



sinovac®

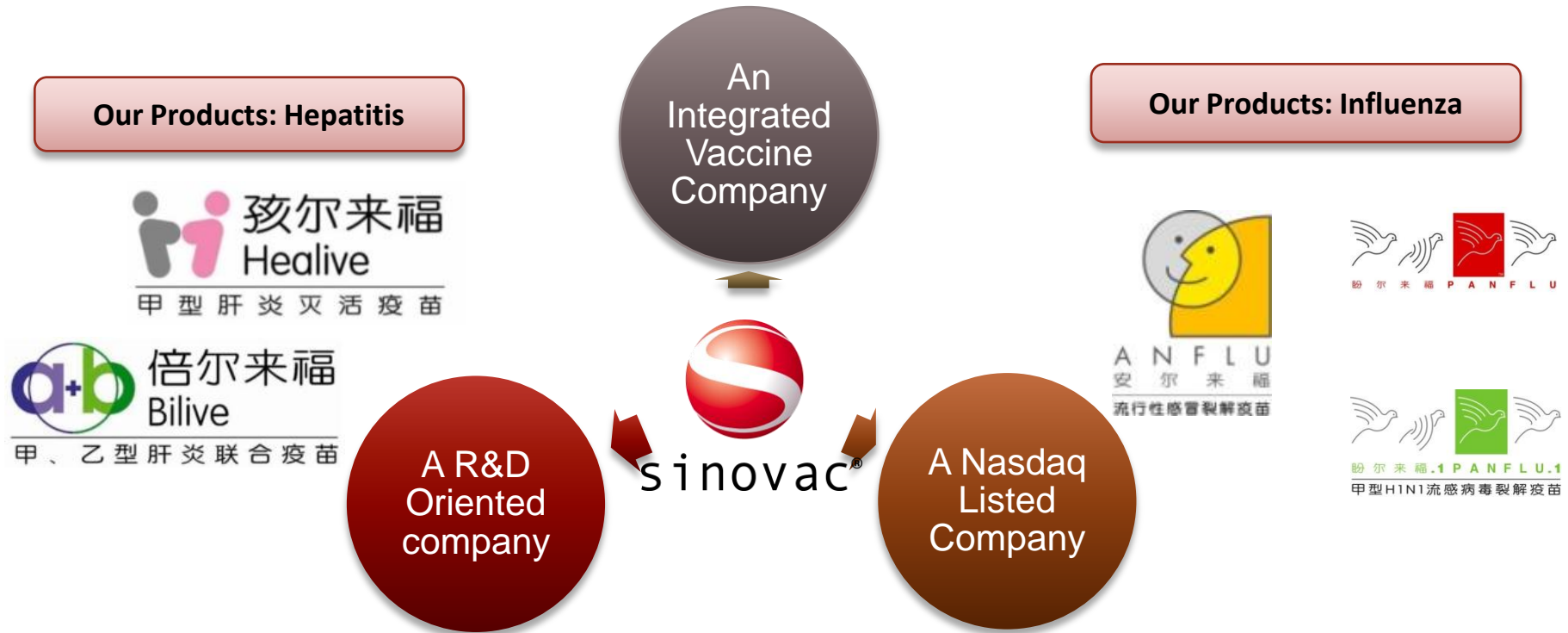
Inactivated Hepatitis A Vaccine PQ Preparation- Clinical Aspect

Weining Meng
15 March 2016

Outline

- ❑ Sinovac and HepA Vaccine-Healive
- ❑ Clinical Studies Program
- ❑ Preparation of PQ Application

Sinovac-A leading vaccine company in China



We are:

- 1st company to develop **inactivated hepatitis A** vaccine in China
- 1st company to develop **combined hepatitis A and B** vaccine in China
- 1st company to complete phase I clinical trial on **SARS vaccine** worldwide
- 1st company to develop **H5N1 vaccine** in China
- 1st company to develop and get license of **H1N1 vaccine** worldwide
- 1st and only Chinese vaccine company listed in Nasdaq

Our Mission

Supply Vaccines To Eliminate Human Diseases

- Provide Chinese Population with International Quality Vaccines
- Provide Vaccines Made in China to Worldwide

Our Products: Hepatitis



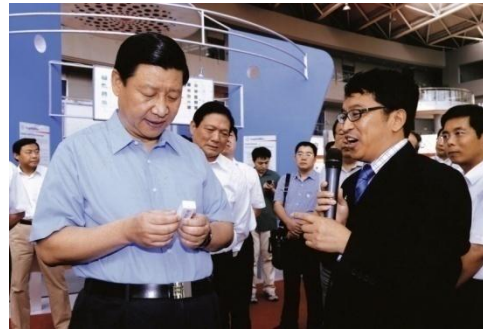
Our Products: HFMD

Inlive

Our Products: Influenza



International R&D Platform



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Vaccine xxx (2007) xxx–xxx

Preparation and characterization of S in-house reference antiserum

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Articles

THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Safety and Effectiveness of a 2009 H1N1 Vaccine in Beijing

Beijing, China



Manufacturing Facilities

Manufacturing Plants

Headquarter- Beijing

Healive production plant



Capacity: 10 million

Filling & Packaging Plant



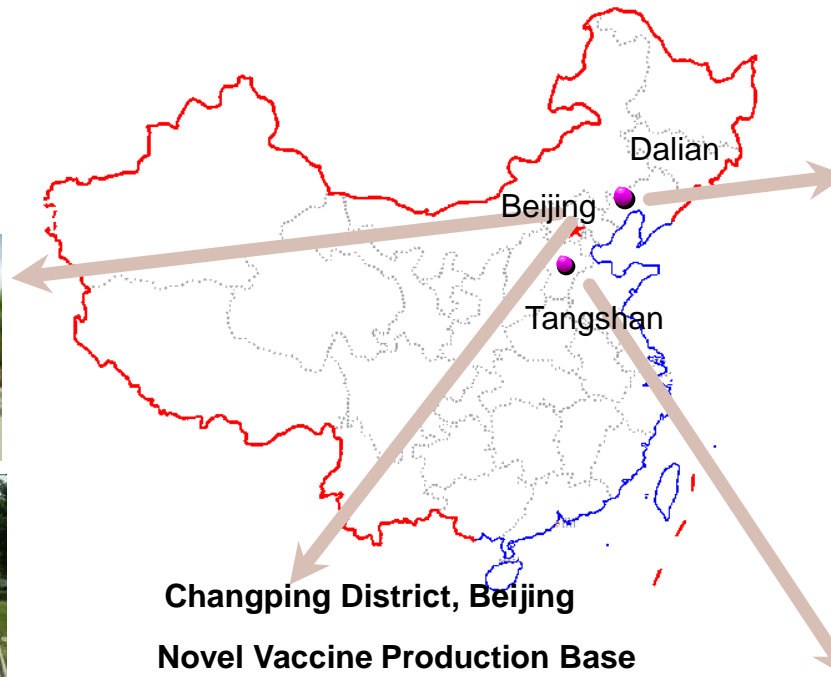
Capacity : 20 million

Anflu Production plant



Capacity : 8 million

R & D Center



Capacity of Filling and Packaging: 100 million

Capacity of EV71: 10-20 million



Building Area: 29,000 square meters

Dalian

Vero Cell Cultured Vaccine and Live Attenuated Vaccine

Capacity : 6-15 million



Building Area: 95,000 square meters

Tangshan

Yi'an Animal Vaccine



Capacity: 5-20 million

Building Area: 13,500 square meters

Hepatitis A vaccine——Healive



- Liquid injection, single dose in vial or syringe;
- Each dose containing 1.0 ml (over 16) or 0.5 ml (1-15 years old);
- Immunization schedule: 0, 6 month, i.m.;
- Storage condition: 2-8°C protection from light;
- Shelf life: 42 months;

Distribution Net of Healive



- Healive has been registered in China, Nepal, Mongolia, Chile and Turkey.
- Healive is being registered in India, Mexico, Korea, Philippine, Pakistan...
- More than 40 million doses of Healive have been distributed in the world

WHO Position and Recommendation

- WHO position paper on Hepatitis A vaccine Published in the weekly epid.2012
- Inactivated Hep A vaccine are safe and induce long lasting, possibly life-long protection against A in all age groups
- Vaccination should be part of comprehensive plan for prevention/control of viral hepatitis
- If indicated (cf local EPI and cost effectiveness data) Hep A vaccination for children ≥ 1 y should be integrated into NIP
- Inactivated HepA vaccine are licensed for IM use in a 2-dose schedule. May be co-administered with other vaccines.
- As of today only one HepA vaccine WHO prequalified (Havrix) in 2013.

Strains Used for Hepatitis A vaccine

Table 1: Monovalent inactivated hepatitis A vaccines available worldwide.

Trade name	Attenuated HAV strain	Adjuvant	HAV antigen dose/injection		Manufacturers
			Pediatric	Adult	
HAVRIX®	HM-5	Alum hydroxide	720 EU	1440 EU	GSK
VAQTA®	CR-326	Alum hydroxide	25 U	50 U	MSD
AVAXIM®	GBM	Alum hydroxide	80 U	160 U	Sanofi Pasteur
EPAXAL®	RG-SB	Virosome	12 U	24 U	Crucell

Source: Adapted from WHO 2011

Table 2: Monovalent inactivated and live attenuated hepatitis A vaccines available in China.

Trade name	HAV strain	Adjuvant	HAV antigen dose/injection		Manufacturers
			Pediatric	Adult	
Healive®	TZ84	Alum hydroxide	250 U	500 U	Sinovac Biotech Limited, Beijing
Weisairuian	Lv-8	Alum hydroxide	320 EU	640 EU	Institute of Medical Biology of the Chinese Academy of Medical Sciences; Kunming
Weisairuiji	H2	None	6.5lg TCID50	6.5lg TCID50	Institute of Medical Biology of the Chinese Academy of Medical Sciences; Kunming
NA	H2	None	6.5lg TCID50	6.5lg TCID50	Zhejiang Pukang Biotechnology Company Limited, Zhejiang Academy of Medical Sciences, Hangzhou
NA	L-A-1	None	6.5lg TCID50	6.5lg TCID50	Changchun Institute of Biological Products. & Changchun Changsheng Life Sciences Limited
HAVAC	L-A-1	None	6.5lg TCID50	6.5lg TCID50	Changchun Institute of Biological Products

Healive :Clinical Development Plan

- Pre-licensure Studies
 - Safety
 - Immunogenicity, step down design for age group, dose and schedule immunization selection
- Post-Marketing Studies
 - Non inferiority with Havrix[®]
 - Lot to Lot consistency
 - Long term immunogenicity persistency
 - Interchangeability between Healive[®] and Havrix[®]
 -
- Total 26 clinical trial were conducted in China since 1998, and one trial in India is in the process.

Summary of Clinical Experience



Safety

- More than 60,000 subjects in 27 trials
- Similar safety profile with reference vaccine

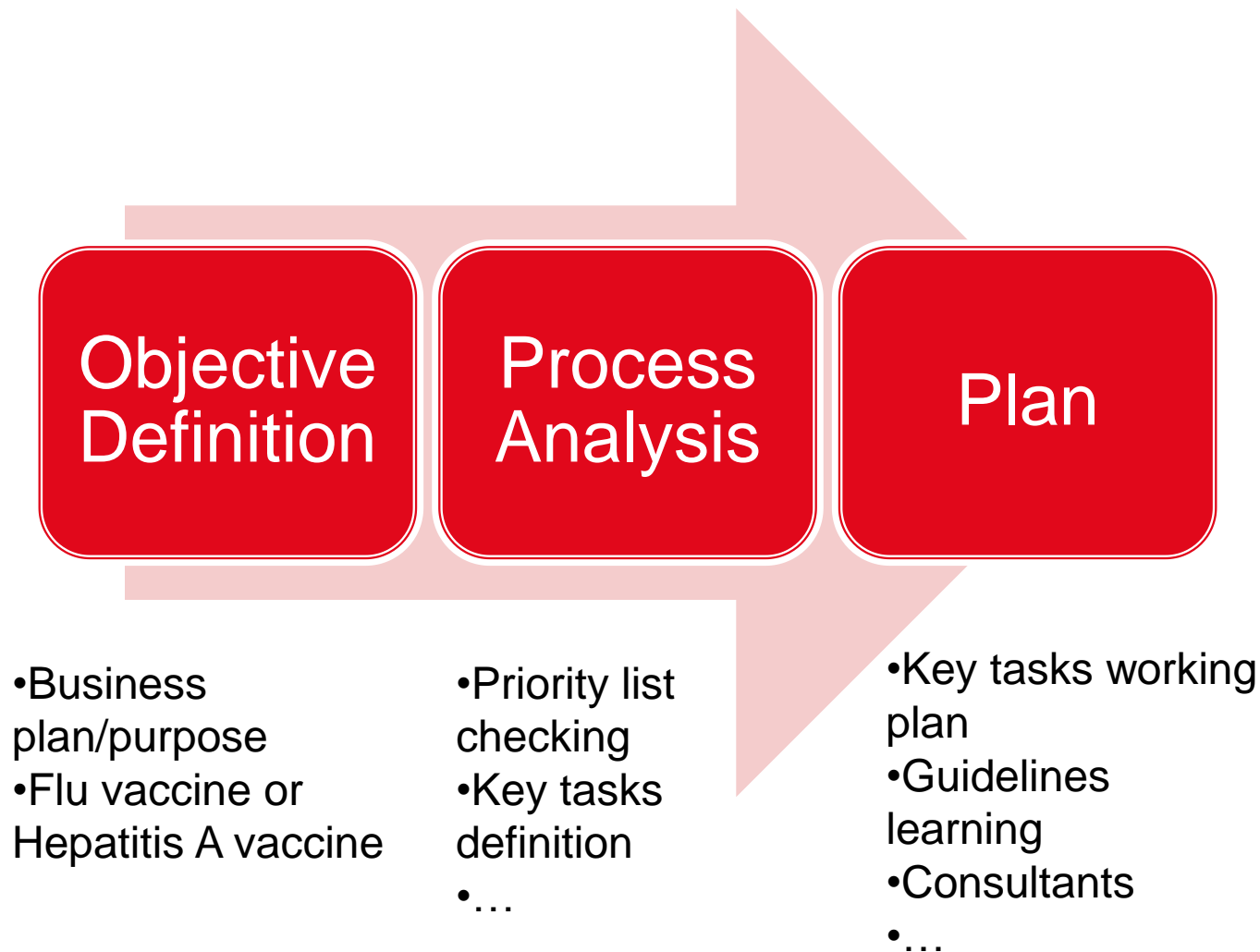
Efficacy

- Non-inferiority with reference vaccine
- Lot to lot consistency

Application

- Long term persistency
- Interchangeability with reference vaccine

Preparation of PQ Application



Preparation of PQ Application-Key task

- ▶ Clinical data sufficiency is the most important task for our hepatitis A vaccine due to the timeline and cost;
 - Take use of Pre-submission meeting to confirm this key task
 - Communication with PQ team in Geneva
 - Meeting materials preparation
 - Meeting on Feb 27, 2015
 - Post submission meeting on Feb 26, 2016

为人类消除疾病提供疫苗

Supply vaccines to eliminate human diseases



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谢谢!



让

中国儿童使用国际水平的疫苗
世界儿童使用中国生产的疫苗

Provide Chinese children with international quality vaccines

Provide children in the world with vaccines made in China