A novel initiative to increase access to adjuvants for developing countries vaccine manufacturers

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3rd Meeting with International Partners for Influenza Vaccine Technology Transfer to DCVM
6 May 2010 – Nha Trang, Vietnam
The challenges of adjuvant access and development

Influenza vaccine adjuvants

UNIL Vaccine Formulation Laboratory

Strategy of UNIL to increase adjuvant access for DCVM
The problem

Limited **access** to adjuvants

+ Lack of **know-how** and **expertise**

Use of inappropriate adjuvants & inappropriate use of adjuvants

Novel adjuvant development:

- Lengthy
- Costly
- Risky

Multiple vaccine products needed for each adjuvant to justify investment

How to increase adjuvant development by DCVM?

- **Public Sector**: a role to play for technology transfer
Adjuvants and influenza vaccines

<table>
<thead>
<tr>
<th>Mineral salts</th>
<th>Water-in-oil emulsions</th>
<th>Oil-in-water emulsions</th>
<th>Liposomes</th>
</tr>
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<tbody>
<tr>
<td>Polysaccharides</td>
<td>Polyelectrolytes</td>
<td>TLR agonists</td>
<td>Others</td>
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<td>(many others!)</td>
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</table>

**For influenza vaccines**

1. Aluminium: modest effect on dose-sparing/immunogenicity
2. Oil-in-water emulsions:

- Remarkable **dose-sparing** effect for pandemic vaccines
- Enhanced immunogenicity and **cross-reactivity** (esp. in naïve individuals)
- **Extensive safety record** for seasonal and pandemic vaccines (> 100 M)
- **Split** and **subunit** influenza vaccines
Benefits of oil-in-water emulsions for pandemic influenza vaccines

. Dose-sparing

MF59™-adjuvanted H5N3 vaccine

Non-adjuvanted H5N3 vaccine

Nicholson et al. 2001
Benefits of oil-in-water emulsions for pandemic influenza vaccines

. Dose-sparing

Clinical trials with AS03- and MF59™- adjuvanted (H1N1) 2009 vaccines: a single low-dose of antigen is sufficient for immunogenicity

![Graph showing GMT of HI antibody against days after dose 1]

**Pandemrix™:** 3.75 μg HA adjuvanted with AS03

**Control:** 15 μg HA (non-adjuvanted)

*Campens et al. 2010*

. Increase of the quality of protective antibodies against pandemic strains

*Khurana S. et al. 2010*
Quick conversion of unadjuvanted seasonal vaccine capacity to adjuvanted pandemic vaccine production

Oil-in-water

Expected multiplication factor for capacity: 5-20 fold
Current existing solutions
(outside of the “big pharma” landscape…)

Numerous biotechs are developing adjuvants with:
- Unproven efficacy
- No significant safety record
- Uncertain utility for influenza
- No regulatory approval perspectives in the short term
- Commercial purposes

Infectious Diseases Research Institute (IDRI, Seattle)
- Non-profit organization, support from BMGF
- Undertakes research / development on new adjuvants:

GLA (Glycopyranosyl lipid Adjuvant)  
SE (Stable Emulsion)
A technologic park in Lausanne

UNIL Department of Biochemistry

Swiss Vaccine Research Institute

WHO Collaborating Centre

Lausanne Hospital Center

Ludwig Institute for Cancer Research
More than 50 years of existence
150 employees
Expertise in: immunology, inflammation, infectious diseases, cancer cell biology
Active collaboration with other centers
Entrepreneurial spirit - several start-ups
Various international collaborations
WHO Research and Training Centre in Immunology
More than 800 trainees from developing countries over 30 years
Access to various platforms, including:
Proteomics and peptide synthesis
SPF Animal Unit (>30,000 mice, inc. transgenic)
Clinical trial unit (malaria trials)
The Vaccine Formulation Laboratory

- Integrated in the UNIL Department of Biochemistry

- A platform for the WHO **Global Adjuvant Development Initiative:**
  1. Supply portfolio of proven adjuvants accessible to public sector
  2. Undertake their evaluation and optimization using harmonized read-outs
  3. Provide vaccine formulation services in the public sector
  4. Provide training courses for vaccinologists from developing countries
Our current activities

**TRANSVAC**: European Network of Vaccine Research and Development

Missions of the laboratory:

- Open-access supply and formulation service
- Assistance to external R&D groups for know-how on vaccine formulation
- Training module on vaccine development
Our objective

- A hub for adjuvant technology transfer / training to developing countries located in Lausanne, Switzerland

- Training and technology transfer on adjuvants including oil-in-water emulsions
  - Demonstrated efficacy and wide safety data

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**For influenza vaccines**

- **IP situation**
  - submicron oil-in-water with tocopherol: patent barrier in most of the world
  - submicron oil-in-water: no patent barrier in Europa; no validity in developing countries

- **Submicron oil-in-water emulsion**
  - Appropriate for pandemic influenza vaccines – extensive safety record (>100M)
  - No IP barrier in developing countries
  - Feasible
Conclusion

The Vaccine Formulation Laboratory at University of Lausanne is:

1. A WHO collaborating centre with expertise on vaccine formulation
2. A service center on vaccine formulation and adjuvant access
3. A training center for vaccinologists from developing countries

Promotion of adjuvant technology transfer to developing countries manufacturers of pandemic influenza vaccines