AN OVERVIEW OF THE PLANS FOR INFLUENZA VACCINE DEVELOPMENT AND EVALUATION IN VIETNAM

Nguyen Thu Van
Vabiotech – Vietnam
Project Overview

Facing with a potential pandemic of avian flu A/H5N1 high pathogenic infection from poultry to human with high mortality rates, Vietnamese Government through The Vietnam Ministry of Health, Ministry of Science and Technology and International Agencies (HHS, CDC, Japan, WHO) have placed the mission and financially supported Grants for R&D Projects on A/H5N1 vaccine for the R&D institutions and Local Manufacturers with different technology approaches, in order for self-sufficiency supply the vaccine for prevention of the disease with high risk outbreak and become pandemic. There were 03 R&D units participated in these Projects.
• VABIOTECH (The Company for Vaccine and biological production No.1)

• POLYVAC (The Scientific Center for Vaccine and Med-Products)

• NICVB– National Institute for Control of Vaccines and Medico-biological products (NCL)

• IVAC (The Vaccine Institute, Nha Trang)

• PASTEUR Institute HCM. City
Current Status: VABIOTECH- A/H5N1

- **Budget source:**
  - Ministry of Science and Technology – 1.2 bill VND (US$ 60,000),
  - HHS/CDC, US. Supported Grant Project: US$ 1 Mil (No:1U01CI000347-01)
- **Duration:** 5 year (2006-2012)
- **Research and development of a Flu A/H5N1 vaccine based on Primary Monkey Kidney Cell Line (PMKC) and Clinical trials**
- **Strain:** rgA/H5N1/Vietnam/1194/2004 developed by the collaboration with Dr. Kawaoka, Tokyo University, Japan.
- **Status:** completed non-clinical study, clinical trial phase I, II and III
- **Next step:** registration and licensing
SUMMARY

• The all produced clinical lots have been tested for release were met the national quality requirements for viral vaccines. All release tests such as toxicology, HA content (SRID), physico-chemical testing, general safety, sterile were validated, standardized for quality control of H5N1 vaccine.

• HHS/CDC, US have awarded a grant of USD 1 mil to VABIOTECH in order to implement the project “Avian Flu A/H5N1 vaccine development in Vietnam”. The objectives of this project are to build capacity for scaling up Flu A/H5N1 vaccine production capacity and assess the safety and immunogenicity of Flu A/H5N1 vaccine, developed by VABIOTECH in phase I and II clinical trial.
IMMUNOGENICITY WITH TWO DOSE SCHEDULE AGAINST CLADE 1

Clinical study phases

Proportion of participants (%)

- GMTs Ratio
- Seroconversion
- Seroprotective
IMMUNOGENICITY WITH TWO DOSE SCHEDULE AGAINST CLADE 2

Clinical study phases

<table>
<thead>
<tr>
<th>Phase</th>
<th>Proportion of participants (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase I</td>
<td>100</td>
</tr>
<tr>
<td>Phase II</td>
<td>80</td>
</tr>
<tr>
<td>Phase III</td>
<td>60</td>
</tr>
</tbody>
</table>

- GMTs Ratio
- Seroconversion
- Seropositive
CONCLUSION

- The safety and immunogenicity of H5N1 vaccine were assessed in phase I, II and III clinical trial. It has been proven that this vaccine is safe and immunogenic in 03 phases. No SAEs has been recorded.
- In phase II, a two dose schedule has been vaccinated to the healthy volunteers aged from 18-45 (30 each and placebo group) with the dose of 30µg HA. The seropositive rates which can be achieved after 2 doses 94.3% against clade 1 and 77.4% against clade 2 strains as reference antigens, respectively.
- In phase III, two dose schedule also has been vaccinated to the healthy groups aged from 18-45 (600 each vaccination and placebo) in 02 centers. The seropositive rates were 92.2% and 79% against clade 1 and 2 respectively.
- All groups (except placebo) had seroconversion factors and seroconversion rates which met the CHMP requirements.
## Current Status: VABIOTECH- A/H1N1

- Technology approach: using PMKC and MDCK based on the Process developed for flu A/H5N1 vaccine
- Budget source: Ministry of Science and Technology: USD 60,000.
- Duration: 2009-2010
- Strain: MYMC-179A (NIBSC, UK)
- Status: completed non-clinical study
  - Established the down-stream process.
  - Developing the in-house reagent for potency test
- Next step: Clinical trial as a component of a seasonal influenza vaccine
VABIOTECH - SEASONAL INFLUENZA VACCINE

Seasonal Influenza vaccine in under development
VABIOTECH : PMKc and MDCK cell line
Strains: Seasonal Influenza from NIBSC
VABIOTECH - Timeline

- Clinical trial of A/H5N1 for children (1-10) and adolescent (11-17), Eldest (46-60), and Pregnant women
  - Dec. 2013
- Licensing for A/H5N1
  - June 2013
- Clinical trial Phase 3 for Seasonal Influenza vaccine (PMK) A/H5N1 for children and adolescent (1-17), Eldest (46-60), and Pregnant women
  - June 2014
- Licensing for SIV
  - June 2015
- First commercial batch of SIV
  - August 2015
IVAC – NHA TRANG – A/H5N1 PROJECT

- Budget source: Ministry of Science and Technology Budget for R & D: 2 bill. VND (USD 100,000)
- Strain: NIBRG-14 (NIBSC, UK)
- Status: complete the Non-clinical study: HI >40 in 100% mice; 77% immunized mice showed HI>320, 100% in Guinea-pig and 96% in chicken. Production of clinical lots is going on in the GMP facility.
- Summary: the clinical lots meet general requirement for a virus vaccine.
- Status: Protocol for Clinical trial phase 1, 2, 3 need to be approved by MOH following GCP guideline.
- Next step: Clinical study phase I.
IVAC – A/H1N1

- Technology: Classic Egg base
- Budget source: Ministry of Health, HHS and Japan through WHO
- Strain: MYMC-179A (NIBSC – UK)
- Status:
  - Completed the down-stream process
  - Produces 03 clinical lots
  - Completed clinical study phase I and the data is under analyzing.
- Next step: Clinical trial phase II and III.
IVAC – WHO/HHS US/JAPAN PROJECT

US and Japanese Governments through WHO have awarded
- Grant USD 2,7 mil for phase I and
- USD 1,5 mil for phase II for construction of a Influenza vaccine production facility, training and technology transfer complains
  - with WHO-GMP with the initial designed capacity = 500,000 doses/year and
  - scaling up in phase II to 1.5 -3 mil doses/year in IVAC, SUOI DAU NHA TRANG.
  - Recently the phase I was completed and clinical lots have been produced, and
  - WHO financial supported in phase II for construction of Clean Egg Facility for Influenza vaccine in the same site (SUOI DAU).
- In the future Influenza vaccines (including seasonal, A/H5N1 and A/H1N1 and seasonal influenza vaccines will be produced in this Production facility.
IVAC – SUOI DAU PRODUCTION FACILITY
PASTEUR INSTITUTE HO CHI MINH CITY

- Budget source: Ministry of Science and Technology Budget for R & D: 4 bill. VND (USD 200,000)
- Title: Research and Development of an avian influenza vaccine a/H5N1 in Vero cell.
- Strain: NIBRG-14 (NIBSC, UK))
- Status: complete the Non-clinical study
- Summary: the clinical lots meet general requirement for a virus vaccine. Low yield
- Next step: NO PLAN
POLYVAC

• Technology: Vero cell base and Primary Chicken Embryo cell line.
• Budget source: Ministry of Science and Technology: USD 200,000
• Duration: 2009-2010
• Strain: MYMC-179A
• Status:
  o Completed the down steam process.
  o Producing clinical lots
• Summary: the clinical lots meet general requirement for a virus vaccine. Low yield
• Next step: NO PLAN
Dependencies and Resources

- BUDGET
- MANUFACTURING
- DAV-MOH
- NICVB FOR QC TESTS
- IRB (MOH)
- CLINICAL TRIALS

Project
THANK YOU FOR YOUR ATTENTION!