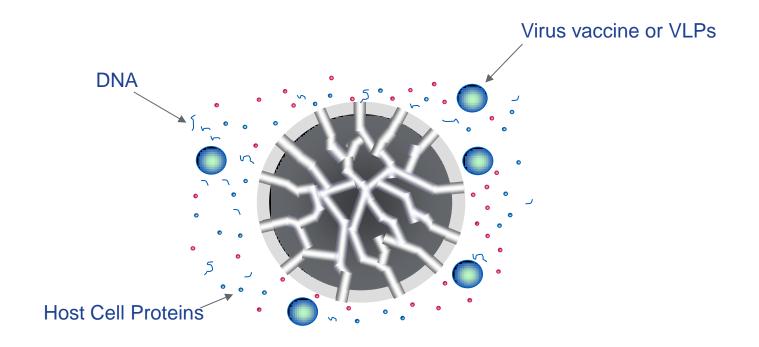


Purification process – EV71 VLP





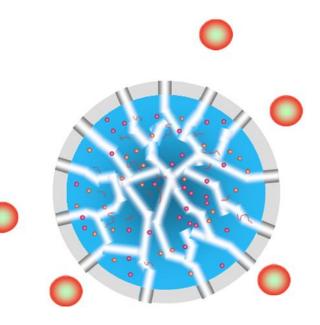
Core beads – the application principle





Application examples Core beads

- Influenza
 - Egg based
 - Cell based
- Dengue, Zika and other Flavivire
- Lentivirus
- Adenovirus
- CMV
- RSV
- Poxvirus vectors
- Polysaccharide conjugates
- · VLPs etc.









Thanks for your attention!