The Vaccine Formulation Laboratory

Adjuvant Hub & Training Center on Vaccine Formulation

Nicolas Collin, Beograd, 28 March 2012
The Challenge of Access to Adjuvants

**Adjuvants:** substances added to vaccines to improve specific immune response

- Increase antibody titers, induce long-lasting immunity
- Trigger cell-mediated immunity
- Enable immunization in weakened immune system
- Reduce antigen dose and number of doses: antigen-sparing

**Essential** components of modern vaccines

**Access** to adjuvants and to vaccine formulation know-how is difficult for:

- Developing Countries Vaccine Manufacturers
- Public Sector
- Biotech Companies
January 2010: creation of the Adjuvant Hub

University of Lausanne, Switzerland
WHO Collaborating Centre in Immunology

October 2010: 1st grant from HHS / BARDA
Technology transfer of oil-in-water adjuvants to DCVMs for pandemic influenza vaccines

March 2012: VFL at a glance
6 grants and respective programmes currently on going
Over 20 collaborations with academics, industries, DCVM
Expansion of adjuvant portfolio, laboratory space & staff
How do we work?

Vaccine developer - DCVM

Choice of adjuvant | Manufacture | Formulation with antigen | QC | Preclinical | Clinical trials

GMP

Lausanne Training platform

Preclinical / GMP-compatible
Trainings at the VFL – a la carte

- **1. Vaccine formulation**: optimized combination of antigens and adjuvants, stability of formulations, etc.

- **2. Quality Control** assays of adjuvanted vaccines

- **3. Preclinical evaluation** of adjuvanted vaccines
  - Stability studies
  - Head-to-head studies in animal models
  - Immunological read-outs (Humoral, T-cell responses)

- **4. Technology transfer** of adjuvant technology
Example: Pandemic influenza vaccine

The BARDA project
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Development and Sustainable Manufacturing of Adjuvanted Pandemic Influenza Vaccines in Developing Countries
Bio Farma - adjuvanted H5N1 vaccine development
Adjuvant for pandemic influenza vaccines

Technology selected: squalene-in-water emulsion

- Emulsions vary in their composition and biology
- Technology used is licensed since 1997: most mature adjuvant technology after aluminium salts
- Tens of millions of doses distributed (seasonal and pandemic influenza vaccines), no severe adverse events

Remarkable dose-sparing effect with H5N1 influenza split / subunit vaccines

2 doses of 90µg (HA) without adjuvant > 2 doses of 7.5µg (HA) with adjuvant
Transfer of adjuvant technology to Bio Farma

- December 2010: Kick-off meeting in Bandung, project team
- March 2011: First training at the VFL
- May 2011: On-site visit in Bandung
- June 2011:
  - Pilot-scale and QC facilities installed - SOP transferred and translated
  - 3 consistency lots manufactured
  - QC performed at both sites
  - GMP documentation list drafted
Oil-in-water emulsion characteristics

- **RP-HPLC squalene content in BF emulsion**

- **Particle size of BF emulsion**

- **Stability of BF emulsion over time (2-8 °C)**

- **Adjuvant activity of emulsion in mice (HI) - formulated with H5N1 turkey/Turkey (2 ug)**
Much more than 3 lots

- Technology transfer completed in 9 months

- Project is continuing:
  - optimization of process development
  - new adjuvant lots produced on regular basis at Bio Farma
  - preclinical evaluation of adjuvanted Bio Farma H5N1 vaccines

- One more step for Indonesia towards Pandemic Preparedness
VFL adjuvant services: to sum-up

1) choose antigen of interest

Example of vaccines that we currently work with: Pandemic influenza, Shigella, E. Coli, MenB, HepB, Inactivated Polio, Malaria, Lupus, HIV, Cancer, etc.

2) choose adjuvants: commercial, manufactured at VFL, MTA

Ex: aluminium salts (hydroxide, phosphate), water-in-oil emulsions, oil-in-water emulsions, saponins, TLR4 agonists, liposomes, etc.

3) customized trainings in Lausanne or at your place of choosing

Current collaborators are from: Vietnam, Germany, Indonesia, The Netherlands, Ireland, France, USA, South Korea, Italy, UK, India, etc.
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