

ANNUAL REPORT 2010

EUROPEAN VACCINE INITIATIVE

FOR DONORS

*Today's
Catalyst For
Tomorrow's
Vaccines*



TABLE OF CONTENTS

LIST OF ABBREVIATIONS	2	PROJECTS FUNDED BY EC AND EDCTP	25
		EMVDA	25
FOREWORD BY THE EXECUTIVE DIRECTOR	5	IDEA	25
		INYVAX	26
EXECUTIVE SUMMARY	6	MVVC	27
		OPTIMALVAC	28
BRIEF HISTORICAL BACKGROUND	7	PHARVAT	29
		TRANSVAC	30
THE BURDEN OF THE DISEASES OF POVERTY	9	GOVERNANCE	32
CHAGAS DISEASE	9	THE DONORS	32
DENGUE	10	FULL MEMBERS	32
HIV/AIDS	11	ASSOCIATED MEMBERS	32
LEISHMANIASIS	12	EVI BOARD OF STAKEHOLDERS	33
MALARIA	12	EVI BOARD	33
TUBERCULOSIS	14	EVI SCIENTIFIC ADVISORY COMMITTEE	34
		EVI SECRETARIAT	35
THE YEAR IN GENERAL	15	INTERNATIONAL FORA	36
VACCINE PORTFOLIO	17	FINANCIAL UPDATE 2010	41
CALL POLICY	18		
CALLS	20	ACKNOWLEDGEMENTS	65
PUBLICATIONS	23		

LIST OF ABBREVIATIONS

ACT	Artemisinin Combination Drug Therapies
Ad	Adenovirus
AdCh	Simian adenovirus
AIDS	Acquired Immune Deficiency Syndrome
AMA	Apical Membrane Antigen
BC	Brighton Collaboration
BoS	Board of Stakeholders
BPRC	Biomedical Primate Research Centre
cGMP	current Good Manufacturing Practice
CoI	Conflict of Interest
CSP	Circumsporozoite Protein
DALY	Disability Adjusted Life Year
DANIDA	Danish Development Agency
DCGI	Drug Controller General of India
DGIS	Directorate General for International Cooperation (at Ministry of Foreign Affairs, The Netherlands)
DiCo	Diversity Covering
DKK	Danish Kroner
DNA	Deoxyribonucleic Acid
EC	European Commission
EDCTP	European and Developing Countries' Clinical Trials Partnership
EEA	European Economic Area
EEIG	European Economic Interest Grouping
EMVDA	European Malaria Vaccine Development Association
EMVI	European Malaria Vaccine Initiative (now European Vaccine Initiative)
EU	European Union
EVI	European Vaccine Initiative
FP6 & FP7	Framework Programme 6 & 7
GAAP	Generally Accepted Accounting Principles
HIV	Human Immunodeficiency Virus
ICGEB	International Centre for Genetic Engineering and Biotechnology
IDEA	African-European Research Initiative on Co-infections of Poverty Related and Neglected Infectious Diseases
IEC	Independent Ethics Committee
INCO DC	International Cooperation Research Programme with Developing Countries

INyVAX	Optimisation of the Development of Poverty Related Diseases Vaccines by a Transversal Approach, Addressing Common Gaps and Challenges
ISHReCA	Initiative to Strengthen Health Research Capacity in Africa
KEMRI	Kenyan Medical Research Institute
LMIC	Low and Middle Income Countries
LoI	Letter of Interest
MDG	Millennium Development Goal
MoU	Memorandum of Understanding
MRC	Medical Research Council
MSP	Merozoite Surface Protein
MVA	Modified Vaccinia Ankara
MVAF	Modern Vaccines/Adjuvants Formulation
MVI	Malaria Vaccine Initiative
MVVC	Malaria Vectored Vaccines Consortium
MVW	Malaria Vaccines for the World
NTD	Neglected Tropical Disease
OECD	Organisation for Economic Co-operation and Development
OPTIMALVAC	Initiative on Optimising Malaria Vaccine Lab Assays Evaluation
PHARVAT	Platform for the Harmonization of Vaccine Adjuvant Testing
PNL	Profit and Loss
PRD	Poverty Related Diseases
R&D	Research and Development
RI	Research Infrastructure
RNA	Ribonucleic Acid
SAC	Scientific Advisory Committee
Sida/SAREC	Swedish Development Agency/ Swedish Committee for Research on developing countries
SSI	Statens Serum Institut
TB	Tuberculosis
TBVI	TuBerculosis Vaccine Initiative
TRANSVAC	European Network of Vaccine Development and Research
USA	United States of America
WHO	World Health Organization
WP	Work Package



FOREWORD BY THE EXECUTIVE DIRECTOR

Our first full year as a legal entity in our own right (a European Economic Interest Grouping [EEIG]) has come to an end, and I can look back with great satisfaction, in the knowledge that the Board decision to create a legal identity has been fulfilled beyond what was originally envisaged. Four new members will be integrated into the EEIG, all prominent European institutions, which together with the two founding universities of Stockholm and Heidelberg, now form the base on which EVI rests. This process was a major success, and without doubt, the greatest achievement of 2010. The eagerness shown by the four new EEIG members - the Biomedical Primate Research Centre, Rijswijk, the Jenner Vaccine Foundation, Oxford, the Netherlands Vaccine Institute, Bilthoven, and the Royal College of Surgeons in Ireland, Dublin – to join the EEIG, bears witness to the credibility and standing of EVI, not just in the European scientific community, but in a global context. This is just the beginning, as the EEIG is open to all relevant and interested European Union (EU) Member State institutions/organisations. The scientific strengthening and broadening of the EVI base will undoubtedly make my position as Executive Director easier, not least in our efforts to find new donors.

In line with EVI's wider mandate, which covers diseases of poverty in low income populations, and our continuing ef-



orts to forge relationships with organisations and institutions, whose activities complement those of EVI, a Memorandum of Understanding (MoU) was signed during the year with TuBerculosis Vaccine Initiative (TBVI) in The Netherlands.

Another rewarding achievement in 2010 was the successful launch of the EVI coordinated TRANSVAC infrastructure project with 11 partners. The success of this far reaching four year project will exert a sustainable cohesive force on the fragmentation of European expertise and facilities, which in some case, can impede vaccine development. It is envisaged that the emerging infrastructure will continue to flourish long after the life of the TRANSVAC project. More information can be found on www.transvac.org

I extend warm thanks to colleagues, partners, donors and friends for their continued unwavering support throughout 2010, and I can look forward to 2011 in the knowledge that EVI stands on a firm scientific foundation from which it can continue to serve the millions of people so sorely in need of effective, affordable vaccines.

EXECUTIVE SUMMARY

The greatest achievement of EVI in 2010 was the start of the integration of four new institutions into the EEIG, which now comprises six members. It is most gratifying to experience the support provided by the enlargement of the EEIG. Having taken the first hurdle to legal identity in 2009, the second and third hurdles - the establishment of professional financial management, and the transfer of projects, contracts and activities from EMVI to EVI in 2010 – were also cleared successfully. EVI is now gaining pace and positioning itself for the challenging hurdles ahead.

EVI is continuing on the path set by EMVI, whose main achievement was to advance 10 vaccine candidates into phase I clinical trials, two of which have been transitioned to partners for further development in Africa.

EVI's core vaccine projects are all on track. The phase I clinical trial of JAIVAC-1 started in August at Lotus Labs Pvt. Ltd., Bangalore, India with no serious adverse events reported to date. The production process of AMA1-DiCo at Fraunhofer Institute, Aachen was scaled up to generate three

clinical batches, and production of P27A commenced at ALMAC.

Likewise, EVI's EC funded projects are running smoothly. The TRANSVAC kick-off meeting was held in January, a call for applications for access to the TRANSVAC infrastructure was launched in November, and TBVI joined the consortium. An important step was achieved on the INY-VAX project with the definition of the critical variables of the vaccine technologies' database, and the harmonisation of safety data collection and analysis for tuberculosis and malaria vaccines.

In October EVI organised a meeting of European Vaccine Stakeholders, bringing together manufacturers, biotechnology companies, public/academic researchers, and funding agencies to identify the needs and gaps in vaccine Research and Development (R&D) in Europe, and to prepare a road-map for vaccine R&D in the European Union.

A busy and rewarding year all in all.

BRIEF HISTORICAL BACKGROUND

In the mid-1990s, the European Commission's International Cooperation Research Programme with Developing Countries (INCO DC) realised that, in spite of decades of national and European Commission (EC) funding of malaria vaccine research, the prospects for the successful development of a European malaria vaccine were bleak. The INCO-DC Programme submitted a proposal to the EU Member States in February 1997. The proposal was approved by oral and written procedure, and led to the establishment of the European Malaria Vaccine Initiative (EMVI). EMVI officially commenced operations in March 1998.

In December 2009 EVI was registered as an independent European Economic Interest Grouping (EEIG) in Germany. Henceforth it will be known as the European Vaccine Initiative – EEIG (EVI). EVI will continue to build on the tremendous success of EMVI, thus contributing to the European Community's effort to combat poverty by improving the health of populations in resource-constrained countries, and so also contributing directly to the Millennium Development Goals.

The main objectives for which EVI was established are:

TO CONTRIBUTE to the global efforts to control diseases of poverty by:

- Creating an environment conducive to accelerating the development and clinical assessment of vaccine candidates for diseases of poverty;
- Promoting affordability and accessibility of vaccines for diseases of poverty in low income populations;
- Aligning all major stakeholders and acting as a focal point in order to ensure successful development of vaccine candidates for diseases of poverty-for low income populations;
- Communicating to the stakeholders and the general public the importance of EVI's mission, goals, and progress towards the deployment of affordable and efficacious vaccines for diseases of poverty.

TO PROVIDE:

- A mechanism to facilitate concerted interaction between EC core activities and EU Member States' investments;
- A mechanism to accelerate the process of bringing promising research results, i.e. experimental vaccines for diseases of poverty, via limited industrial production to clinical evaluation in European volunteers and subsequent clinical evaluation in close collaboration with clinical research networks in endemic areas.

TO BRIDGE:

- The conceptual and operational gaps between the bench product, i.e. candidate molecules, and further validation, limited production, and clinical testing, thus making further industrial development and production feasible. EVI shall position itself as the European Vaccines Development Agency for Diseases of Poverty, and be recognised as such by all stakeholders;
- To fund research and development, including clinical trials, with a supra national focus;
- To create a conducive technical and financial environment in which vaccine candidates for diseases of poverty can

be brought to clinical trials in humans, linking research, education and training, development, manufacturing and clinical trials expertise from both European and disease endemic countries;

- To improve the flow of information between the European scientific community, partners in Developing Countries, relevant organisations/institutions, and vaccine manufacturers (private and public), in order to facilitate co-operation;
- To provide a forum and networks to enhance general and political awareness of the importance of controlling diseases of poverty;
- To provide a forum for the EC and EU Member States' R&D Ministries/Agencies for consultation on the role and development of vaccines for diseases of poverty in the wider context of diseases control.



THE BURDEN OF THE DISEASES OF POVERTY

Diseases of Poverty are defined as diseases that are more prevalent in low income populations than in wealthier populations. They are both causes and consequences of poverty. The three most devastating diseases of poverty are Malaria, HIV/AIDS and Tuberculosis, but more than one billion people are affected by one or more of the Neglected Tropical Diseases (NTDs), so called as they persist exclusively in the poorest and the most marginalised communities, and have been largely eliminated elsewhere, and are thus often forgotten.¹

The past decade has seen unprecedented global investment in the control of these diseases, both in roll out of proven technologies and research into new interventions. There have been some successes, but perennial issues such as drug and insecticide resistance remain. Achieving significant, sustained reductions in disease burden and transmission, let alone elimination, will in most cases require an effective and affordable vaccine.

The challenges for development of vaccines for diseases of poverty are significant for researchers, donors and industry. EVI intends to continue the excellent work of EMVI by acting as a highly visible and dependable partner in the global fight against diseases of poverty.

The following list of diseases is not exhaustive, and the mandate of EVI covers all diseases of poverty.

CHAGAS DISEASE

Chagas Disease, also known as American Trypanosomiasis, is a parasitic disease mainly confined to the Americas and notably to Latin America. Increasing population mobility in past decades has led to the spread of the disease to other continents. Although the disease may be prevented by vector control, a large reservoir of the parasite in wild animals makes eradication impossible. The parasite's inherent capacity to evade the human immune system makes the development of vaccines difficult. New hopes focus on Deoxyribonucleic Acid (DNA) vaccines.

The disease is caused by a protozoan parasite, *Trypanosoma cruzi* (*T.cruzi*). The parasites are usually transmitted via the faeces of infected triatomine bugs, so called "kissing bugs" because of their tendency to suck blood on people's faces. *T.cruzi* can also be transmitted via blood transfusions.

The acute first phase is in the first weeks or months after infection, when a large number of parasites circulate in the blood, often only produces unspecific symptoms such as fever, headache, enlarged lymph glands, pallor, muscle pain, difficulty in breathing, swelling and abdominal or chest pain or vomiting. One characteristic marker, which appears in about 50% of infected people, is a skin lesion or purplish swelling of the eyelid on the side of the face near the bite wound. These symptoms usually resolve spontaneously. The infection persists and proceeds to the chronic phase, when the parasite is hidden in the heart and digestive muscle. Cell deaths in these target tissues lead to inflammation and cellular lesions caus-

¹ Ten Facts on Neglected Tropical Diseases, TDR, WHO DATE

ing cardiac and digestive disorders in about 40% of patients. Progressive damage to the heart muscle may ultimately lead to heart failure and sudden death.

About 10 million people living in Latin American countries are affected, with an additional estimated 400,000 living in non-endemic countries such as Spain and the United States of America (USA). Each year there are an estimated 40,000 new infections and 20,000 deaths attributed to Chagas disease.

Chagas disease can be effectively treated with benznidazole and nifurtimox when administered soon after infection, but efficacy of the treatment diminishes rapidly with time. Neither medicines are suitable for pregnant women or people with kidney or liver failure. Nifurtimox is also not indicated for people with neurological disorders. The current and most effective methods for prevention of the disease are vector control by insecticide spraying, bednets or house improvements to exclude the vector, and blood screening. There is no vaccine against Chagas disease at present, but recently the potential of DNA vaccines for immunotherapy of acute and chronic Chagas disease is being tested by several research groups.

DENGUE

Dengue has spread rapidly across tropical and sub-tropical urban and semi-urban areas in the past 50 years, driven by urbanisation and population growth. Up to 40% of the world's population (2.5 billion people), are now at risk in over 100 countries. Hopes for a vaccine are high but natural immunity to the four viral serotypes is complex and poorly understood. Infection with one of these serotypes provides immunity to only that serotype for life, so persons living in a

dengue-endemic area can experience more than one dengue infection during their lifetime. The lack of an animal model for the disease is also a barrier to the development of an effective vaccine.

The agent of dengue is a flavivirus, a Ribonucleic Acid (RNA) virus of the kind that causes yellow fever, transmitted in the saliva of infected biting *Aedes* mosquitoes, most commonly *Aedes aegypti*.

Dengue fever is a severe flu-like illness which presents as a 'fever-arthralgia-rash' syndrome, sometimes with mild internal/external bleeding.

Severe dengue known as Dengue Haemorrhagic Fever (World Health Organization (WHO) now recommends that dengue be classified as 'dengue fever' for the mild forms and 'severe dengue' for the more severe forms) causes severe internal/external bleeding, serious dysfunction of organs, and - most seriously - circulatory failure. Such 'dengue shock syndrome' tends to affect children in Asia but all ages in the Americas. It can kill within hours of the onset of symptoms.

Although recovery from infection confers lifelong immunity to the same viral serotype, of concern to vaccine developers is the fact that infection may also sensitise patients to severe disease in a subsequent infection with a different serotype. Thus any dengue vaccine must confer protection against all serotypes.

Each year there are an estimated 50 million dengue infections, some 500,000 hospital cases and 15,000-20,000 deaths, pri-

marily in Asia, the Western Pacific and the Americas. Hospital costs alone run to an estimated US\$ 440 million a year.

Dengue, including epidemics of severe disease, is a major public health problem and a significant economic and social burden in many countries. In 2004, dengue was responsible for 663,000 Disability Adjusted Life Years (DALYs) and 18,000 deaths ranking as the 10th highest cause of mortality from NTDs.²

No medications or vaccines are available for treatment or prevention of dengue. Vector control, including elimination of mosquito breeding sites, has not halted the rise of the disease, and a cost effective vaccine is needed.

A dengue vaccine might appear an easy goal: the virus is simple and a vaccine against yellow fever is already available. A dengue vaccine would mimic natural immunity and elicit protective antibodies to neutralise the virus. However, a vaccine needs to induce simultaneous protection against all four dengue viral serotypes, or risk sensitizing people to severe disease. Other challenges are the poor understanding of how natural immunity works, and the lack of a good animal model.³

Hiv/Aids

Human Immunodeficiency Virus / Acquired Immunodeficiency Syndrome (HIV/AIDS) still represents one of the most severe public health burdens in low and middle income countries. According to Uniting the World against AIDS (UNAIDS) an estimated 33.4 million people were living with HIV at the end of 2007⁴, with 2.7 million new infections, and two million deaths every year from AIDS. Two

thirds of HIV infections are in sub-Saharan Africa, and the disease is considered pandemic by WHO. With no cure for AIDS, research into an HIV vaccine is one of several approaches to reduce the global burden of AIDS, in addition to antiviral treatment and the promotion of safe sex.

HIV is a complex retrovirus that is transmitted mainly through unprotected sexual relations, when infected sexual secretions of one partner enter in contact with mucous membranes of the other partner. It can also be transmitted by infected blood coming into contact with an open wound, e.g. blood transfusions or the reuse of hypodermic needles. The virus may also be transmitted from mother to child during pregnancy, at childbirth, or in breast milk.

HIV infects key immune cells such as CD4 T Helper cells, macrophages and dendritic cells. After a short acute phase, characterised by influenza-like symptoms, the disease enters a latent phase, on average nine to eleven years, during which, without causing symptoms, the virus slowly replicates. The increasing virus load leads to a progressive destruction of the immune system, ultimately permitting the appearance of so-called opportunistic infections or HIV-related cancers, such as Kaposi's sarcoma. The presence of any of more than 20 characteristic signs/symptoms is the basis for the diagnosis of AIDS. Most patients die from opportunistic infections or malignancies. The largest cause of AIDS morbidity today is tuberculosis co-infection.

A variety of vaccine strategies are currently in development and several are in clinical trials. There is no effective vaccine to date.

2 G-Finder 2008

3 Guidelines for diagnosis, treatment, prevention and control - New edition, Geneva: WHO/TDR, 2009

4 www.who.int/hiv/data/2009_global_summary.gif

LEISHMANIASIS

Leishmaniasis affects mainly the poor and occurs in India, Bangladesh, Peru, Nepal, Ethiopia, Sudan and Brazil, with increasing resistance to existing treatments, and no new drugs at advanced stages of development. No vaccine has ever been developed for Visceral Leishmaniasis.

Leishmaniasis infection is caused by the *Leishmania* protozoan parasites. Transmission is by the bite of the female vector phlebotomine sandfly, which becomes infected by biting and sucking blood from a person or animal infected with the leishmania parasite.

Infection with *Leishmania* manifests itself in various forms; cutaneous, mucocutaneous and visceral, the latter being the most severe form of the disease. Cutaneous infection is most common with numerous ulcers developing on exposed parts of the body (face, arms, and legs). The healing ulcers leave permanent scars on the affected areas of the body. Mucocutaneous infection results in destruction of the mucous membranes of the nose, mouth and throat. Symptoms of Visceral Leishmaniasis (Kalar-Azar) include irregular bouts of fever, enlargement of the liver and spleen, marked weight loss and if left untreated can lead to death. In general, Leishmaniasis infection is associated with pain, debilitating illnesses, permanent scarring, social rejection and death.

Over 300 million people are at risk with 12 million people believed to be currently infected. Approximately 70,000 deaths in children and young adults occur annually. Visceral Leishmaniasis ranks second only to malaria for mortality, and is one of the top ten infectious diseases globally for DALYs lost.⁵

5 WHO World Health Report 2002

There are currently no vaccines for the treatment or prevention of Leishmaniasis. With the development of a marked resistance to available drugs, the development of a vaccine needs to be accelerated. Efforts at developing an effective vaccine have recently been given prominence by WHO. However, difficulties arise in inducing the strong Th1-type cytokine immune responses, which is required, as it is known that Th2-type responses are induced in chronic Leishmaniasis.

MALARIA

Malaria has long been an entrenched and debilitating feature of the tropical landscape. Efforts to develop a vaccine have a winding and rather chequered history, but during the past decade a concerted international effort is now finally coming to fruition. Increased funding by private and governmental organisations has resulted in accelerated clinical development of malaria vaccine candidates targeting various stages of the malaria parasite life cycle.

Malaria is caused by four species of the single-celled parasite *Plasmodium*, which has a complex life cycle in humans, passing initially through the liver, but causing all its clinical effects when it enters the bloodstream and destroys red blood cells. Transmission of *Plasmodium* is by a vector female *Anopheles* mosquito feeding on the blood of an infected human and transferring the disease when biting another human.

The impact of malaria in sub-Saharan Africa, where the most lethal form *Plasmodium falciparum* is found, is mainly on children under five (90% of cases worldwide), and pregnant women, particularly in poor rural areas. In its rarer severe

form, malaria can cause coma, respiratory distress, metabolic disorders and severe anaemia. For those who survive, impaired learning or neurological deficits are common, although natural immunity is also gradually built up. Pregnant women and their unborn children suffer from maternal anaemia, low birth weight, prematurity and neonatal deaths. The burden of *P. vivax* malaria, particularly in Asia, is also becoming increasingly apparent.

There are an estimated 350-500 million malaria episodes every year, in more than 100 countries covering more than 40% of the world population.⁶ Malaria is estimated to cost sub-Saharan Africa US\$ 12 billion in Gross Domestic Product every year, and to restrict economic growth by 1.3% per year. Malaria is thus both a cause and a consequence of poverty.⁷

Current malaria control methods, notably new Artemisinin-based Combination Drug Therapies (ACTs), insecticide-treated nets and residual spraying, have led to reduced disease burdens in some countries. However, *P. falciparum* is already showing signs of resistance to ACTs and the mosquito has historically always developed resistance to insecticides. A partially effective vaccine could reduce the global disease burden, but only a highly effective vaccine would offer the prospect of malaria elimination. Approaches to malaria vaccine development target various stages in the parasite life cycle:

- Pre-erythrocytic vaccines target the early stage when the parasite enters the liver
- Asexual blood-stage vaccines aim to reduce infection of red blood cells and consequently prevent clinical disease
- Transmission-blocking vaccines could prevent the parasite from maturing in the mosquito. They would need to be

combined with another type of vaccine to protect the vaccinated individual.

Recent advances in the understanding of malaria in pregnancy also give hope that a vaccine specifically targeting malaria infection of the placenta is feasible.⁸

With a child dying every 30 seconds of malaria in Africa (WHO, 2009), the need for an effective malaria vaccine cannot be over stressed. The first generation malaria vaccine, RTS,S, although the clinically most well advanced of current malaria vaccine candidates, will, according to WHO, need further clinical development as a second generation malaria vaccine, combining different antigens linked to the various stages of the parasite life cycle, to achieve the 80% level of efficacy necessary to combat Malaria. Such a vaccine could prevent 5,482 deaths per 100,000 children vaccinated, leading to a 66% reduction in malaria deaths worldwide, and a saving of 193,926 DALYs. At a cost of US\$14/DALY this would be a manifest economic bonus.

EVI is leading the way in Europe in its efforts to de-



6 Robert W. Snow, Carlos A. Guerra, Abdulsalan M. Noor, Hla Y. Myint & Simon I. Hay. The global distribution of clinical episodes of *Plasmodium falciparum* malaria. *Nature* 434, 214-217 10 March 2005

7 Jeffrey Sachs & Pia Malaney. The economic and social burden of malaria. *Nature* 415, 680-685 7 February 2002

8 Stephen M. Todryk & Adrian V. S. Hill. Malaria vaccines: the stage we are at. *Nature Reviews Microbiology* 5, 487-489 1 July 2007

velop an improved malaria vaccine. The fight against malaria is far from over, and hard work and vigilance lie ahead if this vicious disease is to be overcome. Time is of the essence.

TUBERCULOSIS

Tuberculosis (TB) is the leading cause of death among treatable infectious diseases. TB occurs more frequently in poor regions of world which suffer malnutrition, general poor health, and social disruption.

Tuberculosis is caused by the gram-positive, slow-growing, intracellular bacterium, *Mycobacterium tuberculosis*, which was first isolated in 1882 by a Robert Koch who received a Nobel Prize for his discovery.

TB normally causes pulmonary infections, which is the only infectious form of TB. Transmission occurs through inhalation of infectious droplets dispersed through coughing. TB is normally treated with a combination of specific antibiotics and Directly Observed Treatment Short (DOTS)-course, and is the strategy recommended by WHO. Treatment must be continued for at least six months to be effective. Untreated active cases of TB can infect 10-15 people per year.⁹ The emergence of new strains of drug-resistant *M. tuberculosis* has become a major concern especially in countries of South East Asia and within prison populations. Multidrug-resistant tuberculosis refers to strains resistant to at least two of the first-line drugs, isonicotinyhydrazine (INH) and Rifampicin. Today extensively drug resistant strains, resistant to three or more of the second-line treatment drugs, are found most frequently in the countries of the former Soviet Union and Asia.

There are approximately nine million new cases and two million deaths (1.3 million in 2008) caused by TB infection each year. It is especially prevalent in sub-Saharan Africa and in South East Asia (30% and 34% of global total respectively), and incidence of the disease is higher in Eastern Europe than in Western Europe.

Approximately 70-80% of people who are given the Bacillus Calmette-Guérin (BCG) vaccine are protected against TB. However, in many places vaccination is no longer routinely given as part of childhood immunisation schedules. Although the vaccine provides some protection against severe forms of paediatric TB, it has been shown to be unreliable against adult pulmonary TB, which causes the most disease worldwide. A more effective vaccine that would prevent all forms of TB, including drug resistant strains, in all age groups and among people with HIV is needed urgently. Several new vaccines are being developed using a number of approaches including recombinant vaccines, DNA vaccines, and a TB vaccine, MVA85A, based on a genetically Modified Vaccinia Virus (MVA) developed by the University of Oxford. This vaccine is currently undergoing phase II clinical trials in South Africa. Other strategies being used include sub-unit vaccines such as Hybrid-1, HyVac4, or M72, and recombinant adenoviruses (Ad) such as Ad35.

THE YEAR IN GENERAL

2010 was the first full year for EVI as a legal entity in its own right in its new head quarters at UniversitätsKlinikum, Heidelberg, with whom a hosting agreement has been signed. As such the year could be characterised as a period of settling into this new role in a new country. Not only does EVI have a wider scope, which now includes diseases of poverty other than malaria, EVI is also financially independent with all the responsibilities this implies. Hot news travels fast, and no sooner had EVI been established, than several institutions expressed interest in joining the EEIG that EVI has become. At a Board teleconference in October new Statutes and Rules of Procedure were approved, as well as the integration of the following institutions: the Biomedical Primate Research Centre (BPRC), the Jenner Vaccine Foundation, the Netherlands Vaccine Institute (NVI), and the Royal College of Surgeons in Ireland (RCSI). Together with the founding universities of Stockholm and Heidelberg EVI-EEIG now will comprise six institutions.

Funds related to specific projects were transferred during the year from Statens Serum Institut (SSI), and it is anticipated that the remaining funds will be transferred during the second quarter 2011. As such no new calls were issued in 2010. Please see Financial Update for further details.

A MoU was signed during the year with TBVI.

Due to the pressure of the transition from EMVI to EVI and the move from Denmark to Germany, a firm of consultants has been engaged to draw up a new five year strategy plan

2011 – 2015, which will be put to the Board for approval during the first quarter 2011.

Manta Ray Media, a London based company who focus on international health, was engaged to develop the new web site for EVI, and other project specific web sites, with emphasis on easy access, and a common Content Management System (CMS). The EVI web site www.euvaccine.eu was launched in October, and we hope you have already found it useful and informative. The other web sites are expected to be launched early in the new year. A web based solution for document management is also being investigated with Manta Ray Media, along with a more traditional document management solution with another company.



Several new employees joined EVI during the first part of the year. Sophie Houard took up the position of Product Manager on 4 January, and on the same day Sharmila Bakshi started as Project Manager for the European and Developing Countries' Clinical Trials Partnership (EDCTP) financed project: Malaria Vectored Vaccines Consortium (MVVC). In March Sonja Noss joined EVI as Trainee Project Manager for the EC funded project European Network of Vaccine Research and Development (TRANSVAC), and Elfi Bihler commenced duties as Odile Leroy's sorely needed Personal Assistant. During the year Nathalie Imbault was promoted to Quality Assurance and External Communications Manager and became part of the Senior Management team, and Regitze Thøgersen became Programme Manager with responsibility for TRANSVAC. In September a four day team building exercise was held in Iceland, which apart from the professional benefits, provided the staff, most of whom work alone in various countries, with an excellent opportunity to get to know each other better.

Team Building, Iceland September 2010



A hand book has been developed to aid staff in all matters related to their employment with EVI. Senior staff meetings are held on a regular basis, either as face to face meetings in Heidelberg or via teleconferences.

A European Vaccine Stakeholders meeting was held in Brussels in October, and recommendations in the report will be addressed by TRANSVAC working groups. A face to face EVI Scientific Advisory Committee (SAC) portfolio review meeting was held in Heidelberg in April, at which Roland Dobbelaer took over Chairmanship from Samuel McConkey, and Alister Craig was elected Vice Chair. This was followed shortly after by a meeting in Paris, to develop the questionnaire and define stakeholders to be interviewed by the consultant engaged to draft the strategy plan. One Board teleconference was held in October at which Ingileif Jónsdóttir and Mahamadou Thera were approved as new EVI SAC members after the departure of Marita Troye-Blomberg and Peter Kremsner last year.

VACCINE PORTFOLIO

As EVI's mandate only covers early clinical development, success can be measured by the fact that the clinical development of two malaria vaccine candidates (MSP3 and GMZ2) has been continued by other agencies into phase II clinical trials in Africa.

Since 2007 no fewer than eight EC calls under Framework Programmes FP6 and FP7, and two EDCTP calls have been responded to (as coordinator in all but two), the majority

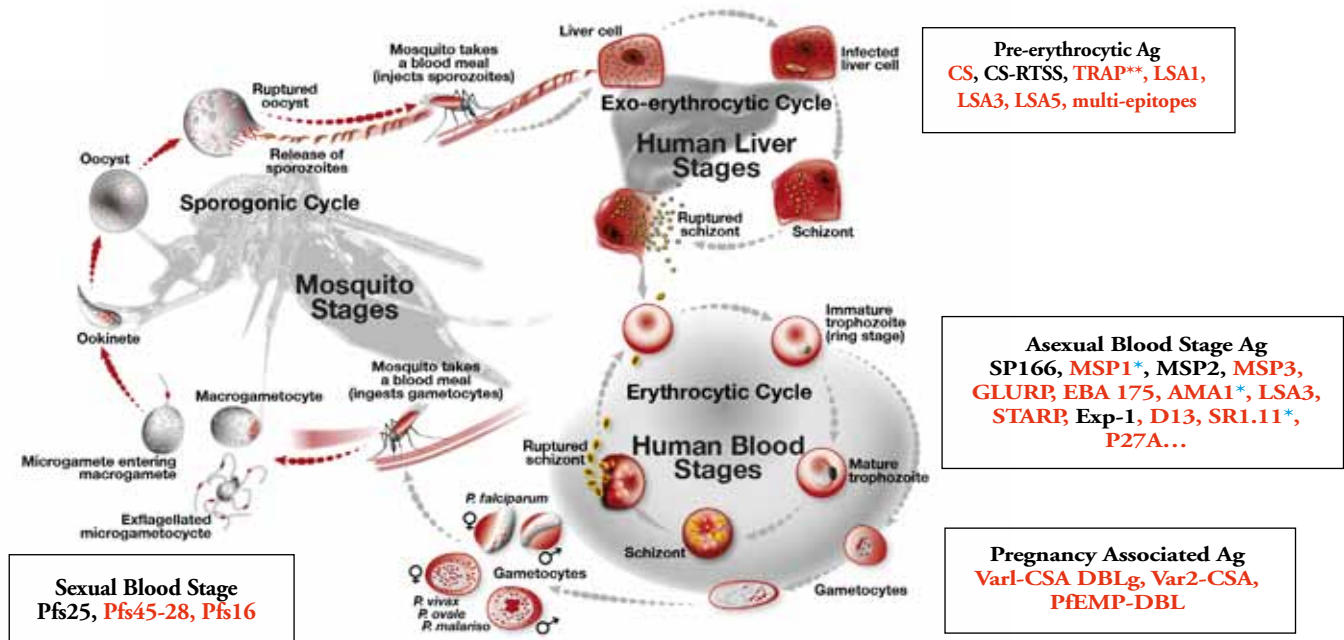
of which address the growing international awareness of the importance of standardisation, harmonisation and coordination within the world of vaccine development.

The EVI vaccine portfolio will continue to expand during the coming years to also include development of vaccines for diseases of poverty. EVI is now recognised by the EC and the European scientific community as the major collaborator for development of vaccines for diseases of poverty; no longer confined to malaria vaccines.

EVI IS LEADING THE WAY IN EUROPE

Malaria Antigens developed by EVI (in red) and funded by EC (*) and EDCTP (**) since 1998, and their target stage

Cycle of Plasmodium



CALL POLICY

EVI's first call is planned for the end of 2011. EMVI issued six open calls between 1998 and 2010. Unsolicited proposals, received by members of the Board of EVI, the Secretariat or the EVI SAC, are subject to the same evaluation procedure as detailed below. Today EVI SAC is involved in the design and text for calls for Letters of Interest (LoI) and/or Proposals. Receipt of LoI/Proposals is acknowledged in writing. At the same time applicants are also provided with the eligibility check procedure, the Conflict of Interest form (CoI) and policy, the Confidentiality Agreement, and the evaluation procedure as background information. After the eligibility check all proposals are forwarded to all EVI SAC members together with the CoI form. Each LoI/Proposal is evaluated by minimum three EVI SAC members, one of which is nominated as rapporteur. Standardised evaluation/rapporteur forms are used, and each EVI SAC member receives the forms relevant to the proposals she/he is to evaluate. Proposals are rated under the headings: originality, scientific significance, clarity, adequacy, feasibility, overall judgement. Numerical ratings are used where helpful. EVI SAC recommendations to the Board of EVI are normally based on written consensus. In the event of widely divergent opinions, additional expertise can be sought. Final approval of EVI SAC recommendations rests with the Board of EVI.

EVI SAC members sign EVI's Confidentiality Agreement.

Please also refer to www.euvaccine.eu/calls-grants and grants for additional information.

EVI FUNDED PROJECTS AND STATUS AT THE END OF 2010

EVI Projects	Process Development	Pilot phase Technology transfer	GMP batch production Formulation	Quality Control Pharmacotoxicology	Regulatory & Ethical Dossier	Phase Ia	Phase Iia	Phase Iib	Phase Iib
AMA1 (AdCh63 and MVA)*	█	█	█	█	█	█			
AMA1-alum	█	█	█	█	█	█	none	█	
AMA1-AS02	█	█	█	█	█	█			
AMA1-DDA-TDB	█	█	█	▧					
AMA1-DiCo	█	█	█						
AMA1-ISA 720	█	█	█	█	█	█			
CSP (AdCh63 and MVA)	█	█	█						
GLURP-alum	█	█	█	█	█	█			
GLURP-ISA 720	█	█	█	█	█	█			
GMZ1	█	█	█	▧					
GMZ2-alum	█	█	█	█	█	█	none	█	█
GMZ2-DDA-TDB	█	█	█	▧					
JAIVAC-ISA 720	█	█	█	█	█	█			
ME-TRAP (AdCh63 and MVA)**	█	█	█	█	█	█	█	█	
MSP1 full size*	█	█	█						
MSP1 (AdCh63 and MVA)*	█	█	█	█	█	█			
MSP3-alum	█	█	█	█	█	█	none	█	█
MSP3-ISA 720	█	█	█	█	█	█			
P27A	█	█	█						
pf45/48	█	▧							
Polyprotein	█	█	█	█	█	█	█	█	
SR11.1*	█	█							
Var CS2A	█	▨							
Var CS2A-DBL-X	█	▨							

* EMVDA funded project
 ** EDCTP funded project

█ Preclinical stage

█ Clinical stage

▧ Projects terminated

▨ Projects transferred

Calls

Call 2000 *Apical Membrane Antigen PfAMA1 in the P. pastoris system*
(first generation)

Funding of AMA1 first generation was discontinued by EVI in 2008 to pursue the Diversity Covering (DiCo) approach which addresses the allele diversity.

PfAMA1 [25-545](DiCo) in the P. pastoris system – second Generation

Inventor: Clemens Kocken (BPRC, The Netherlands)
Project Team Leader: Nicolas Havelange (EVI)
Product Manager: Sophie Houard (EVI)
Process Development: Fraunhofer Institute IME
Manufacturer: Fraunhofer Institute IME

Product Development

Process development has been completed prior to the transfer to current Good Manufacturing Practice (cGMP) production at the Fraunhofer Institute in Aachen. The production process to generate the three DiCo versions of the AMA1 protein has been developed to allow sufficient yield in a stable format of the three proteins to be obtained. In 2010, the production process has been scaled-up and applied in cGMP conditions to generate clinical batches. Clinical batch release of the product is expected in Q2 2011.

Clinical Development

The selection of the investigational site will be completed in Q1 2011 and the phase I clinical trial is planned to start in Q3 2011.

Call 2002 *Combination vaccine based on PfMSP1-19 and Pff2 (EBA 175) JAIVAC-1 in the E. coli expression system*

Inventor: Dr. Chetan Chitnis, Dr. Virander S. Chauhan (ICGEB, New-Delhi, India)
Project Team Leader: Nathalie Imbault (EVI)
Product Leader: Dr. Syed Shams Yazdani (ICGEB, New-Delhi, India),
Manufacturer: Bharat Biotech, Hyderabad, India
Clinical Trial Principal Investigator: Dr. Sandhya Ravi (Lotus Labs Pvt. Ltd., Bangalore, India)
Clinical Trial Management: DiagnoSearch Life Sciences, Mumbai, India

Product Development

Production of three consistency batches by Bharat Biotech, sub-contracted by International Centre for Genetic Engineering and Biotechnology (ICGEB) was completed in December 2007, and the toxicology report was compiled in March 2009 by Intox Pvt. Ltd., Pune, India.

Clinical Development sponsored by ICGEB and EVI

A Phase I, Randomised, Controlled, Dose-Escalating, Single-Blind Clinical Trial to Evaluate the Safety and Immunogenicity of JAIVAC-1 Vaccine (rPpfMSP) -119 and rPpf2) Formulated with Montanide ISA720 in Healthy Indian Males between 18 to 45 Years of Age

The Investigational New Drug (IND) application was made to the Drug Controller General of India (DCGI). The DCGI authorised the clinical trial on 28th April 2010. The Institutional Review Board (IRB) of ICGEB and the Independent Ethics Committee (IEC) of Lotus Labs approved the clinical trial on 7th January and 16th April respectively. The clinical trial started in August 2010 at Lotus Labs Pvt. Ltd., Bangalore, India.

As at the end of the year 45 subjects have been included, who have already received the two-dose primo-vaccination. No serious adverse event has been reported so far.



Call 2007

A circumsporozoite protein vaccine against malaria using the adenovirus Ch63 and MVA vectors: preclinical and phase I safety and immunity studies, CSVAC.

Inventor: Adrian Hill (University of Oxford, UK)
Project Team Leader: Babatunde Imoukhuede (EVI)
Project Manager: Regitze Louise Thøgersen (EVI)
Manufacturer: IDT Biologika Germany and Vivant, USA

Product Development

In July 2009, EVI and the University of Oxford signed a contract for cGMP manufacture and phase I clinical trial of malaria vaccine candidates utilising the Circumsporozoite protein (CSP) antigen vectored by MVA and simian Adenovirus (AdCh). The clinical batch of the CSP vectored MVA vaccine candidate was released in November 2010. For the AdCh63 vectored vaccine candidate, the cGMP production is planned for Q2 2011, with the Quality Control release in Q3-Q4 2011. Toxicology studies are planned for Q2-Q3 2011. Clinical batches should then be ready for the phase I clinical trial in Q1 2012.

Call 2008

Evaluation of the Vaccine Potential of the Fragment P27A of the Novel Malaria Protein

Inventor: Giampietro Corradin (University of Lausanne, Switzerland)
Project Team Leader: Nicolas Havelange (EVI)
Product Manager: Sophie Houard (EVI)
Project Manager: Agnes Kisser (EVI)
Manufacturer: Almac Sciences, UK

Product Development

Production of the P27A peptide vaccine in cGMP conditions is currently ongoing at Almac. A clinical batch is expected to be released in Q2 2011.

Clinical Development

The selection of the investigational site has been completed in Q4 2010, the contract negotiation with the selected sponsor and investigational site is ongoing and the phase I clinical trial is planned to start in Q3 2011.

Unsolicited approach 2009

Development and complete Phase I testing of a thermostable (cGMP) polyvalent meningococcal conjugate vaccine over a five year period

Received from: WHO and PATH (Meningitis Vaccine Project)

The EVI SAC has reviewed the project and has recommended funding provided sufficient funds are available.

PUBLICATIONS

Audran R, Cachat M, Lurati F, Soe S, Leroy O, Corradin G, Druilhe P, Spertini F. Phase I malaria vaccine trial with a long synthetic peptide derived from the merozoite surface protein 3 antigen. *Infect Immun*. 2005 Dec;73(12):8017-26. **(MSP3-LSP)**

Druilhe P, Spertini F, Soesoe D, Corradin G, Mejia P, Singh S, Audran R, Bouzidi A, Oeuvray C, Roussillon C. A malaria vaccine that elicits in humans antibodies able to kill *Plasmodium falciparum*. *PLoS Med*. 2005 Nov;2(11):e344. **(MSP3-LSP)**

Dahlbäck M, Rask TS, Andersen PH, Nielsen MA, Ndam NT, Resende M, Turner L, Deloron P, Hviid L, Lund O, Pedersen AG, Theander TG, Salanti A. Epitope Mapping and Topographic Analysis of VAR2CSA DBL3X Involved in *P. falciparum* Placental Sequestration. *PLoS Pathogens*. 2006 Nov;2(11):e124 **(VAR2CSA DBL3X)**

Sirima SB, Nébié I, Ouédraogo A, Tiono AB, Konaté AT, Gansané A, Dermé AI, Diarra A, Ouédraogo A, Soulama I, Cuzzin-Ouattara N, Cousens S, Leroy O. Safety and immunogenicity of the *Plasmodium falciparum* merozoite surface protein-3 long synthetic peptide (MSP3-LSP) malaria vaccine in healthy, semi-immune adult males in Burkina Faso, West Africa. *Vaccine*. 2007 Mar 30;25(14):2723-32. **(MSP3-LSP)**

Hermsen CC, Verhage DF, Telgt DS, Teelen K, Bousema JT, Roestenberg M, Bolad A, Berzins K, Corradin G, Leroy O, Theisen M, Sauerwein RW. Glutamate-rich protein

(GLURP) induces antibodies that inhibit in vitro growth of *Plasmodium falciparum* in a phase I malaria vaccine trial. *Vaccine*. 2007 Apr 12;25(15):2930-40. **(GLURP-LSP)**

Benoit G, Smith JD, Viebig NK, Gysin J, Scherf A. Pregnancy-associated malaria: Parasite binding natural immunity and vaccine development. *International Journal for Parasitology*. 2007; 273-83. **(Var2-CSA DBL3-X)**

Nielsen MA, Resende M, Alifrangis M, Turner L, Hviid L, Theander T, Salanti A. *Plasmodium falciparum*: VAR2 CSA expressed during pregnancy-associated malaria in partially resistant to proteolytic cleavage by trypsin. *Experimental Parasitology*. 2007; 117: 1-8 **(VAR2 CSA)**

Fernandez P, Viebig NK, Dechavanne S, Lépolard C, Gysin J, Scherf A, Gamain B. Var2CSA DBL6-epsilon domain expressed in HEK293 induces limited cross-reactive and blocking antibodies to CSA binding parasites. *Malaria Journal*. 2008; 7:170 **(Var2CSA DBL6-epsilon)**

Faber BW, Remarque EJ, Kocken CH, Cheront P, Cingolani D, Xhonneux F, Jurado M, Haumont M, Jepsen S, Leroy O, Thomas AW. Production, quality control, stability and pharmacotoxicity of cGMP-produced *Plasmodium falciparum* AMA1 FVO strain ectodomain expressed in *Pichia pastoris*. *Vaccine*. 2008 Nov 11;26(48):6143-50 **(AMA1 FVO)**

Roestenberg M, Remarque E, de Jonge E, Hermsen R, Blythman H, Leroy O, Imoukhuede E, Jepsen S, Ofori-Anyinam O, Faber B, Kocken CHM, Arnold M, Walraven

V, Teelen K, Roeffen W, de Mast Q, Ballou WR, Cohen J, Dubois MC, Ascarateil S, van der Ven A, Thomas A, Sauerwein R. Safety and Immunogenicity of a Recombinant *Plasmodium falciparum* AMA1 Malaria Vaccine Adjuvanted with Alhydrogel™, Montanide ISA 720 or ASO2. PLoS ONE. 2008 Dec; 3(12):e3960. (AMA1)

A Phase I Study to Assess the Safety and Immunogenicity of the Polyprotein Malaria Vaccine Candidates Fp9 PP and MVA PP in Health Adults Using a Prime Boost Delivery Schedule. And Assessment of protection against malaria by sporozoite challenge of healthy adults vaccinated with the polyprotein malaria vaccines “FP9-PP and MVA-PP” and control non-vaccinated volunteers.

A paper is under final review by Vaccine (FP9 PP and MVA PP).



PROJECTS FUNDED BY EC AND EDCTP

EMVDA

The European Malaria Vaccine Development Association (EMVDA) is a five year project funded under EC's FP6, with fifteen consortium members and coordinated by EVI, was signed in April 2007 with a budget of €13,500,000.

EMVDA seeks to accelerate the development of a vaccine to reduce the global burden of malaria by facilitating the combination of resources of leading European research laboratories and bringing an innovative vaccine development infrastructure to Europe. Further, EMVDA complements and supports African efforts in malaria vaccine development through research partnerships and training for African scientists.

In order to most efficiently exploit Europe's fundamental malaria scientific research capacity, EMVDA unites the capabilities of fifteen partners dedicated to the advancement of preclinical malaria vaccine candidates through current cGMP production and early stage clinical trials.

Over the past three years, EMVDA has made impressive progress by moving a substantial number of vaccine candidates along the pipeline.

The first EMVDA funded vaccine candidates were MSP1 (AdCh63 and MVA) and AMA1 (AdCh63 and MVA), which commenced development in late 2008 and early 2009 respectively. These vaccine candidates consist of inactivated viruses - simian adenovirus (AdCh63) or MVA - which have been engineered to include genes encoding the malaria pro-

teins merozoite surface protein-1 (MSP1) or apical membrane antigen-1 (AMA1). After successful completion of cGMP manufacture and toxicology the first MSP1 (AdCh63 and MVA) phase Ia clinical trial was initiated in November 2009 followed by the first AMA1 (AdCh63 and MVA) phase Ia clinical trial in March 2010. Subsequently the phase I/IIa clinical trial was initiated at the University of Oxford in July 2010. The vaccine candidates were found to be safe, and immunogenic for both T-cell and antibody responses when co-administered. Basic immunology readouts are in progress.

Two additional malaria vaccine candidates from other institutions have been selected, and both have shown promising results in preclinical testing, and are currently being developed to enter into cGMP production and subsequent phase Ia clinical trials.

Further information about the project can be found at www.emvda.org.

IDEA

African-European Research Initiative on Co-infections of Related and Neglected Infectious Diseases (IDEA). This five year project funded under EC's FP7 with twenty consortium members started in 2010 and is coordinated by Centre Hospitalier Universitaire Vaudois, University of Lausanne, and has a total budget of €10,300,000

The four major objectives of IDEA are to determine:

1. The worm-induced modulation of the functional and mo-

lecular profile of HIV-, TB- and malaria-specific immune responses. In particular to determine how worm innate and adaptive immune responses instruct the subsequent development of HIV-, TB-, and malaria-specific immune responses;

2. The impact by worm co-infections on measures of disease activity for HIV, TB and malaria. This investigation will promote the understanding of interactions between various pathogens and their influence on disease activity;
3. The immunologic markers of worm-, HIV-, TB-, and the control of pathogen replication and associated disease;
4. The modulation by worm co-infections of vaccine-induced immune responses.

EVI will primarily be involved in the Work Package (WP) concerning the interaction of worm infections with the immune responses induced by experimental malaria, TB and HIV vaccines.

INYVAX

Optimisation of the Development of Poverty Related Diseases Vaccines by a Transversal Approach, Addressing Common Gaps and Challenges (INYVAX) is a €932,335, three year project funded under EC's FP7 with eight participants and coordinated by EVI. The project started in 2009

The development of vaccines against Poverty Related Diseases (PRD) addresses 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 insufficient numbers of trained scientists able to undertake leadership roles in vaccine development.

The objective of INYVAX is to tackle these challenges by establishing a comprehensive database of marketed vaccine technologies, optimising knowledge and resources for the formulation of PRD vaccines, implementing safety standards in clinical trials of PRD vaccines, and funding a training programme in vaccinology. In the following the main results of the first 18 months of the project are summarised.

A panel of experts from various organisations involved in vaccine development has defined the critical variables of the vaccine technologies' database and the methodology of the survey, from data collection to analysis. The draft database is currently being validated and populated by the project members.

The European working group on adjuvants has been formed and has prepared a draft report on the needs and gaps for the optimisation of immune response of PRD vaccines. The AdjuNet Laboratories, which will host the training programme in vaccine formulation, were established and are fully operational.

The provision and promotion of safety standards in clinical trials of PRD vaccines was addressed by a working group of 60 trialists. The group drafted "Guidelines for Collection, Analysis and Presentation of Adverse Events Following Immunisation in Pre-Licensure Clinical Vaccine Trials in Resource Limited Countries", including an "Adverse Events Following Immunisation Case Report Form". Currently, the "template of safety section in clinical trial protocols" is being developed by exchange of draft documents and monthly teleconference for in-depth discussions by the working group members. These efforts are accompanied by a comprehensive literature review of vaccine clinical trials in low income countries to analyse current methods for definition, assessment and reporting of safety data.

With the goal of establishing a critical mass of scientists with sufficiently broad knowledge of vaccinology, and in order to play a leading role in the research and development of new PRD vaccines, INYVAX supports the Advanced Course of Vaccinology organised by Fondation Mérieux and the University of Geneva. Two courses, held in May 2009 and May 2010, hosted 12 INYVAX-funded trainees.

The INYVAX consortium held two face-to-face meetings in March 2009 and March 2010. Delegates from all partner institutions were present; the objectives and work plan were presented and discussed; administrative and managerial issues were clarified. Tasks were allocated and further actions and meetings planned.

The INYVAX Steering Committee met in regular teleconferences every 3-4 months to provide a forum for WP leaders and the coordinator to fine-tune the project activities.

In order to raise awareness of the consortium's work and to present and share the project with the general public, a project website has been established at www.inyvax.eu. To highlight the efforts in safety harmonisation in vaccine clinical trials, a letter to the Editor of the journal "Vaccine" will be submitted early 2011.

Overall, the project is proceeding well towards the objectives, and we expect to meet all objectives and deliverables by the end of the project in January 2012. The main aim is that the efforts and results of INYVAX will substantially contribute to facilitate and accelerate the development of PRD vaccines in Europe.

MVVC

Integrating capacity building and networking in the design and conduct of Phase I and II clinical trials of viral vectored candidate malaria vaccines in East and West African children and infants (Malaria Vectored Vaccines Consortium)

In response to an EDCTP call for development of malaria vaccines, the integrated project was submitted to EDCTP for funding in 2008 with a successful outcome. This four-year project, with eight partners in Europe and Africa, and a budget of € 9,543 310, is coordinated by EVI.

The overall objective of the MVVC is to develop a safe, non-reactogenic, effective and affordable malaria vaccine for use in the malaria endemic countries. The project aims to integrate capacity building and networking in the conduct of clinical trials of AdCh63 ME-TRAP and MVA ME-TRAP administered with the prime-boost strategy. Two phase Ib clinical trials are conducted in Kenya and The Gambia and a multi-centre phase IIb clinical trial will be conducted at two to three sites in Burkina Faso, Kenya, The Gambia or Senegal. Capacity building will be achieved through infrastructure upgrading, and short/long term training. MVVC will establish networks within the consortium partners and with already existing networks.

The phase Ib clinical trials of AdCh63 ME-TRAP and MVA ME-TRAP to obtain preliminary data for use of AdCh63 ME-TRAP followed by MVA ME-TRAP in male adults began in June, 2010 at Kenyan Medical Research Institute (KEMRI), Kenya and Medical Research Council (MRC) The Gambia. The specific objectives of the clinical trials are

to assess the safety, reactogenicity, and immunogenicity of AdCh63 ME-TRAP followed by MVA ME-TRAP and to compare the use of intra-muscular and intra-dermal routes of immunisation of MVA ME-TRAP in male adults. Following ethical approval, community engagement activities began in April, 2010. The study initiation visits were conducted by the clinical trial monitors appointed by the sponsor in May 2010 at both clinical trial sites.

The clinical trials are designed to have a dose escalation for AdCh63 ME-TRAP such that there is a formal safety assessment of the immediate reactogenicity of the lower dose before proceeding to the higher dose. A total of 10 volunteers were vaccinated with low dose AdCh63 ME-TRAP and 10 volunteers were vaccinated with high dose AdCh63 ME-TRAP at KEMRI. Six volunteers have been vaccinated with low dose AdCh3 ME-TRAP and ten volunteers have been vaccinated with high dose AdCh63 ME-TRAP at MRC, The Gambia. All volunteers in Kenya and The Gambia have since received MVA ME-TRAP. To date, no serious adverse events have been reported.

The baseline epidemiological study protocol for the MVVC project has been approved by the IECs in Burkina Faso and Senegal and these studies commenced in October and November 2010 respectively. The studies will include a cohort study involving a longitudinal two-year follow up of infants to characterise the dynamics of malaria maternal antibody, malaria infection, and clinical malaria episodes in infants aged 0 to 2 years residing in a malaria hyperendemic area of Burkina Faso and Senegal. The conduct of these studies is necessary to obtain current reference data that will ultimately guide the final sample size for the multi-centre phase IIb clinical trial. These baseline studies will also be used to

train scientific staff in the conduct of this clinical trial. These data will be fundamental in the understanding of naturally-acquired immunity to malaria for both an evidence-based selection of the appropriate immunisation schedule for the malaria vaccine candidate, and to strengthen the capacity of the respective institutions in conducting cohort studies.

OPTIMALVAC

The Initiative on Optimising Malaria Vaccine Lab Assays Evaluation (OPTIMALVAC) is a three year project funded under EC FP7 with thirteen consortium members coordinated by EVI with a budget of €1,000,000 including complementary contributions from the Malaria Vaccine Initiative (MVI) (€561,395) and the Centres for Disease Control and Prevention (CDC) (€30,000). The Grant Agreement was signed by the EC on 7 September 2009.

The main goal is to harmonise the Immune Fluorescence Assay (IFA), the Antibody-dependent Cellular Inhibition (ADCI) assay, Intracellular Cytokine Staining (ICS) and Enzyme-linked Immunospot (ELISpot)) to facilitate comparison of results and improve decision making on vaccine construct development, product characterisation, down selection of vaccine candidates and/or formulations, and clinical development plans.

A broad-range of malaria vaccine candidates derived from diverse technologies have resulted from the multiple approaches being taken by different groups engaged in developing malaria vaccines. Individual groups have developed assays within the context of the vaccine discovery efforts, with identification of measurable processes for parasite growth and virulence, to test specific antigens. In-house assays are

strain, stage and even process specific and the ability to compare results of various candidates is further limited by diverse methodologies and assay components such as parasites, cells and reagents. Lack of an enabling environment for the comparison of research results generated in different laboratories could unfortunately lead to scepticism of results, which in turn generate uncertainty about the efficacy of the vaccines and rationale of the development pathway.

To compare the relative merits of various vaccine candidates and approaches in a credible and informed manner, efforts must be made to harmonise key assays utilised in a) the evaluation of malaria vaccines, and b) throughout the development process. Consistent, reproducible, and comparable intra- and inter- laboratory performance, and higher accuracy and precision of assay data will strengthen the quality of data on vaccine performance, generate greater confidence in the potential of the vaccine candidate, and will support a rational decision-making process.

In 2010, the OPTIMALVAC partners exchanged standard reagents, protocols, and data analysis programmes, which are available on the Reference Reagents Repository (www.malaria-research.eu), and the project website (www.optimalvac.eu). The first harmonisation rounds were initiated and will be pursued in the coming 18 months. The OPTIMALVAC Steering Committee chaired by Odile Leroy, met in regular teleconferences, and a face-to-face meeting in May 2010. The consortium also decided to extend collaboration to the external laboratories listed right:

- National Institutes of Health (NIH), Bethesda, MD, USA

- Walter Reed Army Institute for Research (WRAIR), Silver Spring, MD, USA
- KEMRI, Kilifi, Kenya
- Infectious Disease Research Institute (IDRI), Seattle, WA, USA
- Seattle Biomedical Research Institute, Seattle, WA, USA
- ICGEB, New Delhi, India

To highlight the efforts in assay harmonisation, an editorial letter was drafted and submitted to “Vaccine”. All the objectives and deliverables of the project are expected to be met by the project termination in March 2012.

PHARVAT

The Platform for the Harmonisation of Vaccine Adjuvant Testing (PHARVAT). This two year project funded under EC's FP7, with three participants and a budget of €300,000, was initiated in November 2009. EVI is managing the global coordination of this project.

The main objective of PHARVAT is to determine the laboratory assays that can be used to harmonise pre-clinical selection of vaccine adjuvants activity based on: 1) an in-depth survey and analysis of best practice currently being employed by members of AdjuNet, 2) an evaluation of lead procedures in collaboration with TRANSVAC, 3) the selection of a panel of assays resulting from the TRANSVAC findings and validation by AdjuNet members, and 4) the dissemination of the harmonised assay by WHO through its websites and conferences. Such tests will allow the activity/safety of adjuvants to be compared directly, and will therefore be a major advantage in PRD vaccine development programmes.

In 2010, PHARVAT was presented at the Modern Vaccines/Adjuvants Formulation (MVAF) Conference, where a survey on the method to compare adjuvants was conducted. It is planned to have a PHARVAT workshop in connection to the Immunopotentiators in Modern Vaccines Conference in Q2 2011, to present and discuss the survey results.

Further information on the project can be found at www.pharvat.eu.

TRANSVAC

The European Network of Vaccine Development and Research (TRANSVAC) is a four year project funded under EC's FP7 with thirteen consortium members, coordinated by EVI and has a total budget of a €9,900,000. The overall objective of TRANSVAC is to accelerate the pharmaceutical and clinical development of promising vaccine candidates for public health use. This will be achieved by bridging the gap between academic research and early phase clinical development through carefully managing the advancement of promising vaccine candidates from preclinical animal experiments to proof-of-principle studies in humans. The project's main activities are:

Research - improving the use of assays, adjuvants, animal models, standardised reagents, microarrays and protein expression in relation to the development of experimental vaccines;

Networking - providing training in vaccine development, harmonising assays, and harmonising microarrays;

Services - providing researchers with free access to: adjuvant formulation, animal models, microarray analysis and assays/standards.

The transnational access services form the core of the project's activities, aims to give researchers from all over Europe the opportunity to use free vaccine development facilities via public calls launched by the project.

In 2010 the focus of EVI's efforts has been on launching the project activities, beginning with the kick-off meeting in January 2010 in Brussels. The User Selection Panel and Scientific Advisory Committee members were selected, and the latter will advise on scientific issues, as well as selecting the Users of the Transnational Access. These two groups include ten internationally recognised vaccine experts, who have agreed to participate and share their experience and expertise.

The call procedure covering applications, evaluation and



selection procedure together with the call schedule were established, and relevant guidelines and forms for both consortium bodies and applicants have been developed.

In November 2010, the project launched a call for applications, together with a re-designed website (www.transvac.org) providing potential users of the TRANSVAC infrastructure with all relevant information on the transnational access services on offer and on the call procedure.

TRANSVAC also added a new partner to the consortium, and is happy to welcome the TBVI on board.

Another highlight of the year was the organisation of the European Vaccine Stakeholders meeting in Brussels in October 2010. EVI brought together manufacturers, biotechnology

companies, public/academic researchers, and funding agencies to identify the gaps in vaccine R&D in Europe. During the meeting, an agenda was formulated containing actions, which should pave the way for putting in place a permanent infrastructure securing vaccine R&D and manufacturing in Europe. From this agenda, a series of workshops will be designed to address specific and tangible deliverables. The first workshop is planned for the autumn 2011. The first deliverables of the project have been completed and all project activities are on track.

*European Vaccine Stakeholders Meeting, Brussels,
October 2010*



GOVERNANCE

The EEIG consists of the following organs: a Board and one manager, the Executive Director, who leads the Secretariat. The EVI SAC advises the Board on scientific and technical matters. Ad hoc working groups can be set up by the Board. The Board of Stakeholders (BoS) supervises the Board and the Executive Director, with the power to make recommendations on governance and good practices.

THE DONORS

EVI is funded by the following EU Member State agencies under their respective Ministries of Foreign Affairs:

The Netherlands:	Directorate General for International Cooperation/Netherlands Ministry of Foreign Affairs (DGIS)
Republic of Ireland:	Irish Aid
Sweden:	Swedish International Development Cooperation Agency (Sida/SAREC)
Denmark:	Danish International Development Agency (DANIDA)

These agencies operate in over thirty Developing Countries, providing aid for a range of activities in areas as diverse as health, education, agriculture, the environment, good governance and human rights just to mention a few. With the eight Millennium Development Goals (MDG), agreed by the United Nations, uppermost on their agendas, their collective efforts can be summed up under the general heading of poverty alleviation. MDG #6: combat HIV/AIDS, malaria

and other diseases, #4: reduction of child mortality rate, and #5 improvement of maternal health all have direct relevance for EVI.

FULL MEMBERS

Full Members are the founding members and additional full members accepted by the Board.

Prospective Full Members are nominated and mandated by the respective Member States of the European Economic Area (EEA). Individual Member States shall not be represented by more than three Full Members, including representatives of pharmaceutical industry.

The Full members as 31 December are Heidelberg University and Stockholm University.

The four new members to be integrated early 2011 are the Biomedical Primate Research Centre, the Jenner Vaccine Foundation, the Netherlands Vaccine Institute, and the Royal College of Surgeons in Ireland.

ASSOCIATED MEMBERS

Associated Members can be admitted, analogous to New Members, from non-EU States, or exceptionally, also from the EEA. If an associated member from a non-EU State, which later becomes an EU Member State, the Associated Member can automatically become a full member, if the Associated Member chooses to do so.

Associated Members, however, do not have voting rights on the Board, unless by Board decision, and they are not respon-

sible to third parties. However, Associated Members shall bear responsibility of joint and several liabilities internally.

There are no Associated Members as at 31st December.

EVI BOARD OF STAKEHOLDERS

The EVI BoS consists of the donors and stakeholders or representatives thereof. The EVI BoS appoints a chairperson and a vice-chair from among its members.

The EVI BoS has the following responsibilities:

- Making recommendations to the Board regarding strategic decisions on new or existing initiatives;
- Making recommendations to the Board regarding the governance and management of the funds;
- Approving the Annual Report;
- Making recommendations to the Board regarding appropriate measures to be taken to prevent irregularity, fraud or corruption related to the use of the resources of EVI. Without limiting the generality of the foregoing, the Board undertakes to ensure that the provisions of this paragraph also apply to any recipient of resources of EVI, as well as to employees, contractors, subcontractors, and agents etc of recipients.

The EVI BoS meets at least once per year. Each member of the EVI BoS has one vote. All resolutions of the EVI BoS require a majority of two thirds of the votes cast.

The EVI BoS may invite persons representing Developing Countries, private organisations or other interested parties to advise the EVI BoS by attending the meetings, but without voting rights.

The EVI BoS is regulated by Rules of Procedure, which delineate the principles of governance that the EEIG should adhere to.

EVI BOARD

The Board comprises all the full members and acts collectively. It is the ultimate decision-making organ of the EEIG. As observers, one representative from the diseases of poverty vaccine research community in a disease endemic area, the chair of the EVI SAC, and the chair of the EVI BoS participate in Board meetings.

The Board decides on financial, governance and legal aspects, and gives final approval for yearly strategic and action plans developed by EVI SAC.

Board meetings shall be convened at the place of the official address, or another location advised by the Secretariat, at least twice a year or as otherwise required.

Decision Making Process in the Board

The following require a unanimous decision by all full members:

- Modification of the Statutes;
- Establishment or alteration of distribution of the internal financial liabilities of the EEIG;
- Transfer of the official address of the EEIG to another EEA Member State;
- Admittance of new members with specified competence and internal liability.

The decisions, as stated in the following paragraphs, are binding with a 2/3 quorum of the full Board members present, or who otherwise take part in the vote. The votes of Associate Members are indicative votes and are recorded separately. Abstentions are not taken into account.

The Board works towards unanimous decisions on the following, and, if necessary, decisions are reached by a majority of 2/3 of the votes of the full members present or otherwise taking part:

- Approval of the yearly action plan and the annual budget;
- Appointment of the Executive Director and senior staff;
- Adoption or the amendment of the Rules of Procedure;
- Establishment or amendment of the general conditions for the acceptance of funds;
- Composition of EVI SAC;
- Composition of the EVI BoS;
- Approval of the EEIG to act as sponsor of a clinical trial as defined in Directive 2001/20/EC;
- Approval of the recommendations of EVI SAC, in the event of first presentation.

Board decisions on the following are binding by simple majority of the votes of the full members present or otherwise taking part:

- Approval of the annual accounts for the preceding year;
- Election of auditors for the EEIG to carry out financial and other audits;
- Approval of the recommendations of EVI SAC, in the event of second presentation.

Decisions by simple majority or majority of 2/3 shall be taken under voting weights determined in the Rules of Procedure,

to ensure that no full member holds a majority of the votes.

So far as these Statutes or the Regulation (European Economic Community [EEC]) No 2137/85 do not specify any other solution, all other decisions of the Board shall be binding with 2/3 majority of the votes of the full members present or otherwise taking part.

A recommendation of EVI SAC is requested before any decision by the Board is taken, in accordance with the procedure described in the Rules of Procedure, on the following items:

- Procedure to appoint the Executive Director;
- Strategic needs and priorities;
- Financial plan;
- Evaluation procedure, including the peer review system;
- Yearly action plan such as the planning of calls for proposals;
- Result of the evaluation and list of selected projects;
- Funding of projects and programmes.

EVI SCIENTIFIC ADVISORY COMMITTEE

The EVI SAC makes recommendations to the Board on scientific direction and technologies as well as on the choice of applications for funding.

SAC Members as at 31st December:

Alister Craig (Vice Chairman)	UK
Roland Dobbelaer (Chairman)	Belgium
Juhani Eskola	Finland
Ingileif Jónsdóttir	Iceland
Samuel McConkey	Republic of Ireland
Mahamadou Thera	Mali
Aissatou Touré	Senegal

EVI SECRETARIAT

The Executive Director is Head of the Secretariat.

The Executive Director and the senior staff are appointed by the Board. The Executive Director represents the EEIG legally, and acts as its officer vis-à-vis third parties, within the limits of the objectives of the EEIG (commitments and payments with a volume up to and including €50,000 require the sole signature of the Executive Director) € The Executive Director is accountable to the Board.

Details of the powers and duties of the Executive Director are specified in the Rules of Procedure.

The Secretariat implements the policies and strategies as recommended by EVI SAC, and approved by the Board, in conformity with the EEIG's stated objectives. Among other things, the Secretariat shall develop the yearly action plan, run independent peer review systems, support SAC's policy development and networking, provide specific organisational support required by SAC, support the work of the Board, handle liaison and negotiations with partners, oversee funded programmes and maintain operational and financial control systems.

Members of the Secretariat as at 31st December:

Odile Leroy, Executive Director

Elfi Bihler, Personal Assistant to the Executive Director

Nicolas Havelange, Production, Director*

Sophie Houard, Product Manager

Nathalie Imbault, Quality Assurance and External Relations Manager

Egeruan Babatunde Imoukhuede, Clinical and Regulatory Affairs, Director

Jill Iversen, Secretary

Agnes Kisser, Project Manager

Sten Larsen, Finance, Director

Sonja Noss, Trainee Project Manager

Regitze Thøgersen, Programme Manager

Harry vanSchooten, Business Development Manager*

* Consultant.

INTERNATIONAL FORA

By participating in international meetings, seminars and workshops etc., EVI is able to keep abreast of state of the art developments in the areas in which EVI is active, as well as reinforcing relationships with international institutions and organisation, and forging new ones with relevant and interested parties and potential donors.

There is growing awareness of the importance of EVI in the world of vaccines in general, and every opportunity must be used to heighten the visibility and awareness of EVI in the scientific community and the vaccine community in particular. EVI actively seeks high visibility at international meetings by making presentations and/or moderating/facilitating vaccine sessions, symposia, abstracts etc.

European Union Parliament Working Group on Innovation, Access to Medicines and Poverty Related Diseases, Brussels established January 2010

The working group wants to see better integration of EU actions on the major developing country diseases and health-related issues, and to raise the profile of PRD among policy makers and third parties. It aims to provide a forum for discussion and to create a “focal point” for Members of the European Parliament (MEP) and policy officials where civil society can act as a source of information.

EVI was represented by Harry van Schooten, EVI’s Business Development Manager, whose consultancy firm EUVADIS is a member of the working group.

Meetings attended in 2010: Inaugural meeting and 18 November

Cross-Europe High Level Conference: Delivering the Right to Health with the Health Millennium Development Goals organised by Action for Global Health, European Parliament Brussels 2 March

The objective of the meeting was to gather input from participants to formulate concrete actions the EC, EU and EU Member States can do to achieve the MDGs.

The meeting was attended by Harry van Schooten.

Spanish Ministry of Science and Innovation and the European Commission - 6th European Conference on Research Infrastructures (ECRI2010), Barcelona 23 - 24 March

The objectives of the conference are to promote discussions on the European Strategy for Research Infrastructures (RIs) and on the decision making process to enable the implementation of the European Strategic Forum on Research Infrastructures roadmap. Management and financial issues, as well as the governance structures of the RIs within the European Research Area, were addressed, and there was also a specific session devoted to e-infrastructure for science dealing with key challenges for the future.

The meeting was attended by Roland Ventura.

Malaria Eradication Research Agency (malERA), Washington DC, USA 23 – 26 March

The Global Malaria Action Plan, launched in September 2008 by the Roll Back Malaria partnership (RBM), provides an overview of the R&D needs for malaria eradication. To build on this action plan, the malaria research and academic community is embarking upon a year-long process of ri-

gorous scientific consultation to identify current knowledge gaps and new tools needed for malaria eradication. The overall goal is to develop a multidisciplinary global R&D agenda that can be actionable by research and public health agencies and sponsors.

The meeting was attended by Odile Leroy.

The Role of Regulatory Agencies on Vaccine Safety, Fondation Mérieux, Veyrier du Lac, France 29 – 31 March

The objective of the meeting was to bring together experts from the regulatory agencies, the vaccine manufacturers and vaccine programmes from both Developed and Low to Middle Income Countries (LMIC) with the aim of:

- a) Reviewing the present status on the role of regulatory agencies in relation to the benefit-risk ratio of vaccines (clinical trials and pharmaco-vigilance) in both western and low to middle income countries; with a discussion on how vaccines are evaluated on the different parts of the dossier: Quality, Non-Clinical, Efficacy, Safety and Risk Management Plan;
- b) Discussing the response of vaccine manufacturers to increasing demands of regulatory agencies in terms of vaccines safety and effectiveness. Indeed once a vaccine is licensed, it is extremely important to measure and follow how the vaccine will behave in real world conditions;
- c) Reviewing the international and regional actions for developing/strengthening regulatory authorities in LMIC and the involvement of the WHO, western regulatory agencies and the manufacturers;
- d) Trying to identify the gaps in the regulatory systems in LMIC;

- e) Trying to identify further actions to be taken to help filling these gaps.

The meeting was attended by Babatunde Imoukhuede.

The Red Cross/EU Office, the International Federation of Red Cross Red Crescent Societies, the PATH Malaria Vaccine Initiative (MVI), Roll Back Malaria and UNICEF: Working lunch to commemorate World Malaria Day 2010: Counting Malaria Out, EU Parliament Brussels 27 April

The theme of the working lunch was universal coverage, health MDGs and vaccines: moving towards malaria eradication.

The lunch was attended by Odile Leroy.

Scientific farewell seminar for Alan Thomas, Delft 20 May

The aim of the seminar was to exchange experiences and perspectives with regard to questions involving malaria and tuberculosis. In connection with this event meetings were arranged with the Executive Director Ronald Bontrup of BPRC and other leading people at BPRC.

The seminar was attended by Odile Leroy, Sophie Houard and Harry van Schooten.

Seventh World Congress on Vaccines, Immunisation and Immunotherapy, Berlin 26 – 28 May

The World Congress, founded in 1997, is for all specialists in global vaccinology, health practice and scientists engaged in research to develop new highly immunogenic, safe vaccines and immunotherapeutics.

The congress was attended by Odile Leroy and Roland Ventura.

Global Business Coalition Annual Conference 2010 - Global Health Action, Washington D.C. 7 - 8 June

The conference convened practitioners, strategists, donors, and government leaders for a hands-on meeting that blended the knowledge and practical skills of corporate and non-corporate leaders, to improve the health and well-being of people around the world.

The conference was attended by Odile Leroy and Babatunde Imoukuede.

EDCTP meeting Connecting the Chain II: Linking Research and Development, Brussels 9 June

The meeting - which was motivated by the Declaration of Paris (2005), Bamako Declaration (2008), the three MDGs on health and the activities of EDCTP in developing partnership and building capacity for clinical trials in sub-Saharan Africa - brought together representatives of EC Directorate General of Development and Research, The African Union Commission of Social Affairs, high level officials from European national research and development aid communities, WHO officials, research funders, representatives from non-governmental organisations and key leaders in the fields of health research and capacity development to explore development of health research and health systems capacity in sub-Saharan Africa. The focus was on exploring ways to better coordinate health-related development aid and health research in sub-Saharan Africa.

The meeting was attended by Odile Leroy.

European Commission: High Level Event on Global Health, Brussels 10 – 11 June

In its recently adopted Communication on Global Health,

the EC proposed areas for action, based on EU principles of solidarity, towards equitable and universal coverage of quality health services. The EC highlighted the main challenges that the EU needs to address: leadership, universal coverage, coherence of EU policies and knowledge. This new policy framework aims to be a turning point in promoting the right to health and better addressing global health challenges.

The meeting was attended by Odile Leroy.

4th General Meeting of the Initiative to Strengthen Health Research Capacity in Africa (ISHReCA), Burkina Faso 11 – 13 July

The aim of the meeting was to map a “menu of options” to meet gaps and opportunities, and identify enablers and barriers of health research in Africa. The forum was moderated by Professor Nelson Sewankambo, ISHReCA Chair. Through this meeting ISHReCA wishes to unveil its plans and welcomes all researchers and stakeholders to join forces for the common goal.

The meeting was attended by Babatunde Imoukuede.

Brighton Collaboration (BC) Science Board Meeting, Brighton 17 - 18 August

The meeting was attended by Odile Leroy, who is a member of the BC Science Board.

The Science Board sets research priorities, oversees the scientific progress, advises the Foundation Board, Management Team and participants, and ensures scientific rigour.

European Commission Colloquium Conference: Neglected Protozoan Diseases - Prevention, Treatment and Control of Leishmaniasis, Trypanosomiasis and Chagas Disease, Paris 24 September

This colloquium brought together scientists interested in research on neglected protozoan diseases. The meeting gathered eight major research projects funded under the EC FP7 in the area of neglected infectious diseases.

OECD Workshop on Better Health through Bio-medicine: Innovative Governance, Berlin 27 – 28 September

This workshop aimed, therefore, to:

- Provide a forum to discuss how biomedicine can lead to better health outcomes;
- Discuss new governance models that are emerging across the Organisation for Economic Co-operation and Development (OECD) area in response to new biomedical developments;
- Consider how they can operate systemically to foster more effective innovation and promote multiple health system objectives within resource and fiscal constraints;
- Consider the role of government in “shaping innovation in governance” to make the most of the benefits of these biomedical developments for both individuals and society.”;
- Gather input from the international community, including international policy-makers and industrial participants
- Determine areas in which the OECD can provide further policy insight and expertise;
- Provide guidance for further work on biomedicine and health innovation at the OECD.

The workshop was attended by Harry van Schooten.

Malaria Vaccines for the World (MVW), Washington DC 28 - 30 September

The second conference in the series was the follow-up to the successful MVW 2008 meeting held in London and again

offered researchers a fresh new forum to discuss the current status of new malaria vaccines initiatives, vaccine candidates and clinical trials. MVW 2010 focused attention on ‘Vaccine Issues’ in relation to Malaria as a worldwide disease. EVI and MVI held a joint reception on 29 September for participants at the meeting. The reception, which was well attended by the malaria community, is in continuation of joint collaboration efforts by EVI and MVI.

The meeting and reception was attended by Sharmila Bakshi and Babatunde Imoukhuede, who gave a presentation on the transition from EMVI to EVI.

4th Vaccine and ISV Annual Global Congress, Vienna 3 – 5 October

The congress has become the forum for the exchange of ideas to accelerate the rate at which vaccines can come to benefit the populations that need them. The key objectives of the congress are:

- To provide a progressive state-of-the-art report for scientists, governmental authorities and healthcare workers with dedicated sessions for each group;
- To accelerate progress in the development of vaccines;
- To encourage a prophylactic approach to healthcare.

The congress was attended by Roland Ventura.

European Vaccine Stakeholders Meeting, Brussels 12 October

The meeting, organised by EVI/TRANSVAC, brought together representatives from vaccine manufacturers, biotech companies, public/academic research, regulatory authorities, product development partnerships and funding agencies, to:

- Identify the gaps and needs in vaccine research and development in Europe;
- Identify which activities or structures could improve the development of new vaccines and technologies in order to sustain and strengthen European leadership in the field of vaccines.

MVAF 2010, Cannes 13 – 15 October

The ever increasing drive to develop new vaccine therapies and their associated adjuvantation and delivery systems has major implications for the design/formulation/stabilisation/preservation of modern vaccines and immunisation strategies. Following the successful meetings held in Prague and Dublin, the follow-up conference MVAF 2010 offered an international forum for the discussion of all aspects of vaccine formulation and focused on:

- Pharmaceutical development of vaccines and adjuvants;
- Safety issues with special emphasis on delivery/administration issues;
- National and international regulatory guidelines.

The meeting was attended by Roland Ventura and Regitze Thøgersen, and more specifically EVI participated with a questionnaire and poster session on the EC funded, EVI coordinated projects PHARVAT and TRANSVAC.

MALVAC Science Forum, WHO Geneva 15 – 16 November

The MALVAC Science Forum dealt with Measures of Efficacy of anti-malarial interventions against malaria transmission, the overall objective of which was to provide consensus-based recommendations on clinical trial designs/approaches for assessment of transmission reduction, for consideration

by the MALVAC committee and by the WHO Global Malaria Programme.

The meetings were attended by Odile Leroy, joined by Agnes Kissler on the last day.

Accelerating Vaccine Development, London 17 – 18 November

This meeting outlined and reviewed the current decision making framework for new vaccine development with input from industrialist, regulators, academics and funders. Incentivisation strategies that have and have not worked were reviewed along with new opportunities. Lowering the regulatory requirements for conditional approval of certain vaccines remains an attractive option, but may be discouraged by increasing public concerns about vaccine safety. The emergence of large scale high quality vaccine manufacturers in several developing countries along with many new national regulatory authorities add new complexity but also opportunities.

The meeting was attended by Odile Leroy.

Eurovaccine 2010, Stockholm 10 December

This one-day conference brought together international experts in the field of vaccinology to provide a platform for information and practice exchange among professionals working in the fields of regulation, policy, implementation, monitoring and evaluation of immunisation activities in European countries.

EVI was represented by Harry van Schooten.

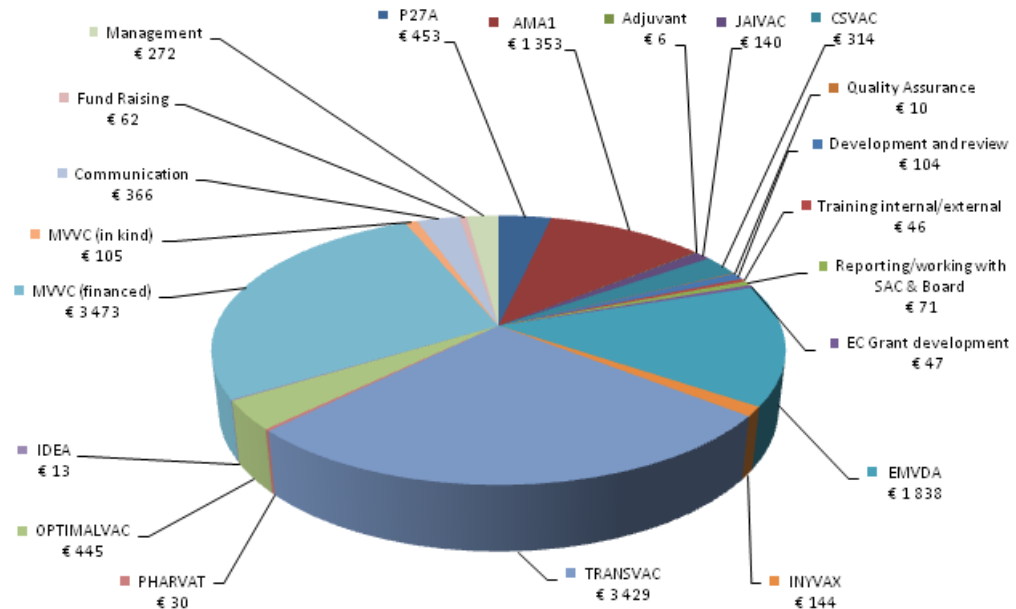
FINANCIAL UPDATE 2010 (OCT09-DEC10)

By: Finance & Human Resources, Director, Sten Larsen

The year 2010 was the first full year of the EEIG. From a financial point of view it's surprising how much activity EVI managed to implement, considering the effort involved in establishing the organisation and hiring new staff. EVI staff has, in the first reporting period, shown diligence and a high level of accomplishment in all areas of EVI activities. In addition, the strong cooperation of stakeholders and partners of EVI has resulted in the unprecedented success in the establishment of EVI. The year 2010 has been an economically difficult year for our donors in these times of economic stagnation in Europe. However, we are grateful for the continued support they have shown us, and we would like to extend our heartfelt thanks to DGIS, Irish Aid, DANIDA, Sida/SAREC, EC & EDCTP.

The figure 1 below shows the cost activity over the current reporting period, where expenditure in a broad portfolio of EVI, EDCTP and EC projects, has technically produced a high level of outcome, in comparison with the level of funding. The financial conclusion of the first reporting period of EVI is that funds have been fully utilised to achieve substantial results, proving that EVI has the right mechanism and setup for developing vaccines efficiently. I would like, in this respect, to point out the exceptionally low level of management costs of only 2.14% (6.42% before EC/EDCTP partner payments), which is an achievement in itself.

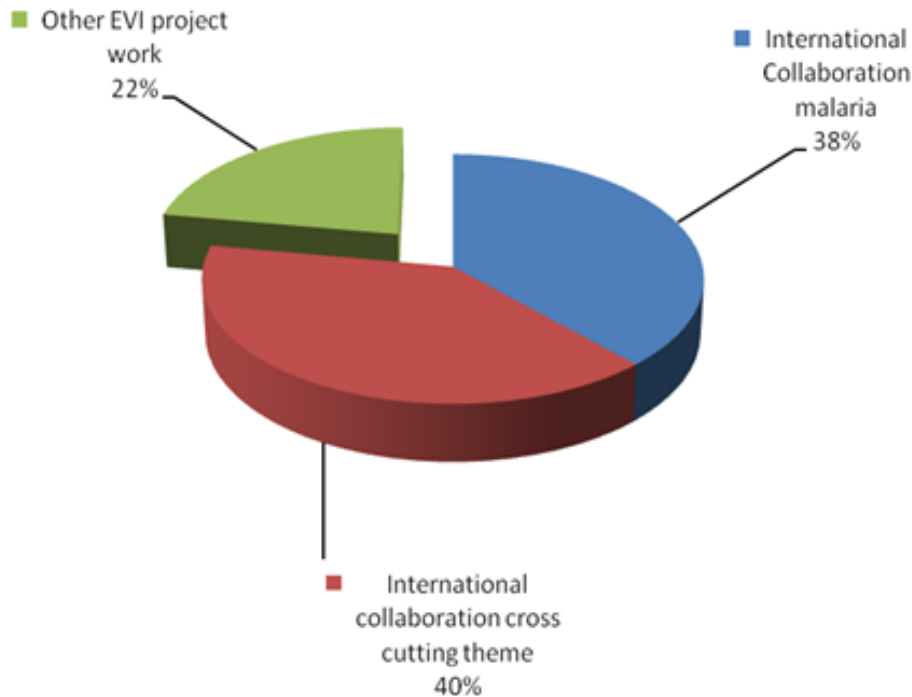
FIGURE 1 - TOTAL EVI ACTIVITY 2010 (€'000)



EVI is a highly international organisation collaborating on malaria and other cross cutting vaccine themes through coordination and networking on vaccine development glo-

bally. 78% of EVI activities are direct international collaboration with partners and stakeholders from Europe, Africa, Asia and North America. See figure 2.

FIGURE 2 – INTERNATIONAL COLLABORATION AND NETWORKING



EVI PROJECT ACTIVITIES

Over the past 15 Months the EVI vaccine portfolio has seen tremendous activity with relatively small investments. cGMP manufacturing is on-going together with clinical trials both in progress and planned for in 2011. During the next 12 months a high level of investment is anticipated, as the projects gain momentum. It should be mentioned that

in the first three months of EVI in 2009, the projects were in the process of being transferred from EMVI to EVI. This constituted a small delay, which EVI and its partners have worked hard to overcome, and as a result all projects are now on schedule and advancing in accordance with planned activity.

FIGURE 3 - EVI PORTFOLIO INVESTMENT (€'000)

The figure 3 depicts investment over the past 15 months dominated by cGMP and process development. Investment over next 12 months will be dominated by cGMP and clinical trials, with very little investment in process development.

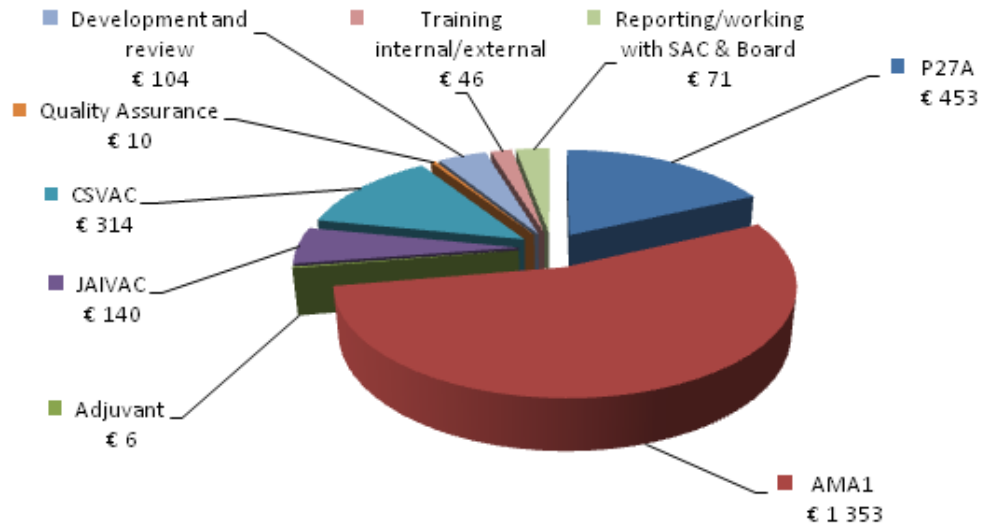
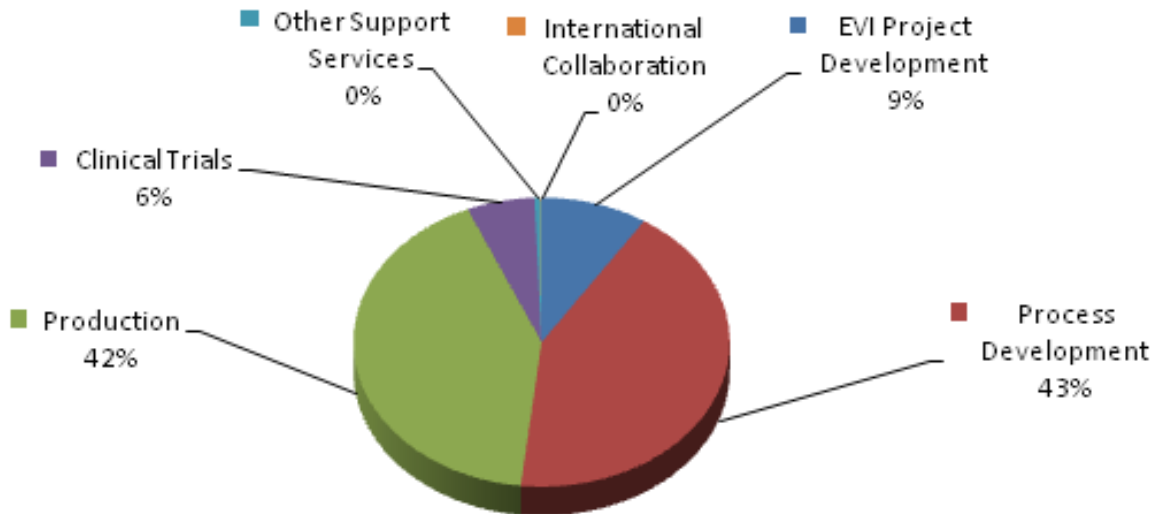


FIGURE 4 - EVI PORTFOLIO INVESTMENT TYPE IN %

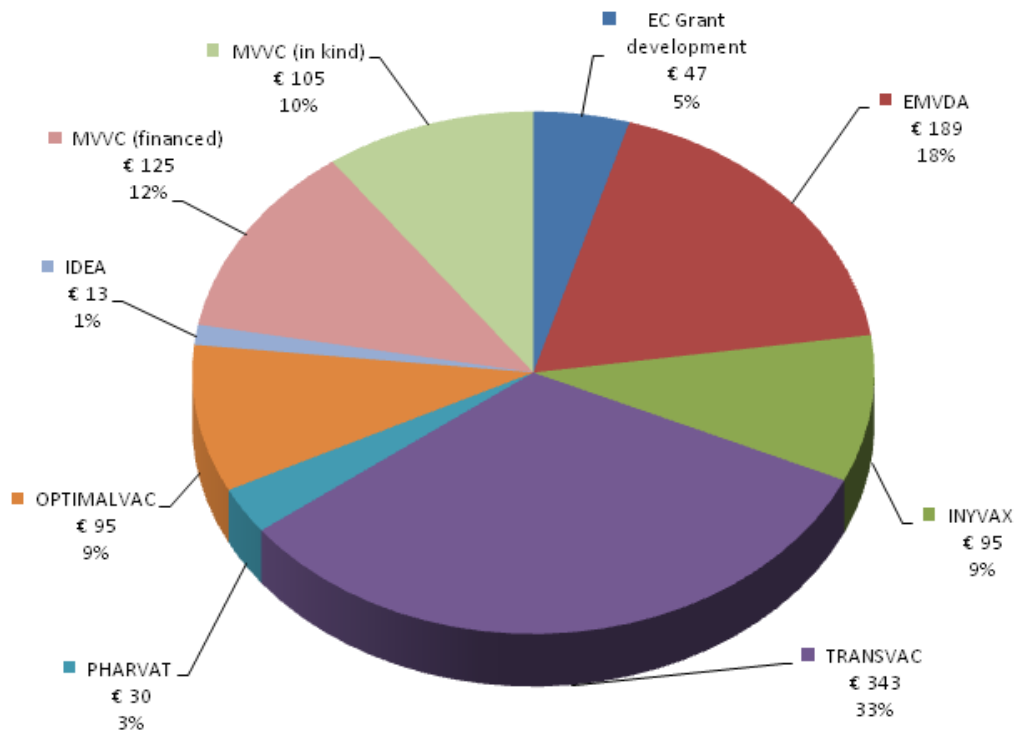


EVI, EC & EDCTP ACTIVITY

Besides EVI's portfolio of specific investment in various vaccine candidate projects, EVI activity is dominated by several EC and EDCTP funded projects. The Figure 5 shows expenditure less partner transfers, solely attributed to EVI. Not surprisingly, the new EC project TRANSVAC (budget €9,9Million) has by far the largest expenditure. In the past 15 months new staff have been hired in connection with this project, which comprises several

large work packages, including a state of the art transitional access component, where services are made available to external users. EMVDA was the last project to be transferred to EVI. The project transfer was not finalised until the Q3 2010. EVI and EMVDA partners are now moving the project steadfastly forward to make up for the delay, ensuring project deliverables are realised according to expectations.

FIGURE 5 - EC AND EDCTP (MVVC) ACTIVITY (€'000)



MVVC is, on the other hand, a success story, with successful completion of the first reporting period with minor under spending, and with a very promising financial and technical forecast. Lastly INYVAX and OPTIMALVAC have successfully completed their first reporting periods, and are entering the final months before conclusion.

THE FINANCIAL CONVERSION OF EMVI INTO EVI.

In a mere 15 months EVI has managed to realign both investment and person months for staff to encompass EVI's broader mandate, which covers all diseases of poverty, not just malaria. Investment in malaria projects will continue

to be high, until new calls result in the funding of projects related to other diseases of poverty. Today more than 60% of staff time is spent on developing vaccines for other diseases of poverty.

FIGURE 6 - INVESTMENT (□ - IN %) MALARIA/OTHER DISEASES OF POVERTY



FIGURE 7 - STAFF ACTIVITY (HOURS) ON MALARIA/OTHER DISEASES OF POVERTY

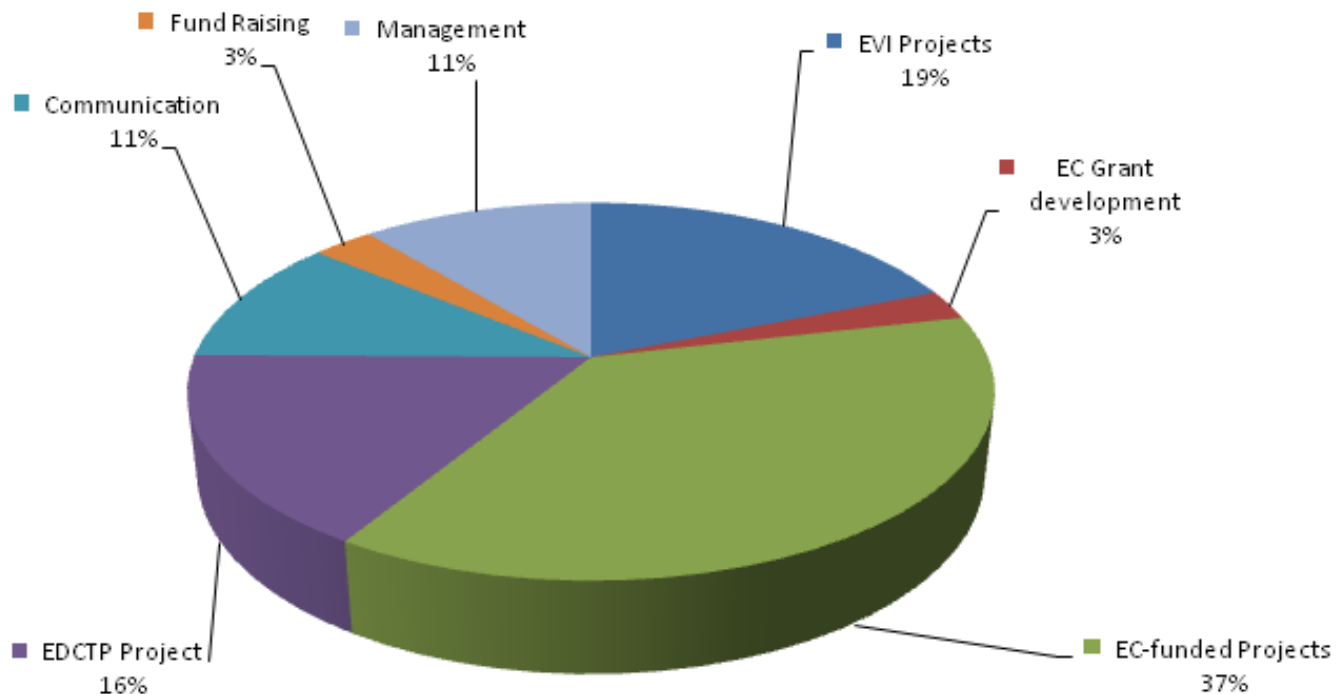


STAFF TIME (HOURS) IN THE CURRENT REPORTING PERIOD

The reorganisation and transfer from EMVI to EVI has resulted in fewer hours being spent on EC funded projects than anticipated. This is expected to be corrected over the next 12 months, where work on EC funded projects will require more staff hours, especially keeping in mind that both INYVAX and OPTIMALVAC are near conclusion. Although staff spent 11% of their time on management, as a direct result of the reorganisation, seen against the overall expenditure of EVI, overall management costs only account for 2.14% of the total global expenditures of EVI.

At the start of EVI's activity, almost all staff were based at offices around Europe, making EVI a de-facto virtual organisation. At the end of 2010 EVI most staff are now based at the EVI Headquarters in Heidelberg, Germany. The expectations are that by end of 2011 only four members of staff will be placed outside of Germany, two of which at the registered office in Denmark. The strategy of EVI is to strengthen the executive office and continuously reduce expenditures on consultants, which has already been implemented in 2010 and will be reflected in the next reporting period for 2011.

FIGURE 8 - STAFF TIME - HOURS - IN PERCENTAGE



FINAL REMARKS

EVI would like to thank all of our stakeholders, subcontractors and partners. We would, from a financial point of view, like to extend our appreciation to the BDO offices in Germany, France, Belgium, Denmark and United Kingdom

for well organised payroll management and tax advice. EVI thanks LETT law firm in Copenhagen for dealing efficiently and professionally with the issue in Denmark, and Falk & co in Heidelberg for accepting the role of auditor for EVI.

THE FOLLOWING SECTION CONTAINS A SUPPORTING DETAILED BREAKDOWN OF THE FIGURES FROM THE PROFIT AND LOSS AND BALANCE SHEET.

PRINCIPAL ACCOUNTING POLICIES

(a) Basis of accounting

The basis of accounting is according to German general accepted accounting principles (GAAP). The reports of the former EMVI were drawn with the International Financial Reporting Standards (IFRS) as standard model and Danish GAAP but with the change of legal entity it has been deemed necessary to change the format into German GAAP. Other accounting policies are described in the EVI handbook together with relevant policies which are known and applied by EVI staff. The change from Danish GAAP/IFRS to German GAAP has not affected normal operations or caused any significant issues.

(b) Transfer from EMVI to EVI

The figures audited refer to the legal entity of EVI, and hence the 2009 comparison relates only to the legal en-

tity of EVI. The figures from EMVI 2009 can be found on the EVI website under 2009 annual report.

(c) Realised income policy

Grants/donations received by EVI are accounted for on the balance until expenditures related to the grant have been recorded, and therefore equally become income for the organisation. Only income generated from sale or other economic activity are directly recognised as income on the Profit and Loss (PNL).

(d) Payables

All amounts payable by EVI are charged to the PNL in the invoice relevant year.

(e) Investment income and interest receivable

Interest received on EVI deposits is included in the PNL in the year for which it is receivable. Interest earned is added to the EVI administration cost centre for core support.

(f) Funds accounting

Funds held by EVI are either:

- Core support funds – these are funds set aside for eligible project relevant expenditures;
- Restricted funds are funds related to specific projects including EC-funded projects.

(g) Foreign currencies

Transactions in foreign currencies are translated into Euro at rates prevailing at the date of the transaction. With the exception of Danish Kroner (DKK) which has a fixed rate of 7.45 based on the kroner being politically and monetarily fixed to the Euro. EVI has for the year 2010 made use of the following currencies: EUR, DKK, Indian Rupees, US\$.

(h) Auditor

EVI is proud to introduce FALK & CO as the auditors of financial activities. FALK & CO form part of the global alliance of independent firms called PRAXITY.

The auditor issues the audit report, which is made available in full to the EVI-EEIG Board and Board of Stakeholders, including all donors and the EC. The audit report contains an analysis of EVI, and relevant recommendations found by the auditor.

In this annual report, the conclusion – the auditor's opinion - together with the audited PNL and balance sheet which is made public. The opinion appears in both German and an English translation prepared by the auditor.

**DONATIONS/GRANTS RECEIVED
(EXCLUDING EMVI TRANSFERS)**

Irish Aid	€	1,000,000
Irish Aid	€	1,000,000
DANIDA	€	268,284
Sida/SAREC	€	286,053
DGIS	€	1,100,000
EC TRANSVAC	€	3,861,000
EC PHARVAT	€	60,500
EC IDEA	€	67,480
EC EMVDA	€	564,336
EDCTP MVVC	€	3,547,141

INTEREST EARNED

Interest Danish Account	€	213
Interest German Account	€	23,227
Total	€	23,440

EVI extends its thankfulness and appreciation to all its Donors and Grant providers

STAFF*List of staff (as of 1 February 2011)*

	First Name	Last Name	Title/Function in EVI	Placement
1	Elfi	Bihler	Personal Assistant	Germany
2	Mark	Geels	Project Manager	Germany
3	Nicolas	Havelange	Production, Director*	Belgium
4	Sophie	Houard	Product Manager	Belgium
5	Nathalie	Imbault	Quality Assurance and External Relations Manager	Germany
6	Egeruan Babatunde	Imoukhuede	Clinical and Regulatory Affairs, Director	UK
7	Jill	Iversen	Secretary	Denmark
8	Agnes	Kisser	Project Manager	Germany
9	Thorsten	Kohaut	Accounting Assistant	Germany
10	Sten	Larsen	Finance & Human Resource, Director	Denmark
11	Odile	Leroy	Executive Director	Germany
12	Sonja	Noss	Project Manager Trainee	Germany
13	Regitze Louise	Thoegersen	Program Manager	Denmark
14	Harry	van Schooten	Business Manager*	The Netherlands

*Consultant

Male	6
Female	8
Total Staff of EVI 1 Feb. 2011	14

DIRECT & INDIRECT PROJECT EXPENDITURES**Grants, contracts, & direct assistance**

Contracts - program-related	€	1,931,139
Grants to other organisations	€	73,000
Benefits paid to or for EDCTP consortium members	€	3,347,335
Benefits paid to or for EC consortium members	€	5,131,334

Salaries & Wage expenses:

Salaries & wages international staff	€	475,439
Salaries & wages German staff	€	215,682
Payroll taxes, etc.	€	272,907
Statutory social security expenses	€	221,050
Employee benefit expenses	€	173

Contract service expenses

Fundraising fees	€	3,136
Accounting fees	€	45,228
Legal fees	€	10,080
Professional fees - other	€	28,899
Consultancies - contract	€	421,779

Facility & equipment maintenance expenses:

Software Licenses	€	6,106
Publishing cost incl. Copy and Printing	€	33,799
Books, subscriptions, references	€	402

Equipment, Hardware & Software

Minor hardware purchases	€	3,112
Minor software purchases	€	5,664
Minor furn, fix, equip, vehicle parts	€	2,263
Depreciation & amortisation	€	2,549

Travel & meetings expenses:

Travel (Flights)	€	109,886
Travel (Train, Ferry, Taxi, other)	€	55,170
Travel (refund for own use of travel means)	€	571
Hotel and other accommodation costs	€	39,771

Conferences, conventions, meetings	€	6,343
EC conferences, conventions, meetings	€	4,838
Travel allowances for employees	€	26,720
Restaurant, catering and other travel provisions	€	7,394
Staff training external costs	€	7,401
Staff teambuilding external costs	€	25,732
Other Direct expenses:		
Recruitment costs	€	9,072
Insurances	€	1,502
Advertising expenses	€	4,476
Other expenses	€	5,419
Indirect Business expenses:		
Telephone & telecommunications	€	19,901
Broadband & other internet connections	€	357
Postage & shipping	€	9,248
Office supplies	€	46,331
Printing & copying	€	870
Fees & charges	€	17,010
Hosting agreement costs	€	3,744
Organisational (corp.) expenses	€	49,390
Overheads from grants (reserved)	€	412,192
General assembly, Board & SAC expenses:		
SAC meetings	€	3,034
SAC strategy cost	€	14,100
SAC travel cost	€	13,235
EC ESAC, SAC, SC expenses:		
ESAC travel cost	€	115
Total Expenses	€	13,124,896

MAJOR PAYABLES

EVI Project Payments	Project relevance	Amount
Biomedical Primate Research Centre-Reservation	AMA1	€ 885,766
Henogen	AMA1	€ 336
Almac Sciences Ltd.	P27A	€ 80,000
Rita Walt Consulting	MVVC	€ 6,393
Diagnosearch Life Science	JAIVAC	€ 11,555
Henogen	AMA1	€ 16,800
Henogen	AMA1	€ 16,800
Henogen	AMA1	€ 12,372
Diagnosearch Life Science	JAIVAC	€ 29,762
Henogen	AMA1	€ 303
Confarma	AMA1	€ 76,344
Diagnosearch Life Science	JAIVAC	€ 5,965
Diagnosearch Life Science	JAIVAC	€ 19,396
Almac Sciences Ltd.	P27A	€ 130,000
Diagnosearch Life Science	JAIVAC	€ 1,809
Henogen	AMA1	€ 410
Henogen	AMA1	€ 33,600
Henogen	AMA1	€ 16,800
Henogen	AMA1	€ 50,400
Henogen	AMA1	€ 2,714
Henogen	AMA1	€ 33,600
University of Oxford	CSVAC	€ 280,300
Almac Sciences Ltd.	P27A	€ 100,000
Prograssima	EMVDA	€ 3,120
Diagnosearch Life Science	JAIVAC	€ 3,200
Fraunhofer IME	AMA1	€ 105,000
NNE Pharmaplan	AMA1	€ 493
NNE Pharmaplan	AMA1	€ 7,900
University of Lausanne	P27A	€ 48,000
University of Lausanne	P27A	€ 5,000

EC Project Payments	Project relevance	Amount
Pevion Biotech AG	EMVDA	€ 15,540
UMC St. Radboud	EMVDA	€ 243,089
Etna Biotech	EMVDA	€ 463,862
Swiss Tropical Institute	EMVDA	€ 9,305
Universitätsklinikum Tübingen	EMVDA	€ 344
Stockholm University	EMVDA	€ 3,573
African Malaria Network Trust	EMVDA	€ 58,709
University of Edinburgh	EMVDA	€ 138,534
University of Heidelberg	EMVDA	€ 712,810
Biomedical Primate Research Centre	INYVAX	€ 49,600
Biomedical Primate Research Centre	OPTIMALVAC	€ 30,373
University of Oxford	OPTIMALVAC	€ 22,437
University of Edinburgh	OPTIMALVAC	€ 44,000
UMC St. Radboud	OPTIMALVAC	€ 71,500
World Health Organization	OPTIMALVAC	€ 99,000
Institut Pasteur	OPTIMALVAC	€ 55,000
Centre de Recerca en Salut Internacional de Barcelona	OPTIMALVAC	€ 27,500
University of Regensburg	TRANSVAC	€ 127,590
ID-Lelystad	TRANSVAC	€ 296,988
Health Protection Agency	TRANSVAC	€ 425,532
Vakzine Projekt Management	TRANSVAC	€ 9,891
Lionex	TRANSVAC	€ 194,632
Helmholtz Zentrum für Infektionsforschung	TRANSVAC	€ 247,266
Biomedical Primate Research Centre	TRANSVAC	€ 602,157
London School of Hygiene and Tropical Medicine	TRANSVAC	€ 145,159
University of Oxford	TRANSVAC	€ 385,589
University of Lausanne	TRANSVAC	€ 220,923
Max Planck Institute for Infection Biology	TRANSVAC	€ 430,432

MVVC Project Payments

	Project relevance	Amount
MRC	MVVC	€ 252,612
University of Oxford	MVVC	€ 1,505,039
UCAD	MVVC	€ 625,222
CNRFP	MVVC	€ 478,445
VSCR	MVVC	€ 65,461
KEMRI	MVVC	€ 411,756
OKAIROS	MVVC	€ 8,800

EXPENDITURES BY PROJECT

Project Code	Amount spent (incl. partner pay)	In percentage
P27A	€ 452,723	3.56%
AMA1	€ 1,353,006	10.64%
Adjuvant	€ 5,777	0.05%
JAIVAC	€ 139,936	1.10%
CSVAC	€ 314,436	2.47%

Quality Assurance	€ 9,762	0.08%
Development and review	€ 103,979	0.82%
Training internal/external	€ 45,716	0.36%
Reporting/working with SAC & Board	€ 71,354	0.56%

EC Grant development	€ 47,421	0.37%
EMVDA	€ 1,837,846	14.46%
INYVAX	€ 144,100	1.13%
TRANSVAC	€ 3,428,978	26.97%
PHARVAT	€ 30,208	0.24%
OPTIMALVAC	€ 444,821	3.50%
IDEA	€ 12,955	0.10%

EDCTP Grant dev.	€ -6,607	-0.05%
EDCTP MVVC (financed)	€ 3,472,624	27.32%
EDCTP MVVC (in kind)	€ 104,513	0.82%

Communication	€	365,906	2.88%
Fund Raising	€	61,734	0.49%
Management	€	271,508	2.14%

BALANCE OVERVIEW OF DONOR AND EC/EDCTP FUNDS

Donor/Grant	Type	EMVI Transfer 2009	Received 2009.2010	Costs 2009.2010	Balance 31st Dec. 2010
Irish Aid	Core	1,999,997	2,000,000	1,614,926	2,385,071
DANIDA	Core	-	268,284	268,284	-
Sida/SAREC	Core	95,220	286,053	381,273	-
EVI Board Funds	Core	1,280,780	-	-	1,280,780
DGIS	Restricted	826,858	1,100,000	1,465,441	461,417
EC TRANSVAC	Restricted	-	3,861,000	3,428,978	432,022
EC PHARVAT	Restricted	-	60,500	30,208	30,292
EC IDEA	Restricted	-	67,480	12,955	54,525
EC INYVAX	Restricted	194,686	-	144,100	50,586
EC OPTIMALVAC	Restricted	533,648	-	444,821	88,827
EC EMVDA	Restricted	2,355,606	564,336	1,837,847	1,082,095
EDCTP MVVC	Restricted	-	3,547,141	3,472,624	74,517
EMVI reserves					
DGIS	Restricted	535,348	-	-	535,348
Irish Aid	Core	535,899	-	-	535,899
EVI Board Funds	Core	1,984,056	-	-	1,984,056
EC Funds	Restricted	3,703	-	-	3,703
Interest	Core	326,514	-	-	326,514
Total Core		6,222,466	2,554,337	2,264,483	6,512,320
Total Restricted		4,449,849	9,200,457	10,836,974	2,813,332
Total EVI Funds		10,672,315	11,754,794	13,101,457	9,325,652

CASH MANAGEMENT (BANK ACCOUNTS) AS OF 31ST DECEMBER 2010

Cash in bank (EUR)	€	2,208,959.46
Cash in Danish Bank (DKK)	€	86,334.51
Savings accounts (EUR)	€	5,000,000.00

HOSTING COSTS

EVI is hosted by the Heidelberg University with the following costs:

Rent of office space and consumables € 65,000 (paid in January 2011)

Other charges (IT, Phone etc.) € 1,589





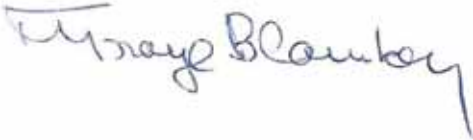



Total 2010 service charges € 66,589 (2009 = €175,958)

REMUNERATION OF GOVERNING BODIES

Travel and subsistence costs are refunded to Board members and EVI SAC members in connection with meetings and conferences including a honorarium to EVI SAC members.

We hereby formally sign and approve the EVI Annual Financial Report for the year 2010 ending 31st December 2010 in accordance with the EVI-EEIG Board decision.

The governing accounting principles and the overall presentation of the Annual Financial Report are deemed to give a true and fair illustration of EVI activities.

 Date : 17-04-2011	
Sten Larsen, EVI Finance, Director	
 Date : 18-04-2011	
Odile Leroy, EVI Executive Director	
 Date : 19-04-2011	
Marita-Troye Blomberg, Chair of EVI-EEIG Board	
 Date : 20-04-2011	
Sodiomon Sirima, Chair of Board of Stakeholders	

FINANCIAL STATEMENTS AS AUDITED FOR THE YEAR ENDING 31ST DECEMBER 2010

Income Statement
for the Period January 1 to December 31, 2010

	EUR	EUR	compared to 2009 K-EUR
1. Other operating income from Grant donors	12.887.073,02		214
2. Miscellaneous operating income	<u>617,00</u>		
3. Subtotal I		12.887.690,02	
4. Personnel expenses			
a) Wages and salaries	-964.200,10		0
b) Social security costs	-221.049,56		0
thereof for pensions: EUR 0,00			(0)
		<u>-1.185.249,66</u>	
5. Depreciation on tangible fixed assets		-3.166,37	0
6. Other operating expenses		<u>-11.722.714,28</u>	-214
7. Subtotal II		-23.440,29	0
8. Other interest and similar income		<u>23.440,29</u>	0
9. Net result		<u><u>0,00</u></u>	<u><u>0</u></u>

Balance Sheet as of December 31, 2010

Assets:	EUR	EUR	compared to 12/31/2009 K-EUR
A. Fixed Assets			
Tangible assets			
Other equipment, office and plant equipment		9.499,05	----- 2
B. Current Assets			
I. Other assets			
Other assets	12.280,33		----- 44
II. Cash in hand, cash in banks	<u>7.295.293,97</u>		<u>5.869</u>
		7.307.574,30	----- 5.913
		7.317.073,35	5.915

Balance Sheet as of December 31, 2010

Liabilities and shareholders' equity:	EUR	EUR	compared to 12/31/2009 K-EUR
A. Accruals			
Other accruals		885.766,00	<u>0</u>
B. Liabilities			
1. Liabilities in relation to grants received			
a) National government grants liabilities	4.099.740,72		2.071
b) European Union and other restricted grant liabilities thereof with a remaining term of up to 1 year: EUR	2.274.281,76 6.374.022,48		3.844 (5.915)
2. Other liabilities thereof from taxes: EUR	57.284,87 14.637,71		0 (0)
thereof from social security: EUR	24.054,28		(0)
thereof with a remaining term of up to 1 year: EUR	57.284,87		(0)
		<u>6.431.307,35</u>	<u>5.915</u>
		<u><u>7.317.073,35</u></u>	<u><u>5.915</u></u>

Bestätigungsvermerk des Abschlussprüfers

An die European Vaccine Initiative-EWIV, Heidelberg:

Wir haben den Jahresabschluss - bestehend aus Bilanz, Gewinn- und Verlustrechnung sowie Anhang - unter Einbeziehung der Buchführung der European Vaccine Initiative-EWIV, Heidelberg, für das Geschäftsjahr vom 1. Januar bis 31. Dezember 2010 geprüft. Die Buchführung und die Aufstellung des Jahresabschlusses nach den deutschen handelsrechtlichen Vorschriften und den ergänzenden Bestimmungen in den Statuten liegen in der Verantwortung der gesetzlichen Vertreter der Gesellschaft. Unsere Aufgabe ist es, auf der Grundlage der von uns durchgeführten Prüfung eine Beurteilung über den Jahresabschluss unter Einbeziehung der Buchführung abzugeben.

Wir haben unsere Jahresabschlussprüfung nach § 317 HGB unter Beachtung der vom Institut der Wirtschaftsprüfer (IDW) festgestellten deutschen Grundsätze ordnungsmäßiger Abschlussprüfung vorgenommen. Danach ist die Prüfung so zu planen und durchzuführen, dass Unrichtigkeiten und Verstöße, die sich auf die Darstellung des durch den Jahresabschluss unter Beachtung der Grundsätze ordnungsmäßiger Buchführung vermittelten Bildes der Vermögens-, Finanz- und Ertragslage wesentlich auswirken, mit hinreichender Sicherheit erkannt werden. Bei der Festlegung der Prüfungshandlungen werden die Kenntnisse über die Geschäftstätigkeit und über das wirtschaftliche und rechtliche Umfeld der Gesellschaft sowie die Erwartungen über mögliche Fehler berücksichtigt. Im Rahmen der Prüfung werden die Wirksamkeit des rechnungslegungsbezogenen internen Kontrollsystems sowie Nachweise für die Angaben in Buchführung und Jahresabschluss überwiegend auf der Basis von Stichproben beurteilt. Die Prüfung umfasst die Beurteilung der angewandten Bilanzierungsgrundsätze und der wesentlichen Einschätzungen der gesetzlichen Vertreter sowie die Würdigung der Gesamtdarstellung des Jahresabschlusses. Wir sind der Auffassung, dass unsere Prüfung eine hinreichend sichere Grundlage für unsere Beurteilung bildet.

Unsere Prüfung hat zu keinen Einwendungen geführt.

FALK GmbH & Co KG
Wirtschaftsprüfungsgesellschaft Steuerberatungsgesellschaft

Appendix 4

Nach unserer Beurteilung aufgrund der bei der Prüfung gewonnenen Erkenntnisse entspricht der Jahresabschluss auf den 31. Dezember 2010 der European Vaccine Initiative- EWIV, Heidelberg, den gesetzlichen Vorschriften und den ergänzenden Bestimmungen in den Statuten und vermittelt unter Beachtung der Grundsätze ordnungsmäßiger Buchführung ein den tatsächlichen Verhältnissen entsprechendes Bild der Vermögens-, Finanz- und Ertragslage der Gesellschaft.

Heidelberg, den 8. April 2011

FALK GmbH & Co KG
Wirtschaftsprüfungsgesellschaft
Steuerberatungsgesellschaft


(Meyer)
Wirtschaftsprüfer


(Ahrens)
Wirtschaftsprüfer

Translation of the Auditor's opinion

To European Vaccine Initiative-EWIV, Heidelberg:

We have audited the annual financial statements, comprising the balance sheet, the income statement and the notes to the financial statements, together with the bookkeeping system of European Vaccine Initiative-EWIV, Heidelberg for the business year from January 1 to December 31, 2010. The maintenance of the books and records and the preparation of the annual financial statements in accordance with German commercial law and supplementary provisions in the statutes are the responsibility of the entity's management. Our responsibility is to express an opinion on the annual financial statements, together with the bookkeeping system, based on our audit.

We conducted our audit of the annual financial statements in accordance with Section 317 of the German Commercial Code and the German generally accepted standards for the audit of financial statements promulgated by the Institut der Wirtschaftsprüfer (Institute of Public Auditors in Germany). Those standards require that we plan and perform the audit such that misstatements materially affecting the presentation of the net assets, financial position and results of operations in the annual financial statements in accordance with German principles of proper accounting are detected with reasonable assurance. Knowledge of the business activities and the economic and legal environment of the entity and expectations as to possible misstatements are taken into account in the determination of audit procedures. The effectiveness of the accounting related internal control system and the evidence supporting the disclosures in the books and records and the annual financial statements are examined primarily on a test basis within the framework of the audit. The audit includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the annual financial statements. We believe that our audit provides a reasonable basis for our opinion.

Our audit has not led to any reservations.

FALK GmbH & Co KG
Wirtschaftsprüfungsgesellschaft Steuerberatungsgesellschaft

Appendix 8

In our opinion, based on the findings of our audit, the annual financial statements as of December 31, 2010 of European Vaccine Initiative-EWIV, Heidelberg, comply with the legal requirements and the supplementary provisions in the statutes and give a true and fair view of the net assets, financial position and results of operations of the entity in accordance with principles of proper accounting.

Heidelberg, April 8, 2011

FALK GmbH & Co KG
Wirtschaftsprüfungsgesellschaft
Steuerberatungsgesellschaft

signed: Meyer
Wirtschaftsprüfer

signed: Ahrens
Wirtschaftsprüfer

ACKNOWLEDGEMENTS

Grateful thanks is extended to the following people, who have contributed significantly to the success of EVI:

The Board and Donors:

France Agid	France
Hannah Akuffo	Sweden
Bjarne Bjorvatn	Norway
Marc de Bruycker	Belgium
Joe Cohen	Belgium
Fulvio Esposito	Italy
Marja Esveld	The Netherlands
Kirsten Havemann	Denmark
Jørn Heldrup	Denmark
Andreas Holtel	Belgium
Joachim Hombach	Belgium
Anna Karaoglou	Belgium
Renée van Kessel	The Netherlands
Wen Kilama	Tanzania
Bernt Lindtjorn	Norway
Charles Mgone	Tanzania
Diarmuid O'Donovan	Republic of Ireland
Nils Strandberg Pedersen	Denmark
Michel Pletschette	Belgium
Harry van Schooten	The Netherlands
Jaak Sinnaeve	Belgium
Charles de Taisne	France
David Weakliam	Republic of Ireland
Klaus Winkel	Denmark

Scientific Advisors:

Pedro Alonso	Spain
Albert Cornelissen	The Netherlands
Paul Hagan	Scotland
Marie-Paule Kieny	Switzerland
Peter Kremsner	Germany
Rose Leke	Cameroun
Pierre Meulien	Republic of Ireland
Louis Molineaux	Switzerland
Piero Olliaro	Switzerland
Artur Scherf	France
Marita Troye-Blomberg	Sweden

Prepared by Jill Iversen and Sten Larsen

Reviewed by Nathalie Imbault and Odile Leroy

Approved by Marita Troye-Blomberg,

Chair of EVI Board

Approved by Sodiomon Sirima,

Chair of EVI Board of Stakeholders



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UniversitätsKlinikum Heidelberg · Im Neuenheimer Feld 326 · 69120 Heidelberg · Germany

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