



Final Report

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1. Abbreviations

AdjuNet	Adjuvant Network
AEFI	Adverse Events Following Immunization
ADVAC	Advanced Course of Vaccinology
BARDA	Biomedical Advanced Research and Development Authority
BPRC	Biomedical Primate Research Centre
DC	Developing Country
EC	European Commission
EMA	European Medicine Agency
EVI	European Vaccine Initiative
FDA	Food and Drug Administration
GADI	Global Adjuvant Development Initiative
GIZ	Deutsche Gesellschaft für internationale Zusammenarbeit GmbH
IDL	Institute for Animal Science and Health Lelystad
NMRC	Naval Medical Research Center
PATH	Program for Appropriate Technology in Health
PRD	Poverty Related Diseases
QC	Quality Control
RLC	Resource Limited Country
WHO	World Health Organization

2. Final Publishable summary report

A. Executive summary

The development of vaccines against poverty-related diseases faces several common gaps and challenges. These include difficulties in accessing know-how and technology platforms in vaccine development, formulation and delivery, difficulties in harmonising safety data collection, and an insufficient numbers of trained scientists able to undertake leadership roles in vaccine development.

The INYVAX project has addressed these challenges by:

- Establishing a comprehensive database of vaccine technologies, available in Europe. This publically accessible database links vaccine researchers with readily accessible formulation and scale-up process development capacity, regulatory support and clinical trial expertise. Everyone involved in the vaccine development chain is encouraged to join the database and upon doing so gains access to a comprehensive collection of vaccine development solutions.
- Optimising knowledge and resources for formulation of PRD vaccines through 1) the opening of the European branch of the global adjuvant network, **AdjuNet**, and 2) the implementation of **Global Adjuvant Development Initiative (GADI)** reference laboratory, which is able to provide several adjuvants and formulations for development of vaccines.
- Development of a training programme on optimisation of vaccines with adjuvant.
- Development of safety standards in clinical trials of PRD vaccines, allowing meta-analysis of the safety of similar vaccine approaches. These standards will be presented to regulatory authorities for worldwide adoption for clinical trials. This also includes Guidelines for Collection, Analysis and Presentation of AEFI in Pre-Licensure Clinical Vaccine Trials in Resource Limited Countries as well as a comprehensive list of AEFI.
- Sponsoring trainees of the Advance Vaccinology Course (**ADVAC**), including the topics: Pre-clinical vaccine research, Design and monitoring of clinical trials, Vaccine safety issues, Selection of new and appropriate vaccination strategies and effective communication.

The project officially started on 1st February 2009 and carried on for three years, ending in January 2012.

B. INYVAX context and objectives

The development of vaccines against poverty-related diseases faces several common gaps and challenges. These include difficulties in accessing know-how and technology platforms in vaccine development, formulation and delivery, difficulties in harmonising safety data collection, and an insufficient numbers of trained scientists able to undertake leadership roles in vaccine development.

Objective 1: Optimisation of knowledge and resources in PRD vaccines technologies

In collaboration with IVR (WHO), to make an inventory of all the European organisations, institutions, biotechs, SMEs and pharmaceutical industries developing vaccine technologies in order to establish a comprehensive database. This inventory include GMP manufacturers as well as organisations/companies able to optimise and transfer technologies developed by academic scientists, validating and optimising the process development and formulation development. This exercise include information from PRD vaccines already in development, as well as relevant information from marketed vaccines when available. When successful at European level, this effort could be pursued towards developing countries, in the perspective of addressing the

industrial scale-up of investigational vaccines, before entering in phase III clinical trials.

Objective 2: Optimisation of knowledge and resources for the Formulation of PRD vaccines

To set-up the European branch of the global adjuvant network ADJUNET, between groups developing adjuvants and public sector organisations evaluating adjuvants in clinical trials.

Among the consortium partners, two are coordinating the EC integrated projects EMVDA, and TBVAC. Through these two projects the partners involved in the work packages on formulation and adjuvant testing will be the foundation of European ADJUNET. This network will also include members of the EAAC (European Adjuvant Advisory Committee) who are adjuvant developers.

To contribute to the Global Adjuvant Development Initiative by providing the first European resources for sharing information and facilitating communication between groups developing adjuvants and public sector organisations evaluating adjuvants in clinical trials (including EMVDA, TBVAC and existing networks such as the European Adjuvant Advisory Committee).

To analyse the needs and the gaps in the development of PRD vaccines formulated with adjuvants. Among others, a special attention will be given to:

- The need for standardised evaluation.
- The identification of technical gaps in antigen optimisation to support the development of high quality antigens with well defined physico-chemical characteristics and standardised immunologic read-outs e.g. functional antibodies, CMI, functional CD8, B-memory.
- An identification of the need for specific pathogen free facilities necessary for minimising inconsistency due to viral infection.
- To develop a strategy specific to malaria and tuberculosis vaccines for the optimisation of immune responses with adjuvants, in order to guide vaccine developers towards better cost-effective pharmaceutical and clinical development, based on an assessment of the different alternatives of formulation work in the course of the clinical development.
- To develop a training program for European PRD vaccine developers and members of ADJUNET to be implemented at Lausanne University (Switzerland) and ICGEB (India) under GADI supervision (the ICGB training is supported by other donors and is not part of this project).

Objective 3. Implementation of Safety standards in clinical trials of PRD vaccines

To identify challenges in the implementation of vaccine safety standards in PRD clinical trials, in Europe and in developing countries.

To generate immediate “user-feedback” for the improvement of BC safety standards in clinical trials.

To identify opportunities to facilitate the usage of BC safety standards in resource-poor settings.

To generate well-defined BC implementation proposals and partnerships.

To identify short term projects for consultancy services in collaboration with international agencies, academic centres, donors and regulators.

With the development of more PRD vaccines around the world, globalisation of vaccine safety efforts has become increasingly important. With a basic set of 29 published Brighton

Collaboration case definitions of Adverse Events Following Immunisation (AEFI), new working groups continue to steadily emerge.

While the generation of case definitions is a remarkable step in the creation of an international vaccine safety terminology, this common language will need to be used and “spoken” in order to be effective in improving vaccine safety around the world. To achieve the goal of global implementation of vaccine safety standards, a specific action plan was developed in 2006 by the

Brighton Collaboration Secretariat, with guidance from their Steering Committee. The major action taken to increase developing country participation was the creation of the Implementation Working Group, which will specifically target developing country issues and concerns. The goal of this group is to facilitate the use of Brighton Collaboration AEFI definitions around the world. The concept of this Working Group is fairly simple:

- There are approved and evidence-based standards available.
- There are people willing to use them.
- There are people who can help and counsel in the process.

Bringing these people to one table is the next logical step to the implementation of vaccine safety standards globally. This project will set-up a working group on the implementation of clinical safety standards in pre-licensure clinical trials of PRD vaccines. This working group will include experts recommended by the WHO, as overseen by the head of IVR in to ensure that these recommendations are transferred to the relevant authorities in the WHO.

Objective 4. Training in vaccinology

This objective deals with training to expose students to the many different facets of vaccinology. Areas of training will relate to:

- Pre-clinical vaccine research (go and no-go decisions, safety assessment, immunological considerations etc.).
- Design and monitoring of clinical trials (ethical issues, calculation of size, monitoring and interpretation of results).
- Vaccine safety issues.
- Selection of new and appropriate vaccination strategies (immunological limitations, epidemiological and economic aspects etc.).
- Effective communication.
- The training will also review advances regarding high priority PRD vaccines: malaria, tuberculosis, HIV/AIDS, diarrhoeal diseases, acute respiratory infections and emerging diseases. It has long been perceived to be of importance that people entering into a career in vaccine R&D be exposed to economic, epidemiological, and logistic issues that will, at a later stage, influence the development and real-life use of the new vaccines.

The course director is Dr Paul-Henri Lambert. The Fondation Mérieux (Scientific Director: Dr Christophe Longuet) are responsible for administrative management, and the curriculum is under the supervision of the Centre of Vaccinology, at University of Geneva (Prof. CA Siegrist).

The course is comprised of top-level lectures, followed by extensive interactive discussions, and specific exercises in small working groups. Care is taken to maintain a full independence from any influence of a commercial nature. English is the official language. This course is the basis for stimulating a large international, cooperation and to favour the development of vaccinology networks. The course is complemented by a follow-up alumni programme, including the establishment of a network based on a specific web forum and information system.

The annual course is restricted to a total of 60 participants, usually comprising of 30 participants from developing countries (mostly with fellowships covering all costs) and 30 participants from industrialised countries (about 20 from governmental agencies or academia, and 10 self-funded from industry). They are selected by an international Scientific Committee that reviews and ranks applications. The global faculty comprises of 50 to 60 leading experts in vaccinology.

This objective has reserved 10 places per year (for three years) for INYVAX-funded students.

The EC, WHO, and other agencies will be asked to propose candidates for sponsorship by INYVAX but general calls for applications will also be made through multiple channels, including advertising in disease-endemic countries. Selection is made by the ADVAC Scientific Committee, as is normal for this course.

C. Main Science & Technology results

a) Comprehensive Inventory of PRD vaccine technologies

Work Package Leader: European Vaccine Initiative, Dr. Odile Leroy

The objective was the development a comprehensive database of European organisations, institutions, biotechnology companies and pharmaceutical industries developing vaccine technologies and to develop a strategy across PRD vaccine for selecting manufacturers and sub-contractors, addressing quality assessment.

With first examination of the published data, it became apparent also, that using literature as a source of information was not going to provide the necessary data for completing the database. The source of the technology and the specific details relevant to the database were rarely stated. It was decided at the time to replace the literature search with expert ad-hoc discussions—these were conducted during the Meeting of Panel Experts. A main clause of this data collection process was to ensure it was compatible with the different European National Laws regulating databases which contain qualitative data. For this reason, the analysis of the advantages, the constraints and the limits of each technologies (including an analysis of intellectual property rights), transferability of the know-how, benchmarking, production costs, regulatory compliance could not be made public or be included in a database, as it was considered as judgements on the companies and were forbidden by law in several European Countries. The risk to enter any unsubstantiated data about a company or organisation which could bring to law case was also assessed.

To avoid these potential legal risks, organisations have been invited to enter their own data or to validate their data into the database. The data are then be validated by EVI staff before being visible online. This process also circumvents the issue of limited availability of data on specific technologies. Whereby it would have been necessary for EVI to contact each service provider, having them fill out a written survey, which would then be entered manually into the database. Being legally forced to have service providers fill in their own public data provides for a much more robust database. Now basic users (companies, organisations, partners, etc.) may enter data to the database only after subscription, their information, validated by an administrator before becoming visible on the site.

The different categories of activities or products are listed in the table below: This list was the support for the development of the database structure. The resulting database is visible at www.euvaccine.org.

In the database have also been included the main European projects dealing with vaccine research or vaccine development.

Table 1: List of activities listed as critical or useful in vaccine development**ADJUVANTS:****Type of Service :** formulation, custom production**Product name :****Manufacturer type:** CMO, GMP, custom, API production, Non-GMP, Clinical, Company Product, Commercial**Adjuvant category:**

- Mineral salts, e.g., aluminium hydroxide and aluminium or calcium phosphate gels.
- Oil emulsions and surfactant based formulations, e.g., MF59 (microfluidised detergent stabilised oil-in-water emulsion), QS21 (purified saponin), AS02 [SBAS2] (oil-in-water emulsion + MPL + QS-21), Montanide ISA-51 and ISA-720 (stabilised water-in-oil emulsion).
- Particulate adjuvants, e.g., virosomes (unilamellar liposomal vehicles incorporating influenza haemagglutinin), AS04([SBAS4] Al salt with MPL), ISCOMS (structured complex of saponins and lipids), polylactide co-glycolide (PLG).
- Microbial derivatives (natural and synthetic), e.g., monophosphoryl lipid A (MPL), Detox (MPL + M. Phlei cell wall skeleton), AGP [RC-529] (synthetic acylated monosaccharide), DC_Chol (lipoidal immunostimulators able to self organize into liposomes), OM-174 (lipid A derivative), CpG motifs (synthetic oligonucleotides containing immunostimulatory CpG motifs), modified LT and CT (genetically modified bacterial toxins to provide non-toxic adjuvant effects).
- Endogenous human immunomodulators, e.g., hGM-CSF or hIL-12 (cytokines that can be administered either as protein or plasmid encoded), Immudaptin (C3d tandem array)
- Inert vehicles, such as gold particles

Adjuvant composition:**USE:** R&D, human use/veterinary**Quality grade:** GMP/GLP/lab scale**Access :** free versus negotiated**Antigen manufacturers (Active Ingredient)****Type of Service:** complete work package, R&D, Process development/ GLP production/GMP production ,USP, DSP, formulation, Fill and Finish,analytics, QC including animal testing, QA, QP release submission**Technology/expertise:**

- living organisms that are naturally avirulent or that have been treated to attenuate their virulence whilst retaining adequate immunogenic properties;
- antigens extracted from or secreted by the infectious agent;
- antigens produced by recombinant DNA technology;
- a live, recombinant vector producing antigens in vivo in the vaccinated host
- plasmid DNA
- antigens produced by chemical synthesis in vitro.

Technology/expertise: Any, cell/tissue, DNA, Live attenuated virus, recombinant sub protein, recomb vector, synthetic peptide/ VLP**Manufacturer type:**R&D, CMO, GMP, custom, API production, Non-GMP, Clinical, Company Product, Commercial**Quality and regulatory Compliance:** FDA cGMP, European Medicines Agency requirements. ICHQ7 GMP API,**Scale:** lab , industrial, mg, kg, liter,**Biosafety level:** BSL1,BSL2, BSL3**Access :** free versus negotiated**Consultants****Expertise:**Process/product development, Due diligence and technology, QA, outsourcing, supply, manufacturing,business strategy, database, market research, commercialisation, preclinical Immunology, clinical Immunology,immunodiagnostic, vaccination, drug delivery,adjuvant, antibody,antigen,immunochemistry, assay, environmental impact, vaccine research, quality assurance (audit GxP compliance,Facility design, quality training, GCP, GMP, GLP)**Contracts Research Laboratories****Service:** Drug discovery, Pre-clinical and clinical sample analysis, Potency assays, Development of preclinical strategies,method development, method validation**Technology:**HPLC, Mass spectrophotometry, Tests of toxicity after acute and repeated administration, Haematology, Histopathology,Immunisation,Bioanalysis, genotoxicity, and safety pharmacology, dose formulation analysis,Toxicokinetics analysis, Pharmacokinetics analysis, Biomarker assay, ligand-bind assay, immunogenicity assays, cell based assays, animal in vitro, animal in vivo,human, mice, small animal, primate, rodent, non-rodents, in vitro**Quality compliance :**ISO17025 (technical competency of analytical laboratories), GLP accreditation, GMP certification, GCLP, BARKA (British Association of Research Quality Assurance)**Clinical Research Organisation (CROs)****Service:** Clinical- phase I, II, III, IV study design, protocol design, consulting, trial and site management, Data Management, electronic capture, Statistical Reporting & Analysis, Biostatistic, biometrics, clinical research report, clinical research manuscript, Serious adverse event reporting, Data Monitoring Committees,Specialized Clinical Consulting, Risk Management Products & Services, regulatory support, pharmacovigilance,qualified person, batch release, clinical trial supplies, clinical trial logistics,**Quality compliance:** ISO 2001 certification

*Table 1 cont'd: List of activities listed as critical or useful in vaccine development***Regulatory support**

Service: Scientific advice, Orphan drug applications, Competitive intelligence surveys, Regulatory strategy definition, Submission strategies, Clinical trial applications, maintenance and trial support, dossier submission to competent authorities, dossier submission to ethic committees, translation, drug label preparation, drug label translation, review of document,

Regulatory Agencies: European Medicines Agency, FDA, Swissmedic

Pharmaco-toxicology studies

Service: safety toxicology, general toxicology, analytical service, microbiology, histopathology, cell culture, immunology,

Animal species: rodent, dog, pig, rabbit, primates, facilities

Quality compliance: GLP certification

Process development

Service: R&D, Process development/ GLP production/ GMP production, USP, DSP, formulation, Fill and Finish, analytics, QC, QA, QP release submission

Technology/expertise: Any, cell/tissue, DNA, Live attenuated virus, recombinant sub-unit protein, recombinant vector, synthetic peptide, Virus Like Protein

Manufacturer type: R&D, CMO, GMP, custom, API production, Non-GMP, Clinical, Company Product, Commercial

Quality Compliance: FDA cGMP, GLP certificate, DIN EN ISO/ IEC 17025 accreditation, GMP ICHQ7 GMP API,

Scale: lab, industrial, commercial, mg, kg, liter,

Biosafety level: BSL1, BSL2, BSL3

Access: free versus negotiated

Project management

Service: process development, API production, clinical trial, QA

Area of expertise: vaccine

Analytical Quality control

Service: Pre-clinical and clinical sample analysis, Stability studies, Pilot in vivo studies, Development of preclinical strategies, method development, method transfer, method validation, potency assay

Technology: HPLC, Mass spectrophotometry, Immunisation, Bioanalysis immunogenicity assays, cell based assays, release testing, animal in vitro, animal in vivo, human, mice, small animal, primate, rodent, non-rodents, in vitro,

Quality compliance: ISO17025 (technical competency of analytical laboratories), GLP accreditation, GMP certification, GCLP, BARKA (British Association of Research Quality Assurance)

Antigen and epitope screening

Service: phage display, epitope screening,

Company type: research, bioinformatics, contract manufacturer

Quality compliance: R&D, GMP/GLP

Access: free versus negotiated

Formulation Fill & Finish

Service: Formulation, development, Fill and Finish, lyophilisation, analytics, QC, QA

Technology/expertise: Any, cell/tissue, DNA, Live attenuated virus, recombinant sub protein, recomb vector, synthetic peptide/ VLP

Manufacturer type: R&D, CMO, GMP, Non-GMP, Clinical,

Quality and regulatory Compliance: FDA cGMP, European Medicines Agency requirements. ICHQ7 GMP API,

Scale: lab, industrial, vials

Biosafety level: BSL1, BSL2, BSL3

Access: free versus negotiated

Vaccine Development

Service and partnering: manufacturer, research collaboration, industrial co-development

Technology: pox virus, adenovirus, expression system, proprietary technology

Manufacturer type: Biopharma, collaboration, licensing, CMO, GMP, custom, API production, Non-GMP, Clinical, Company Product, Commercial

Quality and regulatory Compliance: FDA cGMP, European Medicines Agency requirements. ICHQ7 GMP API,

Scale: lab, industrial, mg, kg, liter,

Access: free versus negotiated

b) Optimisation of knowledge and resources for the formulation of PRD vaccines

Work Package Leader: World Health Organization, Martin Friede

An analysis of the needs and gaps for *optimising the immune response to candidate vaccines against poverty related diseases* was conducted through analysis of the literature supplemented with interviews with vaccine developers. The picture that emerged is as follows:

Developing vaccines against poverty-related diseases is complex, facing first and foremost a lack of financial incentives and available resources, but from a scientific perspective rendered extremely difficult by

- a) The lack of comprehension of which immune response is required to protect against these diseases in target populations
- b) The lack of animal models which reliably mimic the human disease and which could reliably be used to identify the protective immune response and how to induce it
- c) The paucity of vaccine technologies with *demonstrated* safety and activity on which to base these vaccines, and the lack of availability of comparable studies to enable a valid selection of one technology over another
- d) The lack of methods for inducing a strong cytotoxic lymphocyte responses without using live viral vectors, and
- e) The poor reliability of animal models to predict how safe and immunogenic a candidate vaccine will be in the clinic.

Additional gaps identified also included the lack of availability of clinically proven technologies for alternative routes of delivery to facilitate immunisation in resource-poor settings as well as technologies to overcome the need for the cold-chain in these settings. These are discussed.

Since the focus of the exercise, was on gaps in enhancing the immune response, the analysis focused on the formulation challenges. This included reviewing the technologies available to enhance immunity to vaccines, their challenges associated with each of these, and, to assist vaccine developers, the identification of a pathway to formulating vaccines for PRD with the least risk of failure. This pathway focused on the critical importance identified by the vaccine industry on risk-minimisation when using immune-enhancing methods such as adjuvants. Following the failure of numerous vaccine candidates in clinical trials or withdrawals following post-marketing surveillance where the adjuvant has been blamed, the use of adjuvants is identified as carrying risk. This risk is best minimised by either not using adjuvants, or if absolutely required, using adjuvants that have a history of safe and effective use. In order to be able to achieve this, it is essential that significant effort is put into making the antigen as immunogenic as possible, an activity that is generally overlooked.

It is concluded that this activity, enhancing the native immunogenicity of antigens prior to formulating with adjuvants is the most critical step in optimising immunogenicity of candidate vaccines for poverty-related diseases. Based on this, an optimisation strategy is proposed:

1) Optimisation of antigen

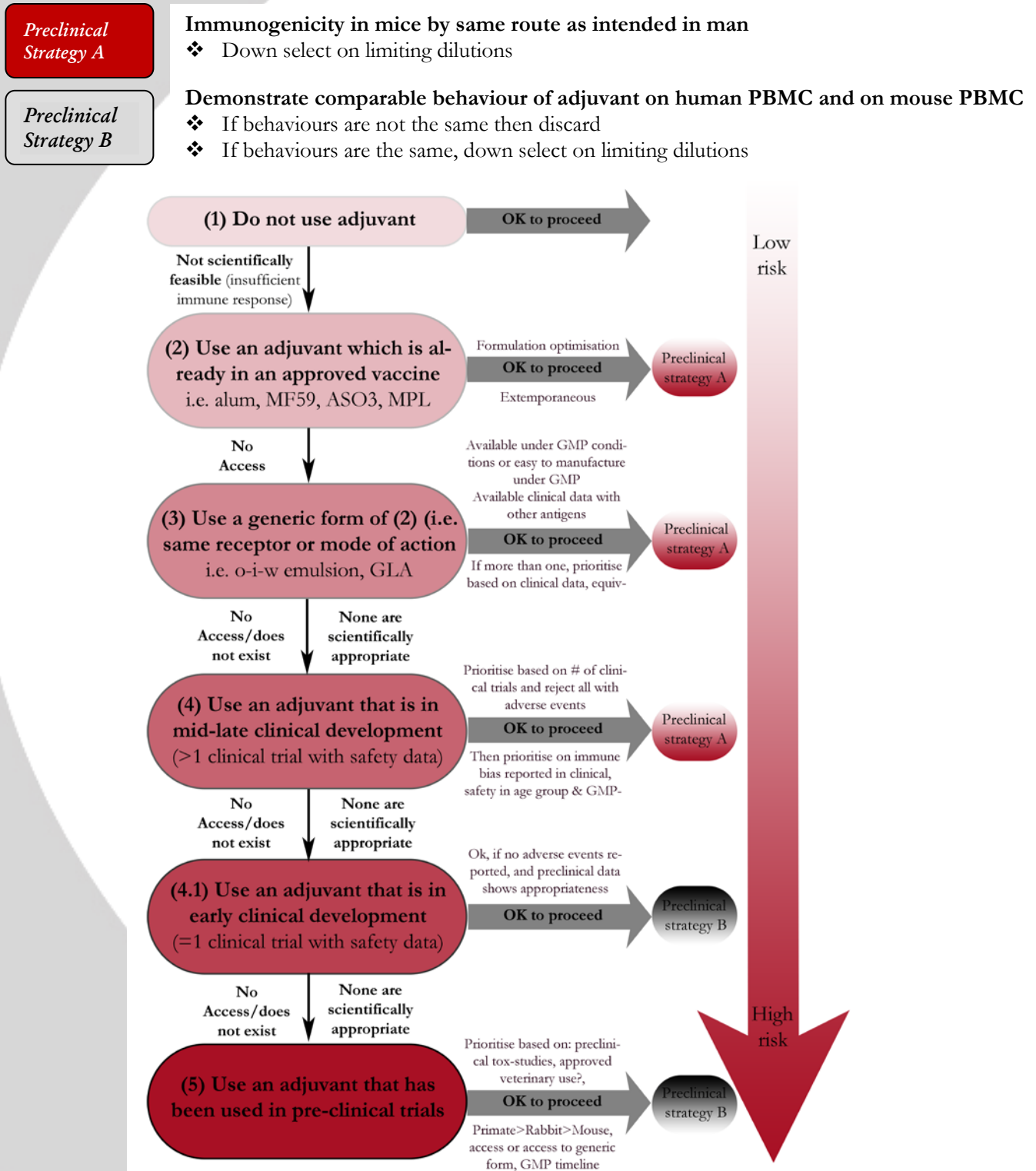
- Soluble monomeric proteins are poor candidates to start with (require very potent adjuvants & therefore risky)
- Evaluation multimeric formulations such as:
 - i. Conjugate to carrier protein (any)
 - ii. Conjugate to virosomes
 - iii. Conjugate to a virus (e.g alpha virus)
- Express as fusion protein in self-assembling system (but NOT human virus origin i.e. not HBsAg, HBc, etc.)

Select one of the above and test both monomeric and multimeric forms.

2) Selection of adjuvant and formulation

- Follow the flowchart on the figure 1 for selection of adjuvant
- Then pre-clinical down selection:

Figure 1: Flow chart for decision making in selection of adjuvant "Inyvax Rules"



The other objectives were to establish the European branch of the global adjuvant network AdjuNet between groups developing adjuvants and public sector organisations evaluating adjuvants in clinical trials, to develop a strategy for the optimisation of malaria and tuberculosis vaccines, and to establish a short training programme on optimisation of vaccine with adjuvants. The work was initiated by the formation of a European working group on adjuvants with an initial core team within the INYVAX participants. The report on the needs and gaps for the optimisation of immune response of PRD vaccines is available, and described as **"INYVAX rules"**.

The Global Adjuvant Development Initiative (GADI) laboratory at the University of Lausanne opened the 4th of January 2010. This laboratory is now a **WHO collaborating centre on Adjuvants and Vaccine formulation**. It provides adjuvants and vaccine formulation to numerous clients; European universities, European biotechnology companies and regulatory agencies. There are also a number of clients expressing interest from the USA, India and China. WHO has lead the creation of an initiative to ensure the availability of adjuvants and know-how on formulation for vaccine developers working on vaccines of public-health importance.

As part of a INYVAX, a **modular training course** has been developed on the preparation of adjuvants and the formulation and quality control of vaccines containing these adjuvants. These training courses are being conducted in collaboration with the WHO collaborating centres on Adjuvants and Vaccine Formulation.

A training program on oil/water emulsion preparation and use was established and will be given to the first round of trainees (table 2). This took place in March 2011 at Biofarma in Indonesia (USA funded). The training programme will be one week long, covering theory, preparation, adjuvant Quality Control (QC), formulation and vaccine QC aspects of both oil-in-water adjuvants and alum salts and a final day on theory of other adjuvants.

Table2: Programme of the adjuvant training

DAY 1		
09:00-12:00	Theory:	
	Background to composition, safety and uses	M. Friede
	Theory of microfluidisation	<i>Microfluidics</i>
	Theory of particle size measurement	<i>Malvern</i>
13:00-17:00	Preparation of batch of squalene-in-water emulsion	
	Microfluidisation:	
	Preparation of emulsion on Microfluidics M110H	<i>L.Brunner</i>
	QC with particle size analysis	<i>L.Brunner</i>
DAY 2		
	QC of oil content by HPLC	<i>L.Brunner</i>
	Measurement of antigen association by Ficoll flotation	<i>L.Brunner</i>
	Antigen quantification / integrity by ELISA /WB	<i>L.Brunner</i>
	Theory: design of stability studies & stability indicating parameters.	<i>M. Friede</i>

A General training program on vaccine formulation with adjuvants has been prepared (course material and speakers). First course will take place September 2012. This will be conducted by the TRANSVAC consortium (EC FP7 funded Infrastructure). The training programme will be one week long, covering theory, preparation, adjuvant Quality Control (QC), formulation and

vaccine QC aspects of both oil-in-water adjuvants and alum salts and a final day on theory of other adjuvants.

Under INYVAX, the selection procedures have been developed for European PRD vaccine developers to participate in these training courses. Courses for these participants will be held at the WHO collaborating centre on Adjuvants and Vaccine Formulation, at the University of Lausanne.

c) Implementation of safety standards in PRD vaccine clinical development

Work Package Leader: Brighton Collaboration Foundation, Ulrich Heininger

The objective of the work package is to provide safety standards in clinical trials of PRD vaccines allowing meta-analysis of the safety of similar vaccine approaches.

The BC/INYVAX working group has been formed by a call for volunteers to which 67 persons worldwide replied, requesting to participate in the work. Monthly conference calls were held with about 20 - 25 people on average attending each meeting.

The “**Guidelines for Collection, Analysis and Presentation of AEFI in Pre-Licensure Clinical Vaccine Trials in Resource Limited Countries**” have been finalised. This report also includes a **list of AEFI prioritised for Resource Limited Countries (RLCs)**. In order to guide the development of AEFI case definitions and vaccine safety studies, the Brighton Collaboration has conducted an email-based survey to all its members, i.e. over 3,000 vaccine safety-relevant professionals from over 120 countries in five continents, collecting proposals for most imminent AEFI to be prioritised for development of a harmonised case definition. The results are stratified by developed countries and RLC (see table 3). In addition, individual AEFI are grouped and then be analysed by organ systems.

Table 3: List of prioritised AEFI case definition

Rank	AEFI overall	AEFI in RLCs
1	Guillain-Barré Syndrome	VAPP
2	Seizures	Seizures
3	Local reactions at injection site	Encephalitis
4	Neuritis	Lymphatic tuberculosis /Lymphadenitis to BCG
5	Fever	Guillain-Barré Syndrome
6	Anaphylaxis	Local reactions at injection site
7	Encephalitis	Fever
8	Bell's Palsy	Anaphylaxis
9	Narcolepsy	Diarrhea
10	Arthritis /arthralgia	HHE
11	ADEM	Disseminated -BCG
12	VAPP (vaccine associated paralytic polio)	
13	Pain	
14	Thrombocytopenia	
15	Lymphatic tuberculosis /Lymphadenitis to BCG	

There is no uniformly accepted template protocol for vaccine clinical trials. The standards used to assess safety in RLC should be as stringent as anywhere else in the world. With the development of the INYVAX template of safety section in clinical trial protocols, BC will petition for these to be undertaken in all RLC CTs. The template along with the content outline should provide an executive summary of the protocol with a dedicated section to outline the

approach to safety assessment of the CT. The summary may be presented in narrative or tabular format.

The literature review of vaccine clinical trials in resource poor countries is in the final stage of preparation. This was done by a group of scientific volunteers from the Naval Medical Research Center (NMRC), Clinical Trials Center, Bethesda, MD, USA and some of the working group members including Vasee Moorthy and Ulrich Heininger.

Methods: To evaluate the degree of standardisation of safety reporting across vaccine clinical trials, we performed a systematic literature review of electronic databases for publications that reported safety data from vaccine clinical trials for malaria, TB and HIV. The scope of this review included publications published in English between 1 January 2000 and 1 July 2009. Search strategies were customised for each publication database. Eligibility of publications identified during the initial search was determined by title and/or abstract review using the following exclusion criteria: publications that 1) did not focus on one of the three selected diseases, 2) did not have safety as a main focus, 3) reported on therapeutic use of a vaccine, 4) reported on Bacillus Calmette-Guérin (BCG) only, 5) reported on HIV vaccine candidates given to infants born to HIV infected mothers or 6) were case reports or case series. Important safety data extracted included: age of trial participants; platform, route and method of vaccine administration; duration of participant follow-up; type, severity and reporting method of adverse events; reporting of laboratory abnormalities.

Results: A search of electronic databases yielded a total of 2,278 publications for screening of which 151 were eligible for inclusion on reviewing the title and abstract. A closer review resulted in the exclusion of an additional 27 publications leaving 124 publications eligible for inclusion (66 malaria, nine TB, and 49 HIV). Overall, the consistency and detail of safety data reporting was found to be suboptimal. A total of 264 different terms were used throughout the publications to describe specific adverse events with 48 describing adverse events at the vaccine injection site alone. Critical safety data was missing in a number of publications. For example, 27% of all manuscripts failed to report serious adverse events (SAEs) and 17% of the publications did not mention fever. In the publications that did mention fever, 44% did not define fever and 63% did not specify the mode for measuring the temperature.

Conclusion: The results of this review demonstrated the nonstandard nature of safety data reporting. The efficiency of developing safe and effective vaccines for poverty related diseases would be facilitated by improved comparability of data across clinical trials. Standardisation of safety data reporting could be an important first step to improving data quality and comparability.

The review paper will be entitled “A Systematic Review of Safety Data Reporting from Vaccine Clinical Trials of Three Poverty Related Diseases: Malaria, Tuberculosis, and Human Immunodeficiency Virus Infection”. This paper will be submitted to VACCINE and due to the BC review process it will require no further peer review before being published. Also to be published in VACCINE will be a paper containing the template described above. Along with the paper published in 2011, addressing the needs and gaps in safety assessment of vaccines during clinical trials in resource limited countries, INYVAX has contributed three papers aimed at identifying and implementing safety standards in PRD clinical trials.

d) Advanced Training in Vaccinology (ADVAC)

Work Package Leader: University of Geneva, Paul-Henri Lambert

The objective of this work package is to generate training opportunities for PRD vaccine researchers by funding students from Europe as well as from Developing Countries (DC) who wish to attend the Advanced Training in Vaccinology (ADVAC) Course offered by Fondation Mérieux in Geneva, Switzerland.

The third ADVAC course in Advanced Training in Vaccinology for European and DC scientists in relation to PRD vaccines has taken place from 16th to 27th May 2011 at the Fondation Mérieux conference centre. To be accepted in the ADVAC course, the INYVAX candidates were required to demonstrate that they were involved in vaccine research, vaccine development or clinical research (vaccine trials, epidemiology), in relation to Poverty-Related Diseases Vaccines (Malaria, TB, HIV, diarrheal and other neglected diseases, respiratory infections, etc.)



A total of thirteen five students were sponsored by INYVAX, coming from 24 countries (13 North, 11 South).

The fourth course will be running in May 2012 for two weeks and will include the five last positions for INYVAX sponsorship. The programme is completed and the lecturers defined by the ADVAC Steering Committee. Many participants are involved in PRD, with many applying for INYVAX funding. The selection of candidates to receive the INYVAX funding has now finished, following the ADVAC procedures.

An example of the programme course is given in Table 4 (2010 module Training)

Table 4: 2010 Module Training ADVAC course

Theme Coordinator : Adam Finn Bristol, UK)	
Opening	Benoit Miribel , General Director, Fondation Mérieux
Definition of the course objectives	Paul-Henri Lambert , Director of the ADVAC Course
SESSION 1.- THE MULTIFACETED NATURE OF VACCINOLOGY	
Chairpersons: Claire-Anne Siegrist, and Paul-Henri Lambert	
Opening Lecture: The history of vaccinology and its global perspectives	Stanley Plotkin , University of Pennsylvania
Impact of vaccination on disease epidemiology	Roy Anderson , Imperial College, London, UK
Herd immunity	John Clemens , IVI, Korea
Public and media perception of vaccination during the course of the H1N1 pandemics	David Salisbury , UK
The Value of Vaccination	Till Baernighausen , Harvard PHS
Theme Coordinator :	Adam Finn (Bristol, UK)
SESSION 2 - HOW VACCINES WORK	
Chairpersons: Adam Finn and Daniel Pinschever (UNIGE)	
How are vaccine responses elicited? What a vaccinologist should know about the basic aspects of immunological responses a- B-cell responses	Claire-Anne Siegrist , University of Geneva
What a vaccinologist should know about the basic aspects of immunological responses b- T-cell responses	Claire-Anne Siegrist , University of Geneva
Immunological correlates of immunity: use and limitations in vaccinology:	Stanley Plotkin , University of Pennsylvania, Philadelphia
Immunological basis for responses to mucosal vaccines	Adam Finn , University of Bristol
Vaccines and Immunological memory Quiz and general discussion	Claire-Anne Siegrist , University of Geneva
Vaccine-induced Immunological memory	Rafi Ahmed , Emory University
Theme Coordinator : Hanna Nohynek (THL, Helsinki)	
SESSION 3 – DECISION-MAKING IN VACCINE RESEARCH AND PRECLINICAL DEVELOPMENT	
Chairpersons: Luc Hessel & Georges Thiry	
Vaccine adjuvants: pragmatic approaches	Martin Friede , WHO, Geneva
From pre-clinical research to vaccine development: Examples of go-no-go decisions	Georges Thiry , PATH
How do vaccines cause adverse events ?	Neal Halsey , Johns Hopkins B. School of Public Health, Baltimore
Special Lecture: HIV vaccines	Brigitte Autran , INSERM, France
SESSION 4 - ASSESSING VACCINES IN CLINICAL TRIALS (I)	
Chairpersons: Hanna Nohynek	
Sequential stages of clinical trials and overview of issues to be considered	Myron Levine , University of Maryland, Baltimore, USA
Regulatory barriers e.g. re: new adjuvants Round table debate	Norman Baylor (FDA), Pieter Neels (Federal Agency for Medicinal and Health Products Brussels & CHMP-EMEA) – Thomas Verstraeten , GSKBio and Michael Decker (Sanofi Aventis,)
Lessons from pitfalls experienced in the registration process (including role of a DSMB)	Luc Hessel , Sanofi Pasteur MSD, Lyon,
SESSION 5 - ASSESSING VACCINES IN CLINICAL TRIALS (II)	
Chairperson: Juhani Eskola	
Essential practical aspects in conducting phase III trials	Hanna Nohynek , Helsinki
Introduction to statistical aspects of clinical trials	Peter Smith , LSTMH, UK
1- Defining sample size: practical approaches and examples	
How to design, recruit volunteers for, and analyze the results of selected phase II trials	
Small group exercise: How to design a phase II trial -	
Special lectures: New vaccines in development (1)	
New approaches to vaccine development and delivery systems	Carole Heilman , NIH/NIAID
The challenge of developing new tuberculosis vaccines	Stefan Kaufmann (Berlin)
The challenge of malaria vaccines-	Vasee Moorthy WHO
Theme Coordinator : Neal Halsey (Baltimore)	

SESSION 6 – VACCINE SAFETY - ASSESSMENT OF ADVERSE EFFECTS	
Chairpersons: Noni Mc Donald and Neal Halsey	
Lessons from previous adverse effects of vaccination and Assessment of causal relationships	Neal Halsey, Johns Hopkins B. School of Public Health, Baltimore
Immunological safety of vaccination (Autoimmune and allergic diseases)	Paul-Henri Lambert,
Immunization safety in developing country vaccination programs	Philippe Duclos , WHO
Risk communication: An overview	Noni McDonald, Dalhousie Univ, Halifax Canada
Introduction to statistical aspects of clinical trials- 2- Statistical assessment of phase 3 trials- 30 min	Peter Smith , LSTMH, UK
Population-based post-licensure surveillance	Steve Black, Cincinnati Children's Hospital Medical Center
Small group exercise 2: Designing and analysing the results of 3 selected phase III trial (pneumococcal conjugate vaccine in The Gambia, among Navajo Indians in the U.S. and in South Africa)	Objective: To understand how to critically appraise and compare phase III trial results
Introduction to the group work Exercise:	Hanna Nohynek
Group 1:- Facilitator: Edwin Asturias Group 2: - Facilitator: Hanna Nohynek Group 3: - Facilitator: Steve Black Group 4: - Facilitator: Rana Haji Group 5: - Facilitator: Peter Smith	
Theme Coordinator :	Edwin Asturias (Guatemala City)
SESSION 7- ETHICAL ISSUES	
Ethical issues related to clinical trials – Revisiting the Helsinki Declaration	
Chairpersons: Betty Dodet and Catherine Slack	
Clinical trials in developing countries: Ethical issues basic principles & practical approaches	Catherine Slack (University of KwaZulu-Natal, South Africa)
Small group exercise 3: Ethical issues – Access to treatment for participants who seroconvert during the conduct of an HIV vaccine trial talk with her	Coordinated by Catherine Slack And Betty Dodet (Lyon)
Group 1:- Facilitator: Hanna Nohynek Group 2: - Facilitator: Catherine Slack Group 3: - Facilitator: Noni McDonald Group 4: - Facilitator: Betty Dodet Group 5: - Facilitator: TBA Group 6: - Facilitator: Rana Haji	
Theme Coordinator :	Mark Miller (Bethesda)
Review and conclusions of the 23 May Ethics session	Cathy Slack
SESSION 8.1- INTRODUCING NEW VACCINES INTO VACCINATION PROGRAMMES	
Approaches to help the decision-making process	
Chairperson: Juhani Eskola	
Integration of Science, Public Health and Economics - Critical Assessment of Vaccine Policy Options	Mark Miller, Fogarty International Center
Role of disease burden assessment in the decision-making process	Brad Gessner AMP
Challenge of making evidence-based vaccination policies in developing countries	Rana Hajjeh, CDC,
Access to vaccines : economic aspects, GAVI and AMC	Nina Schwalbe , GAVI
Case-specific study #1: Meningococcal vaccines	
Infant responses to polysaccharide and conjugate vaccines	David Goldblatt, Institute of Child Health, London
Approaches towards new Meningococcal vaccines	
Future vaccination strategies to prevent meningococcal epidemics in Africa	Brian Greenwood (UK)
Special lecture: The population biology of bacterial pathogens and its importance for vaccination strategies	Richard Moxon, Oxford University
SESSION 8.2 - INTRODUCING NEW VACCINES INTO VACCINATION PROGRAMMES (2)	
Chairperson: Alan Shaw (Vaxinnate) and Bernard Fritzell (Wyeth)	
Case-specific study #2: pneumococcal conjugates	
Pneumococcal conjugate vaccines: overview	Ron Dagan, Soroka Medical Center, Beer Sheva and Keith Klugman (Emory Univ)
Case-specific study #3: Influenza- vaccination strategies and pandemic disease preparedness	
Influenza biology and vaccination strategies	Kathy Neuzil, PATH, Seattle
Development of new influenza vaccines	Kathy Neuzil, PATH, Seattle
Vaccines for pandemic response: a global vision	Marie-Paule Kiény (WHO)

Varicella and Zoster vaccines: what are the issues ?	Myron Levin UCD_Denver
Case-specific study #4 Rotavirus vaccines:	
Present status and introduction in industrialized and developing countries	Umesh Parashar (CDC)
Small group exercise 4: Decision-making for the use of new vaccines in selected countries: safety and effectiveness	organized by Juhani Eskola and Hanna Nohynek
Objective: To learn what facts are needed in a decision-making process and how other factors influence the outcome	
Group 1 Rota Umesh Parashar	
Group 2 Rota Rana Haji	
Group 3 HPV Alan Shawn	
Group 4 HPV Edwin Asturias	
Group 5 PCV Juhani Eskola	
Group 6 PCV Bernard Fritzell	
Theme Coordinator : Neal Halsey (Baltimore)	
SESSION 9 - SELECTING APPROPRIATE VACCINATION STRATEGIES	
Chairpersons: Janet Englund	
1. Vaccination in the elderly	
Vaccination and Immuno-senescence	Richard Aspinall , Imperial College London
2. Vaccination in early life	
Advantages and limitations	Claire-Anne Siegrist , University of Geneva
3. Vaccination and pregnancy	
Main issues and applications in developed and developing countries	Janet Englund , Children's Hospital and Regional Medical Center, Seattle
Parallel working group sessions	
1. Identifying Capacity Building needs in Developing Countries Special - Working group setting-up recommendations for EC & other funding agencies	Charles Mgone (Executive Director EDCTP) Arnd Hoeveler , EC, Brussels, and Alan Shaw , Vaxinate
2.National decision making for immunization programmes	Melinda Wharton , CDC, and Philippe Duclos (WHO)
3.Clinical vaccinology : patients' problem solving	CA Siegrist and Alessandro Diana
4. Vaccination schedules	Neal Halsey & Edwin Asturias
Past, present and future – Is there some rationale?	
Info on main ADVAC sponsors activities-	Arnd Hoeveler , Head, Health and Biotechnology, EC, Brussels
Research perspectives in vaccinology: The EC FP7 programme	
5- Vaccination in immune-compromised individuals, including HIV positive patients	Claire-Anne Siegrist , University of Geneva
PLOTKIN LECTURE	Peter Hotez , Sabin Vaccine Institute, Washington DC
The challenge of developing vaccines for neglected tropical diseases	
Theme Coordinator : Edwin Asturias (Guatemala City)	
Special lectures: New vaccines	
Prospects for dengue and JE vaccines	Hal Margolis IVI, Seoul
Lessons from HIV trials in developing countries	Jean William Pape , Gheskio, Haiti
HPV vaccines	John Schiller (NIH)
Elimination or Eradication strategies?	
Polio, measles, malaria,rubella	Bruce Aylward WHO ; Walt Orenstein ; Stanley Plotkin
Special Lecture	Suresh Jadhav , Serum Institute of India, Chair DCVMN
Industry Views on Future Vaccines for the Global Community	
Presentations by participants and poster discussion	
Brief presentations by participants and poster discussio	
SESSION 10: FACING THE MEDIA	
Interactive session	Chairperson: Edwin Asturias
	Deborah Hall , Broadcaster and media affairs consultant, London,
Introduction to media dynamics: How to best deliver vaccinology r elated messages to different interest groups	(organized by Edwin Asturias)
CME credits	Stanley Plotkin and Paul Henri Lambert
Diploma ceremony –	
Distribution of CD Roms with course slides	
Closure of the Course	
The educational quality of the course will be certified by Prof. Claire-Anne Siegrist and Dr Hanna Nohynek (CME related issues)	

D. Potential impact and dissemination activities

INYVAX is remarkable in his immediate impact on the creation of directly available resources for vaccine researchers and developers.

a) Potential Impact

Capacity building

The creation of **the WHO collaborating centre on Adjuvant Formulation** has been possible mainly because of the seed funding of INYVAX. This has allowed the UNIL group to raise more funds from Wellcome Trust and then were eligible for a grant from GIZ and BARDA. Now the centre is recognised as a main resource centre. (see <http://www.unil.ch/ib/page81028.html>) The group has developed several partnerships, with the World Health Organization, Geneva, Switzerland, the Developing Countries Vaccine Manufacturers' Network, the National Institute for Public Health and the Environment, Bilthoven, The Netherlands, the European Vaccine Initiative, Heidelberg, Germany, The Biomedical Primate Research Center, Rijswijk, The Netherlands and Bio Farma, Bandung, Indonesia.

The centre is now delivering services to the whole scientific community, helping scientists in developing their antigen-adjuvant formulation, within the respect of standard for quality assurance and control; through another EC funded project those services are currently provided for free in Europe.

Two main activities have been put in place for the **training**:

Inyvac has supported 35 trainees from 2009 to 2012 in the **ADVAC** course, ie one third of the total trainees for the period. The ADVAC course is an unique course, with highly recognised quality, which not only is important for the knowledge acquiring but is one of the key network in vaccinology.

Inyvac has develop a new cursus in vaccine training, focussing on **adjuvant formulation at UNIL**. This cursus has already been put in place and the training has started with fundings coming from other sources.

Harmonisation

For the first time in the history of vaccine development, a effort of harmonisation the safety assessment in pre-licensure clinical trials has taken place in INYVAX. This harmonisation has mainly focussed on the tuberculosis and malaria vaccines, but it could be easily transfer to other vaccine development. The implementation phase to validate the guidelines and the templates of clinical trial protocols and the case report forms will take place in two malaria phase Ia/b clinical trials in Europe and Africa. Those guidelines have been developed under the supervision of the Brighton Collaboration, which has already safety definition guidelines recognised by FDA and EMA.

After the validation phase, those guidelines will be submitted by the Brighton collaboration to the relevant regulatory agencies.

Knowledge sharing and networking

The INYVAX database will be an important source of information and will also contribute to strengthen the vaccinologist network by putting in relation scientists who are facing the same technology or optimisation challenges.

The AdjuNet activities have been also strengthened by INYVAX, and has been instrumental in the guidance for the development of the database.

b) Dissemination activities

The publications are listed in section 3.

Communication materials:

Leaflets, posters, and websites have been developed.

The INYVAX activities have been presented in several conference and meeting

Data base:

EVI Rendez vous, Heidelberg, November 2011, Malaria Vaccine Funders group, Geneva Switzerland 2012, NEWTBVAC meeting in *Les Diablerets*, Switzerland, February 2011

Adjuvant:

EVI Rendez vous, Heidelberg, November 2011, Global Vaccine Forum Geneva 2011; MALVAC meeting Geneva Switzerland 2012; NEWTBVAC meeting in *Les Diablerets*, Switzerland, February 2011, Hamburg March 2012

Safety:

EVI Rendez vous, Heidelberg, November 2011, Malaria Vaccine Funders group, Geneva Switzerland 2012, NEWTBVAC meeting in *Les Diablerets*, Switzerland, February 2011

Training:

EVI Rendez vous, Heidelberg, November 2011, TRANSVAC annual conference, Hamburg March 2012

E. Website

For more information on INYVAX, please visit www.inyvax.eu

3. Use and dissemination of foreground

Section A - Public

LIST OF SCIENTIFIC (PEER REVIEWED) PUBLICATIONS, STARTING WITH THE MOST IMPORTANT ONES										
No	Title	Main author	Title of the periodical or the series	Number, date or frequency	Publisher	Place of publication	Year of publication	Relevant pages	Permanent identifiers ¹ (if available)	Is/Will open access ² provided to this publication?
1	<i>Addressing the needs and gaps in safety assessment of vaccines during clinical trials in resource limited countries</i>	<i>Dr Agnes Kisser</i>	<i>Vaccine</i>	<i>Thirty-two no. a year</i>	<i>Butterworths, Guildford, Surrey, UK</i>	<i>Epub</i>	<i>2011</i>	<i>4173-4</i>	<i>PMID: 21473949</i>	<i>Yes</i>
2	<i>A Systematic Review of Safety Data Reporting from Vaccine Clinical Trials of Three Poverty Related Diseases: Malaria, Tuberculosis, and Human Immunodeficiency Virus Infection</i>	<i>Cindy Tamminga</i>	<i>Vaccine</i>	<i>Thirty-two no. a year</i>	<i>Butterworths, Guildford, Surrey, UK</i>	<i>Epub</i>	<i>2012 (Currently in review)</i>			<i>Yes</i>
3	<i>Template of safety section in clinical trial protocols; including data collection, analysis and reporting</i>	<i>Jan Bonhoeffer</i>	<i>Vaccine</i>	<i>Thirty-two no. a year</i>	<i>Butterworths, Guildford, Surrey, UK</i>	<i>Epub</i>	<i>2012 (Currently in review)</i>			<i>Yes</i>

Also in the foreground of the INYVAX project is the Service Provider database. The development of this comprehensive database to collect the existing information will provide a tool to help the academic groups in the early phase of Good Laboratory Practice (GLP) production to develop transferable procedures for QC and vaccine specification, from the perspective of industrial scale-up, etc. has been foreseen as an asset for the European research vaccine community. This publically accessible database will form a network for all those involved in vaccine development throughout Europe and the

¹ A permanent identifier should be a persistent link to the published version (full text if open access or abstract if article is pay per view) or to the final manuscript accepted for publication (link to article in repository).

² Open Access is defined as free of charge access for anyone via the internet. Please answer "yes" if the open access to the publication is already established and also if the embargo period for open access is not yet over but you intend to establish open access afterwards.

world. This database will help academic vaccine developers, to find organisations to either build partnerships or to provide them with services as sub-contractors for developing their vaccine approach.

Section B – Confidential**LIST OF APPLICATIONS FOR PATENTS, TRADEMARKS, REGISTERED DESIGNS, ETC.**

Type of IP Rights: Patents, Trademarks, Registered designs, Utility models, etc.	Application reference(s) (e.g. EP123456)	Subject or title of application	Applicant (s) (as on the application)
<i>NA</i>	<i>NA</i>	<i>NA</i>	<i>NA</i>

OVERVIEW TABLE WITH EXPLOITABLE FOREGROUND

Exploitable Foreground (description)	Exploitable product(s) or measure(s)	Sector(s) of application	Timetable, commercial use	Patents or other IPR exploitation (licences)	Owner & Other Beneficiary(s) involved
<i>NA</i>	<i>NA</i>	<i>NA</i>	<i>NA</i>	<i>NA</i>	<i>NA</i>

4. Report on societal implications

A General Information <i>(completed automatically when Grant Agreement number is entered.)</i>		
Grant Agreement Number:	HEALTH- 2007-223532	
Title of Project:	INYVAX - Optimisation of the development of Poverty-Related-Diseases (PRD) vaccines by a transversal approach, addressing common gaps and challenges	
Name and Title of Coordinator:	Dr Odile Leroy, Executive Director EVI	
B Ethics		
1. Did you have ethicists or others with specific experience of ethical issues involved in the project?	<input checked="" type="radio"/>	<input type="radio"/>
	X	No
2. Please indicate whether your project involved any of the following issues:	tick box	
INFORMED CONSENT		
• Did the project involve children?		
• Did the project involve patients or persons not able to give consent?		
• Did the project involve adult healthy volunteers?		
• Did the project involve Human Genetic Material?		
• Did the project involve Human biological samples?		
• Did the project involve Human data collection?		
RESEARCH ON HUMAN EMBRYO/FOETUS		
• Did the project involve Human Embryos?		
• Did the project involve Human Foetal Tissue / Cells?		
• Did the project involve Human Embryonic Stem Cells?		
PRIVACY		
• Did the project involve processing of genetic information or personal data (eg. health, sexual lifestyle, ethnicity, political opinion, religious or philosophical conviction)		
• Did the project involve tracking the location or observation of people?		
RESEARCH ON ANIMALS		
• Did the project involve research on animals?		
• Were those animals transgenic small laboratory animals?		
• Were those animals transgenic farm animals?		
• Were those animals cloning farm animals?		
• Were those animals non-human primates?		
RESEARCH INVOLVING DEVELOPING COUNTRIES		
• Use of local resources (genetic, animal, plant etc)		
• Benefit to local community (capacity building ie access to healthcare, education etc)		
DUAL USE		
• Research having potential military / terrorist application		

C Workforce Statistics		
3 Workforce statistics for the project: Please indicate in the table below the number of people who worked on the project (on a headcount basis).		
Type of Position	Number of Women	Number of Men
Scientific Coordinator	1	
Work package leader	1	3
Experienced researcher (i.e. PhD holders)		
PhD Students		
Other	7	9
4 How many additional researchers (in companies and universities) were recruited specifically for this project?		
Of which, indicate the number of men:		
Of which, indicate the number of women:		

D Gender Aspects			
5	Did you carry out specific Gender Equality Actions under the project ?	<input type="radio"/> X	Yes No
6	Which of the following actions did you carry out and how effective were they?		
		Not at all effective	Very effective
	<input type="checkbox"/> Design and implement an equal opportunity policy	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/>
	<input type="checkbox"/> Set targets to achieve a gender balance in the workforce	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/>
	<input type="checkbox"/> Organise conferences and workshops on gender	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/>
	<input type="checkbox"/> Actions to improve work-life balance	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	<input type="radio"/>
	<input type="radio"/> Other: <input type="text"/>		
7	Was there a gender dimension associated with the research content – i.e. wherever people were the focus of the research as, for example, consumers, users, patients or in trials, was the issue of gender considered and addressed?		
	<input type="radio"/> Yes- please specify		
	X No		
E Synergies with Science Education			
8	Did your project involve working with students and/or school pupils (e.g. open days, participation in science festivals and events, prizes/competitions or joint projects)?		
	<input type="radio"/> Yes- please specify		
	X No		
9	Did the project generate any science education material (e.g. kits, websites, explanatory booklets, DVDs)?		
	X Yes- Modular course on use of Adjuvants (Deliverable D2.2), Inyvax database website		
	<input type="radio"/> No		
F Interdisciplinarity			
10	Which disciplines (see list below) are involved in your project?		
	X Health science 1.1		
	X Associated discipline Erreur ! Signet non défini.: 3.1	X	Associated discipline Erreur ! Signet non défini.: 3.3
G Engaging with Civil society and policy makers			
11a	Did your project engage with societal actors beyond the research community? (if 'No', go to Question 14)	<input type="radio"/>	Yes No
11b	If yes, did you engage with citizens (citizens' panels / juries) or organised civil society (NGOs, patients' groups etc.)?		
	X No		
	<input type="radio"/> Yes- in determining what research should be performed		
	<input type="radio"/> Yes - in implementing the research		
	<input type="radio"/> Yes, in communicating / disseminating / using the results of the project		

11c In doing so, did your project involve actors whose role is mainly to organise the dialogue with citizens and organised civil society (e.g. professional mediator; communication company, science museums)?	<input type="radio"/> <input type="radio"/>	Yes No	
12 Did you engage with government / public bodies or policy makers (including international organisations)			
<input type="radio"/> No <input type="radio"/> Yes- in framing the research agenda <input type="radio"/> Yes - in implementing the research agenda <input checked="" type="radio"/> Yes, in communicating /disseminating / using the results of the project			
13a Will the project generate outputs (expertise or scientific advice) which could be used by policy makers? <input type="radio"/> Yes – as a primary objective (please indicate areas below- multiple answers possible) <input checked="" type="radio"/> Yes – as a secondary objective (please indicate areas below - multiple answer possible) <input type="radio"/> No			
13b If Yes, in which fields?			
Agriculture Audiovisual and Media Budget Competition Consumers Culture Customs Development Economic and Monetary Affairs Education, Training, Youth Employment and Social Affairs	Energy Enlargement Enterprise Environment External Relations External Trade Fisheries and Maritime Affairs Food Safety Foreign and Security Policy Fraud Humanitarian aid	Human rights Information Society Institutional affairs Internal Market Justice, freedom and security Public Health Regional Policy Research and Innovation Space Taxation Transport	X
13c If Yes, at which level? <input type="radio"/> Local / regional levels <input type="radio"/> National level <input type="radio"/> European level <input checked="" type="radio"/> International level			

H Use and dissemination			
14	How many Articles were published/accepted for publication in peer-reviewed journals?	1 (two more in review)	
	To how many of these is open access³ provided?	3	
	How many of these are published in open access journals?	3	
	How many of these are published in open repositories?	3	
	To how many of these is open access not provided?	0	
	Please check all applicable reasons for not providing open access:		
	<input type="checkbox"/> publisher's licensing agreement would not permit publishing in a repository <input type="checkbox"/> no suitable repository available <input type="checkbox"/> no suitable open access journal available <input type="checkbox"/> no funds available to publish in an open access journal <input type="checkbox"/> lack of time and resources <input type="checkbox"/> lack of information on open access <input type="checkbox"/> other:		
15	How many new patent applications ('priority filings') have been made? <i>("Technologically unique": multiple applications for the same invention in different jurisdictions should be counted as just one application of grant).</i>	0	
16	Indicate how many of the following Intellectual Property Rights were applied for (give number in each box).	Trademark	0
		Registered design	0
		Other	0
17	How many spin-off companies were created / are planned as a direct result of the project?	0	
		<i>Indicate the approximate number of additional jobs in these companies:</i> 0	
18	Please indicate whether your project has a potential impact on employment, in comparison with the situation before your project:		
	<input checked="" type="checkbox"/> Increase in employment, or <input type="checkbox"/> Safeguard employment, or <input type="checkbox"/> Decrease in employment, <input type="checkbox"/> Difficult to estimate / not possible to quantify	<input type="checkbox"/> In small & medium-sized enterprises <input type="checkbox"/> In large companies <input checked="" type="checkbox"/> None of the above / not relevant to the project <input type="checkbox"/>	
19	For your project partnership please estimate the employment effect resulting directly from your participation in Full Time Equivalent (FTE = one person working fulltime for a year) jobs:	<i>Indicate figure:</i>	
	<i>X Difficult to estimate / not possible to quantify</i>		

³ Open Access is defined as free of charge access for anyone via the internet.

I Media and Communication to the general public	
20	As part of the project, were any of the beneficiaries professionals in communication or media relations? <input type="radio"/> Yes <input checked="" type="radio"/> No
21	As part of the project, have any beneficiaries received professional media / communication training / advice to improve communication with the general public? <input type="radio"/> Yes <input checked="" type="radio"/> No
22	Which of the following have been used to communicate information about your project to the general public, or have resulted from your project?
<input type="checkbox"/> Press Release	<input checked="" type="checkbox"/> Coverage in specialist press
<input type="checkbox"/> Media briefing	<input type="checkbox"/> Coverage in general (non-specialist) press
<input type="checkbox"/> TV coverage / report	<input type="checkbox"/> Coverage in national press
<input type="checkbox"/> Radio coverage / report	<input type="checkbox"/> Coverage in international press
<input checked="" type="checkbox"/> Brochures / posters / flyers	<input checked="" type="checkbox"/> Website for the general public / internet
<input type="checkbox"/> DVD /Film /Multimedia	<input type="checkbox"/> Event targeting general public (festival, conference, exhibition, science café)
23	In which languages are the information products for the general public produced?
<input type="checkbox"/> Language of the coordinator	<input checked="" type="checkbox"/> English
<input type="checkbox"/> Other language(s)	

Question F-10: Classification of Scientific Disciplines according to the Frascati Manual 2002 (Proposed Standard Practice for Surveys on Research and Experimental Development, OECD 2002):

FIELDS OF SCIENCE AND TECHNOLOGY

1. NATURAL SCIENCES

- 1.1 Mathematics and computer sciences [mathematics and other allied fields: computer sciences and other allied subjects (software development only; hardware development should be classified in the engineering fields)]
- 1.2 Physical sciences (astronomy and space sciences, physics and other allied subjects)
- 1.3 Chemical sciences (chemistry, other allied subjects)
- 1.4 Earth and related environmental sciences (geology, geophysics, mineralogy, physical geography and other geosciences, meteorology and other atmospheric sciences including climatic research, oceanography, vulcanology, palaeoecology, other allied sciences)
- 1.5 Biological sciences (biology, botany, bacteriology, microbiology, zoology, entomology, genetics, biochemistry, biophysics, other allied sciences, excluding clinical and veterinary sciences)

2. ENGINEERING AND TECHNOLOGY

- 2.1 Civil engineering (architecture engineering, building science and engineering, construction engineering, municipal and structural engineering and other allied subjects)
- 2.2 Electrical engineering, electronics [electrical engineering, electronics, communication engineering and systems, computer engineering (hardware only) and other allied subjects]
- 2.3 Other engineering sciences (such as chemical, aeronautical and space, mechanical, metallurgical and materials engineering, and their specialised subdivisions; forest products; applied sciences such as geodesy, industrial chemistry, etc.; the science and technology of food production; specialised technologies of interdisciplinary fields, e.g. systems analysis, metallurgy, mining, textile technology and other applied subjects)

3. MEDICAL SCIENCES

- 3.1 Basic medicine (anatomy, cytology, physiology, genetics, pharmacy, pharmacology, toxicology, immunology and immunohaematology, clinical chemistry, clinical microbiology, pathology)
- 3.2 Clinical medicine (anaesthesiology, paediatrics, obstetrics and gynaecology, internal medicine, surgery, dentistry, neurology, psychiatry, radiology, therapeutics, otorhinolaryngology, ophthalmology)
- 3.3 Health sciences (public health services, social medicine, hygiene, nursing, epidemiology)

4. AGRICULTURAL SCIENCES

- 4.1 Agriculture, forestry, fisheries and allied sciences (agronomy, animal husbandry, fisheries, forestry, horticulture, other allied subjects)
- 4.2 Veterinary medicine

5. SOCIAL SCIENCES

- 5.1 Psychology
- 5.2 Economics
- 5.3 Educational sciences (education and training and other allied subjects)
- 5.4 Other social sciences [anthropology (social and cultural) and ethnology, demography, geography (human, economic and social), town and country planning, management, law, linguistics, political sciences, sociology, organisation and methods, miscellaneous social sciences and interdisciplinary , methodological and historical S1T activities relating to subjects in this group. Physical anthropology, physical geography and psychophysiology should normally be classified with the natural sciences].

6. HUMANITIES

- 6.1 History (history, prehistory and history, together with auxiliary historical disciplines such as archaeology, numismatics, palaeography, genealogy, etc.)
- 6.2 Languages and literature (ancient and modern)
- 6.3 Other humanities [philosophy (including the history of science and technology) arts, history of art, art criticism, painting, sculpture, musicology, dramatic art excluding artistic "research" of any kind, religion, theology, other fields and subjects pertaining to the humanities, methodological, historical and other S1T activities relating to the subjects in this group] .