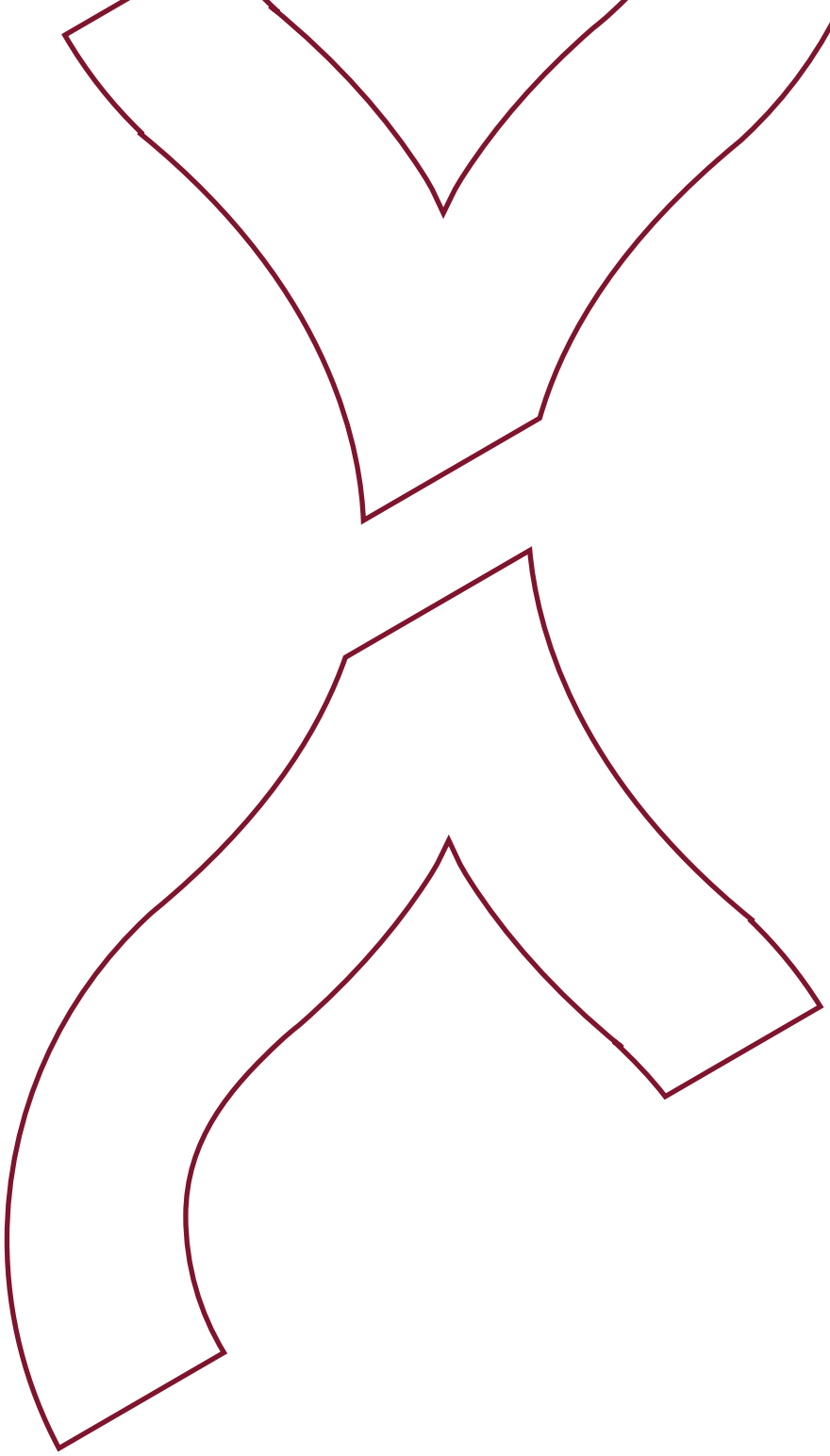


European Vaccine Initiative

Annual Report 2019

Contents

Message from the Chairman and Executive Director

The year 2019 was an eventful year for EVI. Early in the year we had to say goodbye to EVI's Executive Director, Odile Leroy, who decided to retire following a long and successful career. Odile had been leading EVI since 2006 and guiding it to the position it currently holds. We are really grateful for her many years of leadership, dedication and hard work that have put EVI in a great position for the future. Dr Hilde Depraetere filled the position of Acting Executive Director through most of 2019 before we had the pleasure of welcoming Dr. Ole Olesen as the new Executive Director, starting January 1st, 2020.

The EVI Board also saw changes during 2019. Professor Marita Troye-Blomberg, who is one of the founders of EVI, retired from the Board by the end of the year after a long and dutiful membership, most recently as Vice-Chair. We warmly thank Marita for all her support, commitment and wisdom in support of EVI over the years. The Institute for Translational Vaccinology (NL) had to terminate its membership of EVI due to a change in legal status, and therefore we also had to say good-bye to their representative on the Board, Dr Corine Kruiswijk. Finally, Dr Claude Leclerc was replaced by Dr Christiane Gerke as Board representative for Institut Pasteur, Paris. We thank Corine and Claude for their help and service to EVI and warmly welcome Christiane on the Board.

EVI embarked in 2019 on five new collaborative projects with a total budget of 1.76 M EUR and with three of the projects having EVI as the coordinating organisation. These three projects were funded by the GHIT Fund (PfRipr5 project), Horizon 2020 (SHIGETECVAX), and EDCTP2 (ShigOraVax). While PfRipr5 focuses on developing a malaria vaccine candidate, SHIGETECVAX and ShigOraVax are both focusing on vaccines against bacterial diarrhoeal infections and thus consolidate EVI's position in this important disease area.

Apart from the newly started projects, progress of some of the ongoing projects is worth highlighting. In the PRIMALVAC project, an important milestone was reached when first-in-human Phase 1 trials demonstrated that adjuvanted PRIMVAC was safe and well tolerated in 18-35-year-old women who were malaria naive in France, and in women who were naturally exposed to *P. falciparum* and nulligravid in Burkina Faso. These results will be further analysed in 2020 and future development plans will be drafted.

In the ZIKAVAX project, a phase I clinical trial with the lead vaccine candidate against ZIKA virus was initiated in Austria in mid-2019. Results are expected to be available in 2020.

Finally, in the SEmalvac2 project, the interim analysis report assessing the safety and the immunogenicity of the BK-SE36/CpG vaccine one month after the last vaccination has been prepared. The results indicate that the vaccine is well tolerated and immunogenic and support the continuation of the clinical development of the vaccine.

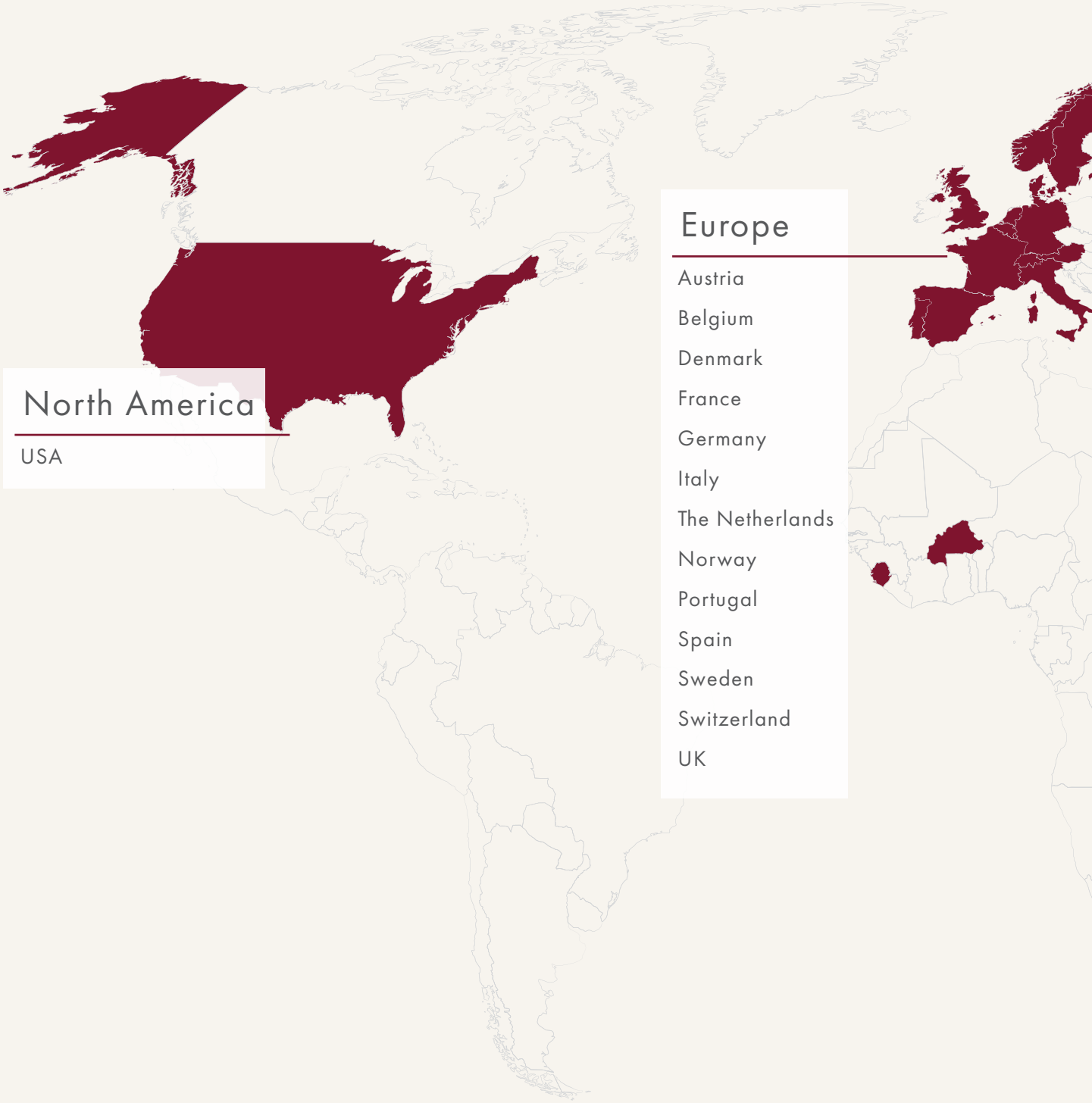
As we look back on 2019, the COVID-19 pandemic is ravaging the world and leaving behind a terrible toll of death, disease and financial ruin. More than ever, the crucial role of vaccines in global public health has become apparent. EVI's commitment to develop efficient and affordable vaccines for all people has therefore never been more important than now.

Dr Clemens Kocken
Chairman of the EVI Board

Dr Ole. F. Olesen
Executive Director


© Julie Johnson, Unsplash.

GLOBAL PARTNERS AND ACTIVITIES MAP

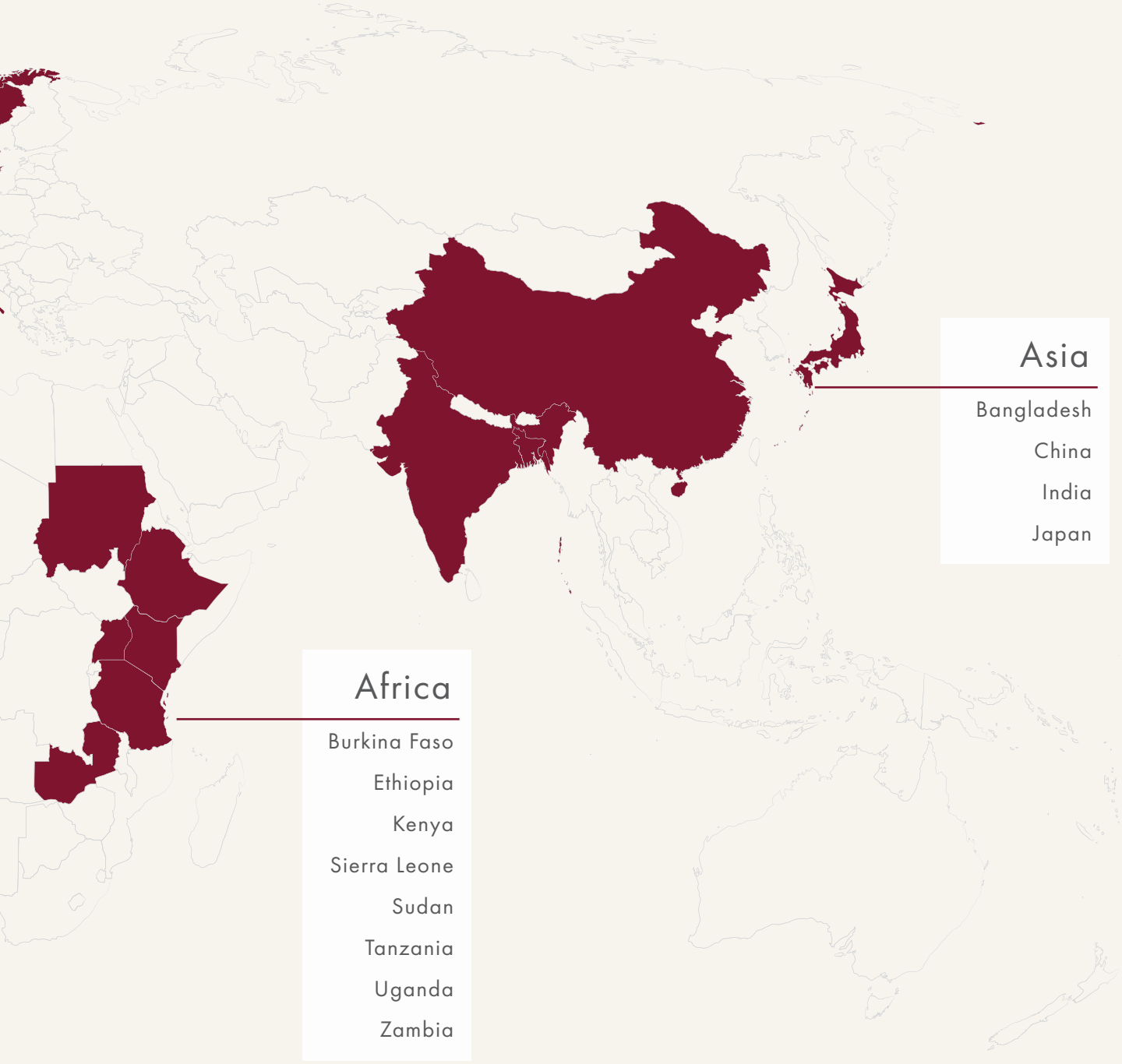


North America

USA

Europe

Austria
Belgium
Denmark
France
Germany
Italy
The Netherlands
Norway
Portugal
Spain
Sweden
Switzerland
UK



Asia

Bangladesh

China

India

Japan

Africa

Burkina Faso

Ethiopia

Kenya

Sierra Leone

Sudan

Tanzania

Uganda

Zambia

2019 EVI VACCINE PROJECTS

MALARIA

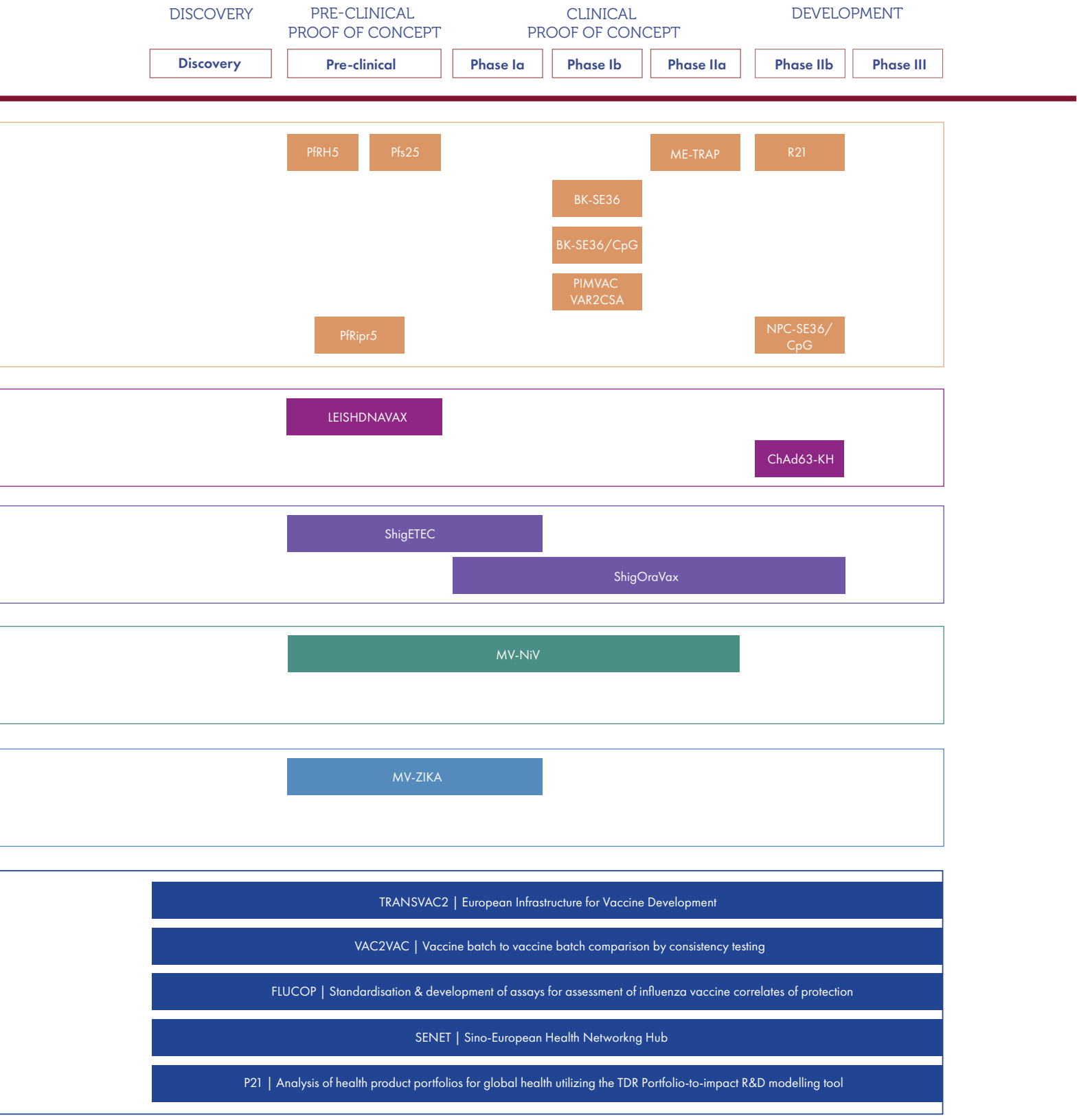
LEISHMANIASIS

DIARRHOEAL DISEASES

NIPAH VIRUS

ZIKA VIRUS

CROSS CUTTING ACTIVITIES


DISCOVERY
PRE-CLINICAL PROOF OF CONCEPT
CLINICAL PROOF OF CONCEPT
DEVELOPMENT
Discovery
Pre-clinical
Phase Ia
Phase Ib
Phase IIa
Phase IIb
Phase III
PfRH5
Pfs25
ME-TRAP
R21
BK-SE36
BK-SE36/CpG
PIMVAC VAR2CSA
PfRipr5
NPC-SE36/ CpG
LEISHDNAVAX
ChAd63-KH
ShigETEC
ShigOraVax
MV-NiV
MV-ZIKA
TRANSVAC2 | European Infrastructure for Vaccine Development
VAC2VAC | Vaccine batch to vaccine batch comparison by consistency testing
FLUCOP | Standardisation & development of assays for assessment of influenza vaccine correlates of protection
SENET | Sino-European Health Networkng Hub
P21 | Analysis of health product portfolios for global health utilizing the TDR Portfolio-to-impact R&D modelling tool

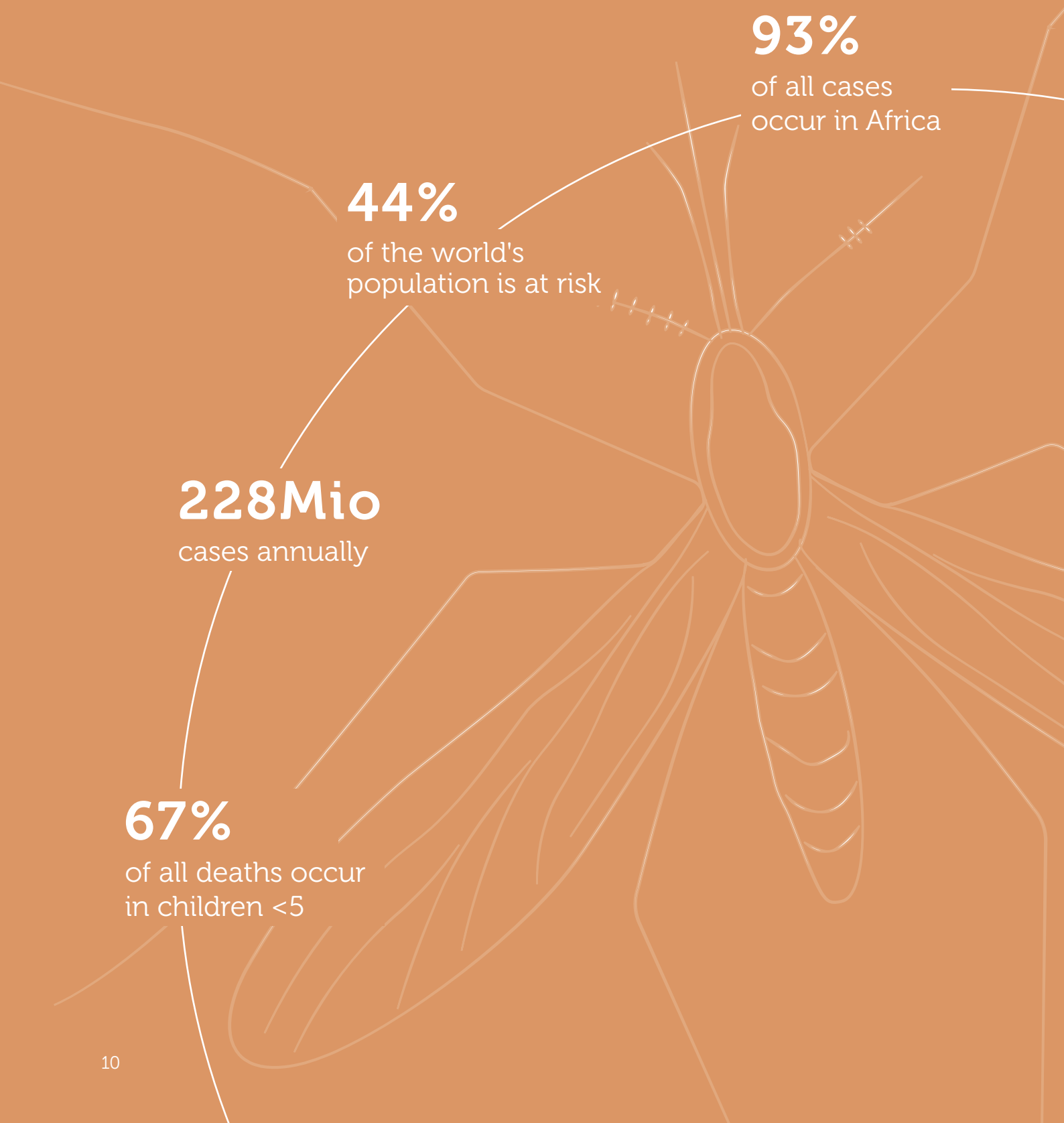
Malaria

93%
of all cases occur in Africa

44%
of the world's population is at risk

228Mio
cases annually

67%
of all deaths occur in children <5



at a glance

Malaria is a mosquito-borne infectious disease. Symptoms typically include fever, chills, tiredness, vomiting, and headaches, ranging from no or very mild symptoms to severe disease and even death. *Plasmodium falciparum* is the most prevalent malaria parasite in the WHO African Region, accounting for 99.7% of estimated malaria cases in 2018, while *P. vivax* is the predominant parasite in the WHO Region of the Americas, causing 75% of malaria cases.

Malaria is a preventable disease and malaria control strategies rely on the use of insecticide treated bed nets and indoor residual spraying to limit human contact with the mosquito vectors, as well as seasonal malaria chemoprevention (SMC) programmes, combined with early detection and treatment of malaria patients. Over the past couple of decades, a significant reduction in transmission rates and malaria incidence was observed due to the implementation of these malaria control measures. However, these control measures need to be applied continuously, are resource-intensive and do not reach all in need, especially during e.g. other disease outbreaks, natural disasters, and wars. Moreover, the rise and spread of drug resistant *P. falciparum* strains threatens the efficacy of the currently used malaria therapy. Natural immunity to *P. falciparum* malaria only develops slowly and leads to partial and short-lived immunity in response to repeated infections. Therefore, the development of vaccines targeting *P. falciparum* malaria would provide an extremely valuable, cost-effective tool complementary to current malaria control methods, and could add significantly to efforts to the eliminate and ultimately eradicate malaria.

SEMALVAC

Target:
Malaria
(Blood-stage)

Timeline:
01 August 2014- 31 July 2020

Development phase in 2019:
Phase Ib

Summary

Clinical development of the BK-SE36 malaria vaccine candidate

The SEmalvac project aims at advancing the clinical development of the *Plasmodium falciparum* serine repeat antigen-5 (SERA5), a blood-stage malaria vaccine candidate. SERA5 is indispensable during blood-stage growth, is suggested to be involved in parasite egress and in parasite immune evasion. SERA5 may likely overcome two major challenges for malaria vaccine antigens as it shows limited polymorphism and has immunodominant IgG epitopes that do not require strict tertiary structures to elicit protective antibodies. A recombinant form of SERA5 N-terminal domain (SE36) was prepared and formulated with aluminium hydroxide gel to yield BK-SE36 vaccine. The safety and immunogenicity of BK-SE36 was demonstrated in a phase Ia clinical trial in malaria naive Japanese adults, and in a phase Ib trial conducted in healthy subjects aged 6–32 years from a malaria endemic area in Uganda.

The main objective of the project is to assess the safety and immunogenicity of BK-36 vaccine candidate in a younger (1-5 years) healthy population living in malaria endemic region of Burkina Faso.

Key Achievements

The clinical results indicate that the BK-SE36 vaccine is well tolerated and immunogenic. The clinical study report finalisation is underway.

EVI Partners

Centre National de Recherche et de Formation sur le Paludisme (CNRFP) (Burkina Faso); Research Institute for Microbial Diseases (RIMD), Osaka University (Japan).

Key Funders

GHIT Fund and Nobelpharma,

SEMALVAC2

Target:
Malaria
(Blood-stage)

Timeline:
01 November 2016-
31 December 2020

Development phase in 2019:
Phase Ib

Summary

Safety evaluation of BK-SE36/CpG in the malaria endemic population

The *Plasmodium falciparum* serine repeat antigen-5 (SERA-5) is a blood stage antigen that plays an essential role in the parasite life cycle. The SEmalvac2 project aims at continuing the clinical development of the recombinant form of the N-terminal domain of the SERA-5 adsorbed on aluminium hydroxide gel (BK-SE36) as malaria blood-stage vaccine for young children living in malaria endemic area.

In pre-clinical model, the immune response is improved when BK-SE36 is formulated with a TLR 9 ligand consisting of CpG motifs that can selectively promote cellular and/or humoral immune responses. The BK-SE36 vaccine candidate formulated with CpC adjuvant (BK-SE36/CpG) was found safe in a phase Ia clinical trial in healthy adults in Japan and elicited antibody titres 3-4-fold higher than BK-SE36 vaccine alone.

In the SEmalvac2 project, launched in parallel to the SEmalvac project, the safety and immunogenicity of the BK-SE36/CpG vaccine will be assessed in healthy malaria exposed adults and children living in Burkina Faso. In this phase Ib age de-escalating trial, the BK-SE36/CpG vaccine safety will be assessed first in adults aged 21-45 years before proceeding to the evaluation of the vaccine in younger populations: children aged 5-10 years and 12-24 months.

Key Achievements

An interim analyses report assessing the safety and the immunogenicity of the BK-SE36/CpG vaccine one month after the last vaccination has been prepared. The results indicate that the vaccine is well tolerated and immunogenic. The results support the continuation of the clinical development of the vaccine.

EVI Partners

Institut de Recherche en Sciences de la Santé (IRSS) (Burkina Faso); Medical Center for Translational Research (MTR), Osaka University Hospital (Japan); Nobelpharma Co., Ltd. (Japan); Research Institute for Microbial Diseases (RIMD), Osaka University (Japan).

Key Funders

GHIT Fund and Nobelpharma

PfRipr5

Target:
Malaria
(Blood Stage)

Timeline:
01 April 2019-
30 June 2021

Development phase in 2019:
Pre-clinical

Summary

Further development of a new asexual blood-stage malaria vaccine candidate (PfRipr5)

The PfRipr5 antigen is a novel highly conserved asexual-blood stage malaria vaccine candidate that could alleviate the concern of strain-specificity that often hampers the efficacy of vaccines in clinical trials. The antigen was discovered following a large-scale screening of merozoite-specific recombinant proteins of *Plasmodium falciparum*. Antibodies against PfRipr showed growth inhibition activities on both 3D7 and FVO strains of *P. falciparum* in in-vitro studies. The most potent inhibitory fragment of PfRipr (renamed PfRipr5) has also been identified and monoclonal antibodies against this fragment also demonstrated potent growth inhibition activity. This antigen demonstrates a desired profile and is a promising candidate in the development of next-generation malaria vaccines.

This PfRipr5 project aims to further advance the development of this new asexual blood-stage malaria vaccine candidate, which was discovered by researchers in Ehime University in collaboration with Sumitomo Dainippon Pharma Co., Ltd., Japan. Different expression systems for the antigen will be tested and compared, subsequently the immunogenicity of the antigen formulated with three different adjuvants already in use in humans will be tested in different model systems. Ultimately, the project is advancing the development of a novel blood-stage antigen that in the future may form part of a more effective multi-antigen-multistage malaria second-generation malaria vaccine.

Key Achievements

Recombinant PfRipr5 was produced in scalable expression systems and further characterised by Surface Plasmon Resonance (SPR) assay, Western Blot and sandwich ELISA. This characterisation allowed the choice of lead expression system and the formulation conditions for the recombinant protein and larger scale production.

EVI Partners

Ehime University (Japan); Instituto de Biologia Experimental e Tecnológica (iBET) (Portugal).

Key Funders

GHIT Fund

PRIMALVAC

Target:
Placental malaria

Timeline:
01 December 2011 - 31 December 2019

Development phase in 2019:
Phase I

Summary

The aim of the PRIMALVAC project was to obtain the proof of concept that a placental malaria vaccine candidate can be developed. A placental malaria vaccine is expected to induce long-lasting or rapidly boosted cross-reactive antibodies that inhibit the binding of the infected erythrocytes to placental CSA. VAR2CSA variants were recombinantly expressed and characterized for their immunogenic activity, specifically for their ability to elicit functional and cross-reactive antibodies against placental parasite phenotypes. PRIMVAC, the candidate antigen that best met strict immunogenicity criteria was moved into preclinical and clinical development. In a phase Ia/b clinical trial, we assessed the safety and immunogenicity of PRIMVAC adjuvanted with Alhydrogel or glucopyranosyl lipid adjuvant in stable emulsion (GLA-SE) in French and Burkinabe women who were not pregnant.

Key Achievements

This first-in-human phase 1 trial assessed the safety and immunogenicity of adjuvanted PRIMVAC in 18-35-year-old women who were malaria naive in France and in women who were naturally exposed to *P. falciparum* and nulligravid in Burkina Faso. This trial is registered with ClinicalTrials.gov, NCT02658253.

The results of the phase Ia/b clinical trial show that PRIMVAC adjuvanted with Alhydrogel or GLA-SE was well tolerated at all the tested doses. The vaccine candidate induced an immune response in all vaccinated women, with the production of antibodies that persisted for several months. The antibodies were capable of both, recognizing the parasitic antigen on the surface of the infected red blood cells and inhibiting their adhesive capacity. Cross-reactivity against heterologous VAR2CSA variants was limited and only observed in the higher dose group. An alternate schedule of immunisation, antigen dose, and combinations with other VAR2CSA-based vaccines are envisaged to improve the cross-reactivity against heterologous VAR2CSA variants. Planning for the further development of this vaccine candidate is on-going.
Taken together, the study has shown that the vaccine candidate has the capacity to trigger a lasting and potentially protective immune response.

Publications

Preclinical immunogenicity and safety of the cGMP-grade placental malaria vaccine PRIMVAC. Chêne A. et al., EBioMedicine. 2019 Apr; 42:145-156.

EVI Partners

Assistance Publique Hôpitaux de Paris, Hôpital Cochin (France); Centre d'investigation clinique en Vaccinologie Cochin-Pasteur (CIC1417) (France); Centre National de Recherche et de Formation sur le Paludisme (CNRFP) (Burkina Faso); EUCLID/F-CRIN Clinical Trials Platform (France); GTP Technology (France); Infectious Diseases Research Institute (IDRI) (USA); Institut national de la santé et de la recherche médicale (Inserm) (France); Novasep (formerly Henogen) (Belgium).

Key Funders

German Federal Ministry of Education and Research (BMBF) through Kreditanstalt für Wiederaufbau (KfW) and Irish Aid Department of Foreign Affairs and Trade

© Jose Aragones, Pexels.

MMVC

Target:
Malaria
(Multi-stage)

Timeline:
01 April 2018-
30 September 2023

Development phase in 2019:
Phase I/Phase II

Summary

The Multi-Stage Malaria Vaccine Consortium (MMVC)
The MMVC project is targeting this multi-component, multi-stage approach based on antigens that have shown promise in clinical trials assessing the single components, e.g. 1) the RTS,S biosimilar R21 that is expected to elicit an improved malaria-specific immune response, 2) the viral vectored prime-boost strategy where the modified vaccinia Ankara virus (MVA) is used for priming and a chimpanzee adenovirus (ChAd63) is used for boosting immune responses against the ME-TRAP antigen, 3) the PfRH5 in various formulations and delivery systems, as well as 4) a transmission blocking component that is expected to inhibit the transmission of the parasite from humans to mosquitoes.

MMVC will undertake a tightly coordinated series of lead-in trials in 2018-2021 building towards a phase IIb multi-stage vaccine efficacy trial in West and East African infants from late 2021 to 2023.

In parallel MMVC will build new capacity to test the ability of the combination vaccine and/or its transmission-blocking component to block human-to-mosquito transmission in African adults, foreseeing the potential use of the combination vaccine in elimination campaigns.

This consortium, comprising very experienced and new African trial sites with leading northern institutions and companies, offers an unprecedented opportunity for rapid development of a deployable high-efficacy multi-stage malaria vaccine.

Key Achievements

EVI is leading the work related to capacity strengthening and networking. Progress has been made in establishing the controlled human malaria infection models using cryopreserved-vialled sporozoites in Kenya and blood-stage parasites in Tanzania (IHI). Capacity has been strengthened at IRSS in Burkina Faso that will allow field efficacy testing of transmission-blocking vaccines using direct membrane feeding assays. Three African PhD students have started their projects on various MMVC clinical trial related topics. Networking and training activities have been initiated.

The MMVC clinical trials are progressing successfully, with special mention of the vaccine trials assessing adjuvanted R21 in a phase I age de-escalation trial in Kenya (ClinicalTrials.gov Identifier: NCT03580824) and a phase II safety, immunogenicity and efficacy trial in Burkina Faso (ClinicalTrials.gov Identifier: NCT03896724). The planning for a Phase 3 trial is ongoing.

EVI Partners

Epicentre (France); Institut de Recherche en Science de la Santé - Unité de Recherche Clinique de Nanoro (IRSS-URCN) (Burkina Faso); Ifakara Health Institute Trust (IHI) (Tanzania); University of Sierra Leone (USL) (Sierra Leone); Institut de Recherche pour le Développement (IRD) (France), Groupe de Recherche Action en Santé sarl. (GRAS) (Burkina Faso), London School of Hygiene and Tropical Medicine, (LSHTM) (UK); Novavax AB (Sweden), Janssen Vaccines & Prevention B.V (The Netherlands); Serum Institute of India Pvt. Ltd (India); University of Sierra Leone (USL) (Sierra Leone); University of Oxford (UOXF) (UK).

Key Funders

European & Developing Countries Clinical Trials Partnership 2 (EDCTP2)

Leishmaniasis

94%
of all cases occur in Brazil, Ethiopia, India, Kenya, Somalia, South Sudan & Sudan

1 Billion
of the world's population is at risk

700,000 - 1 Mio
cases annually

20,000
deaths annually

*Cases and deaths refer to VL

at a glance

Leishmaniases are caused by a protozoan *Leishmania* parasites, transmitted by the bites of infected female phlebotomine sandfly.

There are three main clinical forms of leishmaniases: i) cutaneous, the most common form of the disease (CL); ii) visceral, also known as kala-azar and the most fatal (VL); and iii) mucocutaneous.

Whereas cutaneous and mucocutaneous leishmaniases are chronic, non-life-threatening but highly stigmatising, visceral leishmaniasis is fatal if left untreated in over 95% of cases.

Post kala-azar dermal leishmaniasis (PKDL) is a sequel of VL which develops in 5-10% of cases but more commonly after completing treatment for VL. It is mainly observed in Sudan and India and plays a central role in VL transmission as people with PKDL are reservoir of *Leishmania* parasites.

Leishmaniasis is classified as one of the "most neglected diseases" due to the limited resources invested in diagnosis, treatment, and control, and its strong association with poverty. It represents a severe barrier to socio-economic development.

To date, there are no vaccines approved for human use against leishmaniases, and control measures rely on chemotherapy to alleviate disease as well as on vector control to reduce transmission. The development of vaccines has been hampered by significant antigenic diversity and the fact that the parasites have a digenetic life cycle in at least two hosts (sandfly vector and human, but also an animal reservoirs). An equally important consideration for the design and implementation of anti-parasite vaccines in general is the contribution of the genetics of the target host population and their susceptibility to infection and disease, i.e. the severity of disease manifestation.

LEISHDNAVAX

Target:
Cutaneous and visceral leishmaniasis

Timeline:
01 September 2017-31 March 2020

Development phase in 2019:
Pre-clinical

Summary

Preclinical and preparation of early clinical testing of a new vaccine candidate against cutaneous leishmaniasis

The objective of this project was to complete the preclinical development of LEISHDNAVAX, a candidate DNA vaccine that has been successfully tested for antigenicity in humans in ex vivo studies, and for efficacy in a mouse model for visceral leishmaniasis, by assessing LEISHDNAVAX efficacy against cutaneous leishmaniasis (CL), as recommended by the German regulatory agency. The project encompassed three specific goals: preclinical evaluation of LEISHDNAVAX to study its (i) prophylactic and (ii) therapeutic potential against CL; and (iii) preparation of a phase I clinical trial. LEISHDNAVAX, a T cell-directed DNA vaccine with minimal expression cassettes for 5 *Leishmania* antigens, vaccination schemes were optimized to be tested against two *Leishmania* species endemic in different regions of the world, *L. major* and *L. mexicana*.

Prophylactic and therapeutic vaccine efficacy was evaluated in resistant C57BL/6 and susceptible BALB/c mouse rump infection CL models. Vaccine efficacy assessment was based on immunological criteria (T-cell response, cytokine and antibody production), lesion size and parasite burden. Production and quality control of pre-GMP vaccine candidate, synthetic peptides, peptide libraries and antigens as well as preparation of phase I clinical trial activities were initiated.

Key achievements

University of Nagasaki has conducted and finalised prophylactic and therapeutic studies to assess the efficacy of the LEISHDNAVAX vaccine candidate in cutaneous leishmaniasis using luciferase-tagged parasite strains. Prophylactic effects of LEISHDNAVAX on *L. major* infection, assessed by immunogenicity and challenge experiments, revealed no significant difference in parasite burden and lesion size between immunized and control group in both a resistant and susceptible mouse model. Immunization induced antibody production to Leishmania antigens and IFN-g production in spleen T-cells in response to most antigen peptide pools. The prophylactic effects with *L. mexicana* challenge were similar to those observed with *L. major*. Two immune monitoring marker panels for analysis of Phase I clinical trial were designed.

EVI Partners

Charité – Universitätsmedizin Berlin (Germany); London School of Hygiene and Tropical Medicine (LSHTM) (UK); Mologen AG (Germany); University of Nagasaki (Japan).

Key Funders

GHIT Fund

PREV_PKDL

Target:
Post kala-azar dermal leishmaniasis

Timeline:
01 April 2018-30 June 2023

Development phase in 2019:
Preparation of phase IIb

Summary

Clinical development of a therapeutic vaccine for prevention of post-kala azar dermal leishmaniasis

The PREV_PKDL project aims at advancing the clinical via the development of ChAd63-KH vaccine for the prevention of post-kala azar dermal leishmaniasis (PKDL). The ChAd63-KH vaccine candidate will be evaluated in clinically cured visceral leishmaniasis patients aged 12-50 years in a safety and efficacy phase IIb clinical trial powered to detect a reduction in PKDL incidence. The results of this trial will be decisive in the future development of the ChAd63-KH vaccine candidate. Additionally, to better understand the disease as well as drug and vaccine responses, multidimensional, multiparameter phenotyping will be conducted on patient cohorts recruited across the countries of the Leishmaniasis East Africa Platform (LEAP; Ethiopia, Kenya, Sudan and Uganda). A major aim of the PREV_PKDL project is to support LEAP in its ambitions by extending its research capacity in immunology and vaccine development. This will be achieved through a program to strengthen immunology research capacity through the development of a flow cytometry network across LEAP. This capacity strengthening will help LEAP to develop as a major force for research and training on poverty-related neglected diseases in the East African Region.

Key achievements

The preparation of the phase IIb clinical trial at IEND, Sudan is ongoing. Generic and site-specific protocols, participant's documents for the multidimensional, multiparameter phenotyping research study have been prepared for submission to the relevant ethics committees in Kenya, Uganda, Ethiopia, Sudan and United Kingdom.

Five flow cytometers have been purchased following a tender procedure and have been delivered at University of York allowing a first hands-on training of the flow cytometry managers appointed at the African sites. Following renovation and equipment of laboratories, the delivery of flow cytometers at their final destinations as well as their successful installation are almost completed.

Publications

Cyt-Geist: Current and Future Challenges in Cytometry: Reports of the CYTO 2019 Conference Workshops. Czechowska K et al., Cytometry A. 2019 Dec;95(12):1236-1274

EVI Partners

Institute of Endemic Diseases (IEND) (Sudan); Kenya Medical Research Institute (KEMRI) (Kenya); Makerere University (Uganda); University of Gondar (Ethiopia); University of York (UK).

Key Funders

European & Developing Countries Clinical Trials Partnership 2 (EDCTP2) and co-funded by Wellcome Trust

The first PREV_PKDL annual meeting was successfully organised in Addis Ababa, Ethiopia on 08-10 April 2019.

Diarrhoeal diseases

525,000
deaths annually

1 Billion
of the world's population is at risk

1.7 Billion
cases annually

1 in 10
childhood deaths

*Cases and deaths refer to Childhood Diarrheal Disease

at a glance

According to the World Health Organization (WHO) diarrhoeal disease is the second leading cause of death and high morbidity in children under five years old. Every year, around 525 000 children die of diarrhoeal disease. As diarrhoeal episodes usually follow the ingestion of contaminated food or water, children and individuals living in low- and middle-income countries are particularly at risk. It is estimated that currently about 780 million people lack access to improved drinking-water and 2.5 billion lack improved sanitation.

Shigella and enterotoxigenic *Escherichia coli* (ETEC) account for about 200 million episodes of diarrhoea per year and are directly or indirectly responsible for about 107 500 annual deaths in children under 5-year age. The African region and the South East Asian region have the highest percentage of ETEC episodes, while most *Shigella* cases occur in the African region, Eastern Mediterranean region and Southern Asian region. For those surviving infections, it has been observed that prolonged and/or repeated symptomatic episodes in childhood can have long term consequences such as reduced cognitive development, poorer educational outcomes, reduced wages and increased risk of non-communicable diseases in adulthood.

Conventional treatment includes rehydration therapy and the use of antibiotics. However, given the emergence of multi-drug resistance strains of ETEC and *Shigella* the development of vaccines is becoming increasingly imperative.

SHIGETECVAX

Target:
Diarrheal Disease/ Shigella/ETEC

Timeline:
01 September 2019- 31 August 2024

Development phase in 2019:
Pre-clinical

Summary

Early clinical development of a live, attenuated combination vaccine against *Shigella* and ETEC diarrhoea

SHIGETECVAX is developing a novel oral vaccine against two closely related bacteria that are leading causes of diarrhoea. Based on antigens not targeted in previous vaccines, it is much safer, enabling higher doses. Potentially more effective against both pathogens, this vaccine candidate could save millions of lives.

Although vaccination is an effective way to reduce the huge disease burden associated with diarrhoea caused by enteric pathogens, many attempts to develop vaccines for shigellosis and ETEC infections have failed and a number of current approaches are too complex and costly to provide an adequate solution for LMICs. This Consortium is dedicated to advancing a radically new approach against *Shigella* and ETEC. Instead of targeting the immunodominant, but highly variable *Shigella* LPS O-antigen, elimination of this antigen in this vaccine candidate allows for the immune recognition of minor and highly conserved antigens that are shared among different types of *Shigella* and ETEC.

Key achievements

The project started officially in September 2019. Within the first months of the project, the governance structures were established. The development of immunoassays has commenced. The GMP manufacture of the ShigETEC vaccine candidate was started, along with the selection of the clinical trial site and CRO that will oversee the clinical activities. Icddr,b initiated a sero-epidemiology studies to assess naturally acquired immunity to *Shigella* and ETEC.

EVI Partners

Eveliqure Biotechnologies GmbH (Austria); International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) (Bangladesh); PATH (USA); University of Gothenburg (Sweden).

Key Funders

European Union (Horizon 2020 Programme)

SHIGETECVAX kick-off meeting at the Eveliqure facilities in Vienna, Austria on 14 October 2019.

ShigOravax

Target:
Diarrheal Disease/ Shigellosis

Timeline:
01 October 2019-
30 September 2024

Development phase in 2019:
Preparation of phase Ia/Ib

Summary:

Early clinical development of an oral Shigella vaccine through phase II study in Africa

The ShigOraVax project aims at advancing the clinical development of a safe, efficacious and affordable Shigella vaccine. The project aims at developing an oral Shigella vaccine called 'ShigOraVax' against three serotypes of *Shigella flexneri* (2a, 3a, and 6) as well as *Shigella sonnei*. Specific objectives of this project include (i) conduct of a phase Ia/b clinical trial in European and African adults followed by (ii) an age de-escalating phase II in Burkina Faso and a multi-centre phase IIb clinical trial in Burkina Faso and Zambia. Moreover, specific epidemiologic data will be generated on the incidence of Shigella disease in the two African countries among children under five. The results of this project will strengthen the vaccine pipeline against a major diarrhoeal disease and making it available for late stage clinical development.

Key achievements

The kick off meeting was organized in Burkina Faso, just after the project official start in October 2019. The development of the immunological assays to assess the immune response after vaccination has started at University of Gothenburg. The preparation of the protocol for the phase Ia/Ib clinical trial and for the epidemiology study has started.

ShigOraVax kick off meeting in Ouagadougou, Burkina Faso on 23-24 October 2019.

EVI Partners

Centre for Infectious Disease Research in Zambia (Zambia); Groupe de Recherche Action en Santé (GRAS) (Burkina Faso); Hilleman Laboratories (India); Leiden University Medical Center (LUMC) (The Netherlands); University of Gothenburg (Sweden).

Key Funders

European & Developing Countries Clinical Trials Partnership 2 (EDCTP2)

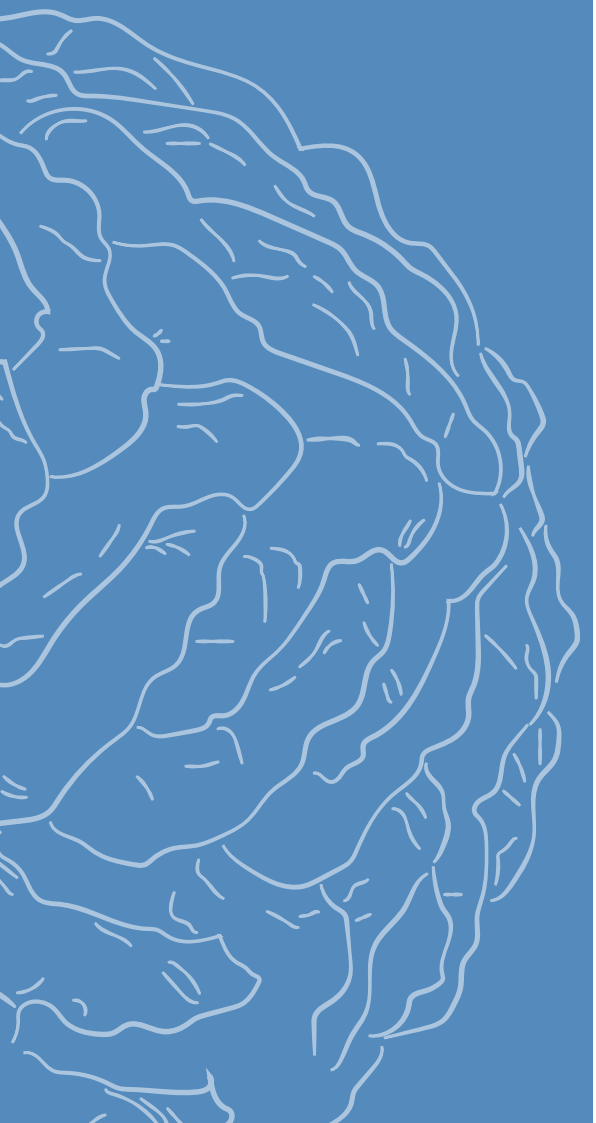
Zika Virus

86
countries reported mosquito-transmitted Zika infection

2.7 Billion
of the world's population is at risk

1 in 5
people infected develop symptoms

5-15%
infants with Zika-associated defects



at a glance

Zika virus is a mosquito-borne flavivirus. The virus is transmitted through the bite of an infected Aedes mosquito, mainly *Aedes aegypti*, in tropical and subtropical regions. The same mosquito also transmits the viruses causing dengue, chikungunya and yellow fever. Zika virus is also transmitted from mother to fetus during pregnancy, through sexual contact, transfusion of blood and blood products, and organ transplantation. The incubation period (the time from exposure to symptoms) of Zika virus disease is estimated to be 3–14 days.

Symptoms are similar to other arbovirus infections, and include fever, skin rashes, conjunctivitis, muscle and joint pain, malaise, and headache. These symptoms are usually mild and last for 2-7 days and often do not require any specific treatment. However, Zika virus infection during pregnancy is a cause of microcephaly and other congenital abnormalities in the developing fetus and newborn and can lead to pregnancy complications such as fetal loss, stillbirth, and preterm birth. Zika virus was shown to be a trigger of the Guillain-Barré syndrome neuropathy and myelitis, particularly in adults and older children. Zika virus infection can only be confirmed by laboratory tests of blood or other body fluids, such as urine or semen.

Currently, there is no therapy available to treat or prevent Zika virus infection or its associated diseases. Protection against mosquito bites remains a key preventive measure.

ZIKAVAX

Target:
Zika virus disease

Timeline:
01 October 2016-
30 September 2020

Development phase in 2019:
Phase I clinical trial

Summary

Fast track development of a Zika vaccine based on measles vector

The ZIKAVAX project aims at developing a safe, effective, and affordable preventive vaccine against Zika virus infection. To achieve this goal, ZIKAVAX uses a delivery platform technology based on a measles vector (MV) with demonstrated proof of principle in humans and a preclinical track record of rapid adaptability and effectiveness for a variety of pathogens. In ZIKAVAX, following antigen selection and expression, immunisation studies were conducted with the Zika vaccine candidate in mice and in a non-human primates' challenge model that was developed by the consortium. The ultimate goal of ZIKAVAX is the demonstration of safety and immunogenicity of a recombinant measles-Zika vaccine candidate (MV-ZIKA) in adult volunteers in a phase Ia clinical trial.

Key achievements

Different vaccine constructs were cloned and characterised in cellular assays. Replicating recombinant vectors were then generated by reverse genetics using a cell-based system developed by Institut Pasteur and were further characterised for antigen expression, growth characteristics and genetic stability.

Based on these data, three constructs were selected for further immunogenicity and efficacy studies in mice. These studies allowed the identification of a lead vaccine candidate, MV-Zika.

Immunogenicity and protective efficacy of MV-Zika was further demonstrated in a non-human primate challenge model for Zika virus infection.

Profiting from the knowledge acquired on manufacturing its MV-based Chikungunya vaccine candidate (MV-CHIK), Themis GMP manufactured the selected MV-Zika vaccine candidate erase was performed and the product was released in 2019.

The phase I clinical trial with the lead vaccine candidate was initiated in Austria in Mid-2019 (ClinicalTrials.gov Identifier: NCT04033068). Results are expected in 2020.

EVI Partners

Commissariat à l'énergie atomique et aux énergies alternatives (CEA) (France); Institut Pasteur (France); Themis Bioscience (Austria).

Key Funders

European Union (Horizon 2020 Programme)

© Pop & Zebra, Unsplash.

Nipah Virus

Outbreaks
Malaysia, Bangladesh, Singapore, India and Philippines

2 Billion
people at risk

300
cases in Bangladesh

40% - 100%
case fatality rate

at a glance

Nipah virus (NiV) is a zoonotic virus, for which the primary reservoirs are bats and pigs. Transmission can also occur through contaminated food or directly from person to person. It belongs to a family of viruses that also includes Hendra virus, another bat-borne virus that cause lethal infection in horses and humans. The natural hosts of the virus are Pteropus fruit bats, commonly known as flying foxes.

Nipah disease symptoms begin 5 to 14 days after infection and initially include fever, headaches, muscle pain, vomiting and sore throat. The disease then progresses rapidly, causing a combination of brain inflammation (encephalitis) and serious respiratory problems such as pneumonia. Patients who recover can suffer long-term neurological conditions, including seizures and personality changes. Initial diagnosis is difficult because the early signs and symptoms are non-specific. Nipah virus was first identified in 1999 during an outbreak of illness affecting pig farmers and others having close contact with pigs in Malaysia and Singapore.

Nipah causes severe disease, with case fatality rates in Malaysia, Bangladesh and India of between 40% and 100%, being one of the deadliest viruses known to infect humans.

Nipah has caused only a few known outbreaks in South and Southeast Asia, but the potential for much larger exposure is significant since more than 2 billion people live in areas where Pteropus bats are found. There is a risk it could also be spread to areas where fruit bats do not live via transmission between people. Thus, Nipah virus has the biological potential to be a truly global threat.

MV-NIV

Target:
Nipah virus infection

Timeline:
01 March 2019- 31 March 2021

Development phase in 2019:
Preclinical

Summary

The CEPI-funded Nipah vaccine candidate is a live attenuated measles vector-based vaccine containing the Nipah-virus G gene (Malaysia strain). The recombinant vaccine candidate was developed at The Institute of Medical Science, University of Tokyo, and has shown to induce humoral and cellular responses in a preclinical study. In addition, the vaccine protected against lethal nipah virus infection in a hamster and non-human primate model. Process development and manufacturing is under development at Batavia Biosciences.

Key achievements

The kick-off meeting took place in Leiden in March 2019, marking the official start of the CEPI-funded Nipah project.

Partners also met face-to-face in October to discuss and address the latest progress on the project and to attend the Symposium "New Vaccines for Saving Lives: Focusing on Nipah Virus Infection", organised by University of Tokyo.

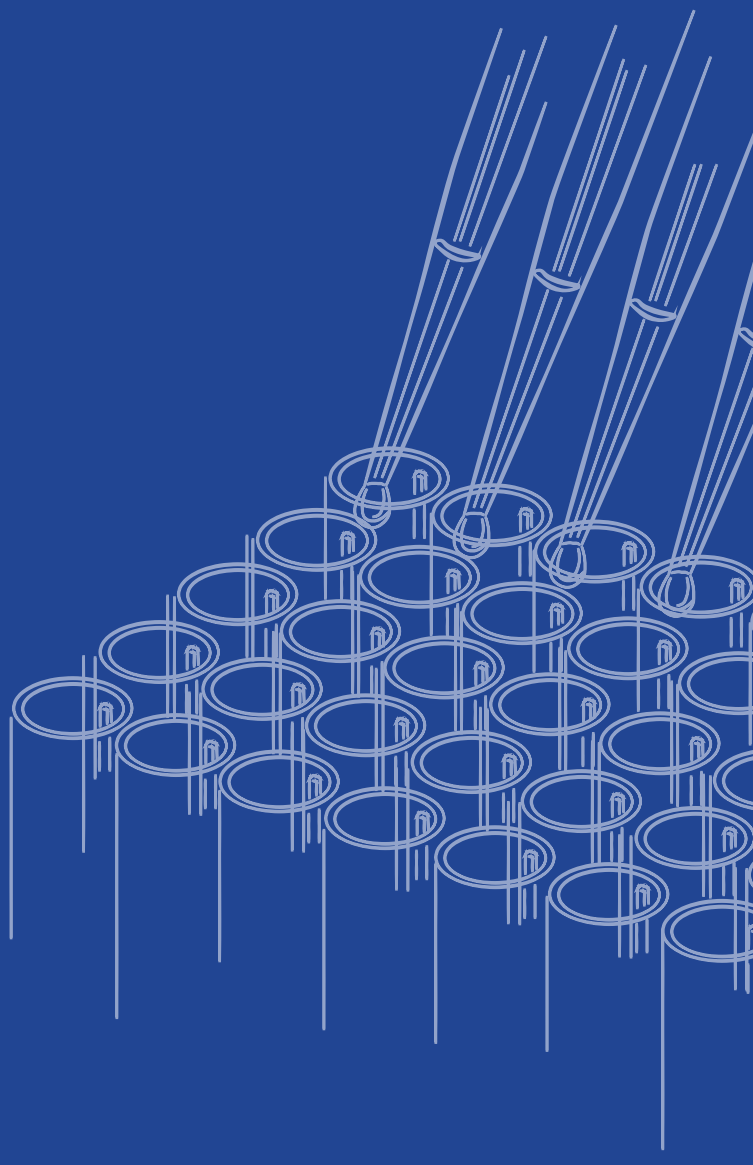
EVI Partners

Batavia Biosciences B.V. (The Netherlands); University of Stanford (USA); University of Tokyo (Japan).

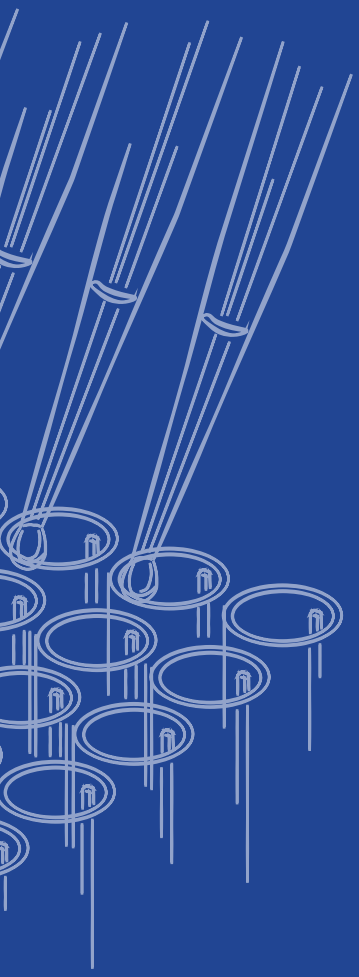
Key Funders

Coalition for Epidemic Preparedness Innovations (CEPI)

Cross-cutting activities



In addition to the different activities that EVI undertakes to advance the development of vaccines for specific diseases, EVI also coordinates and promotes a number of projects that address disease-overarching issues that are common and relevant for vaccine R&D in general.



TRANSVAC2

Target:
Vaccine R&D infrastructure and Capacity Building

Timeline:
01 May 2017- 30 April 2022

Summary

European Vaccine Research and Development Infrastructure
TRANSVAC2 is a joint effort of leading European research groups and SME's and is designed to accelerate the vaccine development by strengthening vaccine research and training in vaccinology:

- TRANSVAC2 offers a wide range of services, the majority of which can be accessed free-of-charge, organised in four different platforms: Technology, Immunocorrelates and System Biology, Animal Models and Clinical Trial Support.
- TRANSVAC2 consortium has set up 14 training modules at leading European centres that can be combined to create customised international courses on vaccine R&D with the aim to train scientists in vaccine research and development in order to sustain Europe's excellence in this field.

Currently, TRANSVAC2 is implementing three types of activities: (i) Transnational Access, (ii) Joint Research Activities and (iii) Networking Activities. Transnational Access provides scientific-technical services that support the development of vaccines. These services are complemented by Joint Research Activities, conducted by the consortium partners, that address current major gaps in vaccine development knowledge and are designed to improve and support the scientific-technical services. The TRANSVAC research activities focus heavily on improving adjuvants, predictive assays, systems biology and animal models. In addition, the Networking Activities further strengthen cooperation between the scientific community, industry and other key stakeholders, for example by offering training and organizing workshops and conferences.

Key achievements

In 2019 six trainings for about 70 researchers were organised by TRANSVAC2 partners in areas as analytical science, clinical and process development, statistics and adjuvants.
In 2019 3 calls were launched for TNA services where 8 projects requesting 11 services were granted. Additionally, three projects awarded in previous years have been successfully completed enabling users to reach specified milestones and take further steps in the development of their vaccine candidates. As part of the Networking Activities, a database of types of sample collections available at partner institutes has been established. These collections include different animal study derived products (sera, tissues etc.), mainly involving a biohazard level 3 or 4 for mice, NHP and non-rodent animals. These samples are offered to be shared with other researchers in the spirit of 3Rs to reduce number of animals used in research studies (www.transvac.org/biobank-sample-sharing).

Finally, a workshop on "In vivo imaging of host response to vaccines and infections" was held on 29 March 2019 at CEA-IDMIT (Paris, France) gathering 50 researchers from Europe working on infectious diseases and vaccine development.

All partners had a great opportunity to share their experience gathered in the project during the Annual Meeting that was held 15-16th May 2019 in Lyon, France, hosted by Bioaster (https://www.bioaster.org/).

EVI Partners

BIOASTER - Fondation de Cooperation Scientifique (France); Biomedical Primate Research Centre (BPRC) (The Netherlands); Commissariat a l'energie atomique et aux energies alternatives (CEA/IDMIT) (France); ETH Zürich (Switzerland); European Clinical Research Infrastructure Network (ECRIN) (France); European Infrastructure for Translational Medicine (EATRIS) (The Netherlands); Fraunhofer Institute for Molecular Biology and Applied Ecology (IME) (Germany); Genlbet Biopharmaceuticals, S.A. (Portugal); Helmholtz Centre for Infection Research (HZI) (Germany); Institut national de la Recherche agronomique (INRA) (France); Institute for Translational Vaccinology (ITV) – Intravacc, (The Netherlands); Instituto de Biologia Experimental e Tecnológica (iBET) (Portugal); Institut de Recerca i Tecnologia Agroalimentàries (IRTA) (Spain); Instruct Academic Services Limited (UK); Leiden

University (The Netherlands); Leiden University Medical Center, (LUMC) (The Netherlands); London School of Hygiene and Tropical Medicine (LSHTM) (UK); Public Health England (PHE) (UK); Sclavo Vaccine Association (SVA) (Italy); Statens Serum Institut (SSI) (Denmark); The National Institute for Biological Standards and Control (NIBSC) (UK); University of Oxford (UOXF) (UK); University of Siena (UNISI) (Italy); Vaccine Formulation Institute (VFI) (UK); Wageningen University & Research (SWR) (The Netherlands).

Key Funders

European Union (Horizon 2020 Programme)

VAC2VAC

Target:
Batch to Batch Control Testing

Timeline:
01 March 2016- 28 February 2021

Summary

Vaccine batch to vaccine batch comparison by consistency testing

VAC2VAC aims to develop and validate quality testing approaches for human and veterinary vaccines using non-animal methods. The initiative will provide data to support the "Consistency Approach" for quality control of established vaccines, where current quality control approaches are often relying on *in vivo* methods.

VAC2VAC involves experts from veterinary and human vaccine industry in a partnership with official medicines control laboratories, academia, translational research organisations, and vaccinology alliances. The project partners are developing, optimising and evaluating physicochemical methods, immunochemical methods, cell-based assays and multiparametric and bioinformatics assays for routine control testing of vaccines. This effort is being conducted in collaboration and consultation with regulatory agencies.

Key achievements

Method development

A cell-based assay (monocyte-activation test) based on the use of human peripheral mononuclear cells (PBMC) has been validated and transferred to the respective industrial partner. The assay has been adapted to GMP standards and a variation has been submitted to regulatory authorities for approval and final implementation of the assay in routine quality control. The development of an inflammasome activation assay has been finalized. The assay could be helpful for characterization of intermediate alum-containing products. Additionally, proof of concept and specificity of a B-cell assay based on human PBMC for consistency testing of DTaP antigens was shown. Multiparametric assays and bioinformatics were applied for the characterization of tetani seed strains at DNA, RNA and protein level. A two-stage DNA-based method has been established and method validation will be initiated. Validation of a Mass Spectrometry-based method has been finalized. In order to study the interaction of vaccine/antigens with antigen presenting cells, cellular platforms were identified and protocols for obtaining and differentiating cells from human, dog and chicken were established.

Work on Pre-validation of selected methods

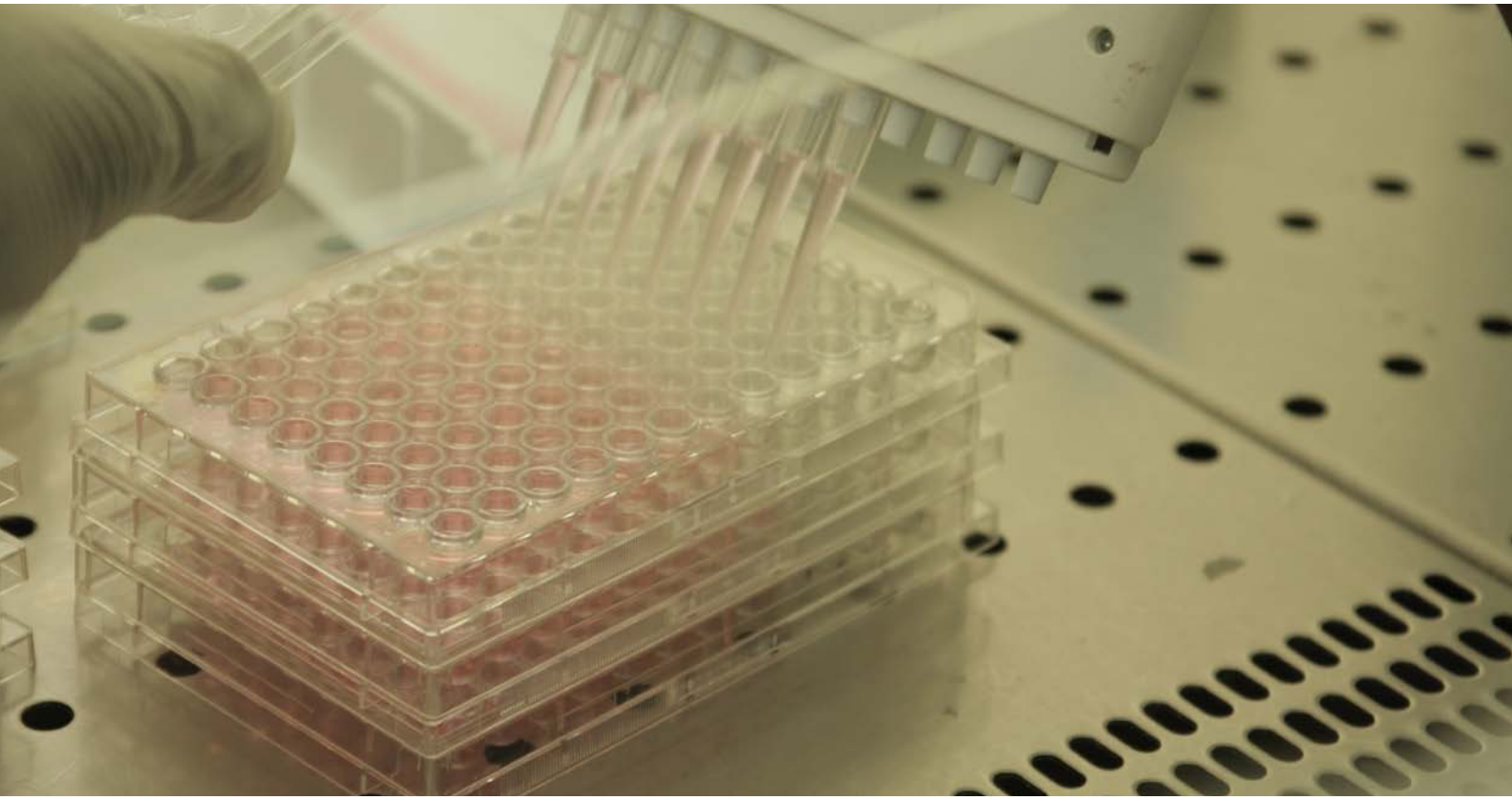
Two ELISA methods for potency testing of TBEV vaccines have been selected to enter the validation phase.

Work on Regulatory acceptance of the consistency approach

Contacts with regulatory agencies and international organisations during last year confirmed that VAC2VAC approach receives global interest: in addition to the national regulatory authorities of the EU, North American authorities (FDA and Health Canada as SEAC Members) as well as USDA, EDQM (also SEAC member), interest was shown by WHO, OIE (The world organisation for Animal Health), the Bill and Melinda Gates Foundation, Human Society International (HSI) as well as by upcoming economies, particularly in Asia.

EVI Partners

Biomedical Primate Research Centre (BPRC) (The Netherlands);Boehringer Ingelheim (BI) (Germany); College ter Beoordeling van Geneesmiddelen (CBG/ MEB) (Netherlands); Joint Research Centre (JRC) (Italy); GSK Biologicals (GSKBio) (Belgium); Institute for Translational Vaccinology (Intravacc) (Netherlands); International Alliance for Biological Standardization for Europe (IABS-EU) (France); Istituto Superiore di Sanità (ISS) (Italy); Merck Sharp & Dohme (MSD) (Netherlands); Boehringer Ingelheim Animal Health (France); National Institute for Biological Standards and Control (DH-NIBSC) (UK); National Institute for Public Health and the Environment (RIVM) (The Netherlands); Austrian Agency for Health and Food Safety: AGES (Austria); Paul-Ehrlich Institute (PEI) (Germany); Pfizer (Austria); Sanofi Pasteur (France); Sciensano (Belgium); University Medical Center Groningen (UMCG) (The Netherlands); University of Applied Sciences



Utrecht (HU) (The Netherlands); University of Utrecht (The Netherlands); Zoetis Belgium SA. (Belgium).

Key Funders

Innovative Medicines Initiative 2 (IMI2) and European Federation of Pharmaceutical Industries and Associations (EFPIA)

FLUCOP

Target:
Harmonization

Timeline:
01 March 2015- 29 February 2020

Summary

Standardization and Development of Assays for Assessment of Influenza Vaccines Correlates of Protection

Despite the development and licensure of influenza vaccines, the potential correlates of protection induced by these vaccines are still not fully elucidated. FLUCOP aims to improve and standardise existing immunological assays for the definition of correlates of protection in future efficacy trials and, whenever feasible, to develop new assays to better evaluate influenza vaccine immunogenicity.

Key achievements

The contribution of anti-Neuraminidase (NA) responses to the immunogenicity of influenza vaccines has recently gained increased attention amongst manufacturers, researchers and regulators. In 2019, the work in FLUCOP has focused on the Enzyme-Linked-Lectin-Assay (ELLA) for which a comprehensive compilation of all variable parameters has been established and a common protocol and narrow the list of variable parameters to focus on could be defined.

EVI Partners

Abbott (The Netherlands); Artemis Bio-Support B.V.(Netherlands); AstraZeneca AB (Sweden);Biomedical Primate Research Centre (BPRC) (The Netherlands); Erasmus Universitair Medisch Centrum Rotterdam (EUMCR) (The Netherlands); European Medicines Agency (EMA) (The Netherlands); Fondazione IRCCS Ca Granda Ospedale Maggiore Policlinico (Italy); GlaxoSmithKline (GSK) (Belgium); Istituto Superiore di Sanità (Italy); Janssen (The Netherlands); MHRA-Department of Health (UK); Paul-Ehrlich-Institut (Germany); QUINTEN (France); Sanofi Pasteur (France); Sclavo Vaccines Association (Italy); Sequirus (USA); University of Oxford (UK);Università degli Studi di Siena (UNISI) (Italy); Universiteit Gen Universitetet i Bergen (Norway); University of Perugia (Italy); University of Surrey (UK).

Key Funders

Innovative Medicines Initiative (IMI) and European Federation of Pharmaceutical Industries and Associations (EFPIA)

P2I TDR

Target:
Various diseases of poverty and emerging infectious

Timeline:
01 January 2019 – 31 May 2019

Summary

Analysis of health product portfolios for global health utilizing the TDR Portfolio-to-impact R&D modelling tool

The Portfolio-To-Impact P2I model is a recently developed product portfolio tool that enables users to estimate the funding needs to move a portfolio of candidate health products, such as vaccines and drugs, along the product development path from late stage preclinical to phase III clinical trials, as well as potential product launches over time.

Key achievements

The study conducted describes the use of the P2I tool for analysing the vaccine portfolio of the European Vaccine Initiative (EVI). Vaccine candidates for various diseases of poverty and emerging infectious diseases at different stages of development were included in the analysis.

Publications

Pipeline analysis of a vaccine candidate portfolio for diseases of poverty using the Portfolio-To-Impact modelling tool. Gunn, A. et al: F1000 Research 11 Jul 2019, 8:1066 (first published)

EVI Partners

Center for Policy Impact in Global Health (USA), Duke Global Health Institute, Duke University (USA);

Key Funders

TDR, the Special Programme for Research and Training in Tropical Diseases, co-sponsored by UNICEF, UNDP, the World Bank and WHO.

SENET

Target:
Policy and EU-China Collaboration

Timeline:
01 January 2019- 30 June 2021

Summary

Strengthening international R&I cooperations between China and the EU

This policy project aims to create and facilitate a sustainable dialogue between health research and innovation actors from the EU and China, and to facilitate the collaboration with Chinese researchers in the context of European research and innovation programmes.

Key achievements

An assessment of the strategic health priorities and the health research and innovation landscape in Europe and China was conducted. Moreover, a first stakeholder meeting was organised in Beijing, China.

EVI Partners

Beijing Science and Technology Linkedin CO LTD, S&T (China); Beijing University of Chinese Medicine (BUCM) (China); Centre for Genomic Regulation (CRG) (Spain); China National Center for Biotechnology Development (CNCBD) (China); China National Health Development Research Center (CNHDRC) (China); inno TSD (France); Sociedade Portuguesa de Inovação (SPI) - Consultadoria Empresarial e Fomento da Inovação S.A. (Portugal); Steinbeis 2i GmbH (S2i) (Germany).

Key Funders

European Union (Horizon 2020 Programme)

TRAINING

EVI is dedicated at strengthening public health and vaccine research capacities in the fight against diseases of poverty and emerging infectious diseases. This is crucial in order to sustain Europe's excellence in this field, but also to strengthen the public health and vaccine research capacities in Low- and Middle-Income Countries (LMICs). Within EVI's research projects, training is included as an integral part, and either offered as webinars, short modular training courses or long-term training of MSc and PhD students.

EVI is also an associated partner of the "Leading International Vaccinology Education" (LIVE) Master programme and is participating in the EDCTP/TDR Clinical Research and Development Fellowship Scheme as a hosting institution.

EDCTP/TDR Fellowships

The training of scientists is key in the empowerment of research institutions in Low- and Middle-Income Countries (LMICs), to address public health challenges and develop and implement appropriate solutions. In 2015, EVI therefore joined the EDCTP/TDR Clinical Research and Development Fellowship Scheme as a hosting institution. The purpose of this fellowship scheme is to provide training to junior to mid-career researchers from LMICs to acquire specialist skills in clinical research and development through placements in pharmaceutical companies and PDPs.

The goal of the placement at EVI is to facilitate critical decision-making in vaccinology by providing fellows with an overview of the field, from antigen discovery to vaccine development and clinical research according to international guidelines particularly for early stage vaccine development. EVI's mentoring concept encourages the trainees to take personal responsibility of project tasks, offers assistance and stimulates individual creativity. Mentorship is maintained by EVI after the return of the fellows to their home institution, including the organisation of joint training sessions.

Nicola Viebig was invited by the former trainees Fassiatou Tairou to UCAD in Dakar, Senegal to provide training on "Project management for clinical research" to young scientists from the university in July 2019 and to remotely co-facilitate a "Clinical Research Project Management Workshop" at the Malaria Research and Training Center in June 2019, organised by the Dr Moussa Niangaly.

Since the beginning of EVI's involvement in the programme, six researchers from sub-Saharan Africa and one researcher from Colombia with different educational background and working experiences were hosted by EVI. In 2019, EVI hosted a young Nigerian researcher, Dr James Onyemata from the Institute of Human Virology, Nigeria. Following the positive experience, EVI is happy to welcome one new trainee in 2020.

Fellow's profiles and their experience at EVI

James Onyemata

The fellowship at EVI was an excellent experience on hands-on training, networking and working in multicultural settings. The unique nature of projects that I was involved in under the supervision of experienced staff at EVI was revealing in a number of ways.

I gained a better practical overview of the preclinical process development, considerations and potential bottle necks therein, through several interactions on preclinical process development of some projects. This exposed me to critical steps of the preclinical development phase and how it contributes to vaccine development. I can apply these experiences to my immediate and future career objectives that requires implementing some proof of concept studies.

I observed critical thinking inputs associated with an ongoing Clinical Trial (CT) project as part of my hands-on training at EVI. This allows me to contribute in a more significant way to vaccine CT projects at my home Institution.

Other key trainings organized through EVI and its networks including viral vaccine process development, single use technologies, assay development and validation-application of surface plasmon resonance technologies in vaccine development and manufacturing, scale-up for recombinant protein vaccines, and requirements for GMP production exposed me to critical thinking strategy and infrastructural requirements for vaccine development.

I gained some additional experience in consortium wide grant application while at EVI. The conversations leading to and focused approach towards developing the grant application were insightful. This positions me to make more meaningful contributions towards developing grant efforts within my home Institution.

I gained some experience on management of projects under the supervision of experienced EVI staff. Understanding the practical methods adopted in project management positions me to contribute to tracking study progress in my home institution.

ADVOCACY AND INTERNATIONAL FORA

EVI participated in a large number of conferences, workshops, symposia and other events with the aim to strengthen and mobilise support for vaccine R&D. Participation in events was followed up by bilateral contacts with funders, policy makers and other stakeholders. Some of the major events that were attended by EVI during 2019 are summarised below.

ADVOCACY

ENRICH Health Care Tour

8-12 April, 2019
Beijing and Wuxi, China

ENRICH, the "European Network of Research and Innovation Centres and Hubs", is an initiative that offers services to European research, technology and business organisations with the aim to connect them to the Chinese market. EVI participated in ENRICH´s Matchmaking Tour to China in the cities of Beijing and Wuxi which provided the opportunity to visit several Chinese vaccine R&D organisations and companies and present EVI to them.

6th Annual meeting of the WHO Product Development for Vaccines Advisory Committee (PDVAC),

26-28 June, 2019
Geneva, Switzerland

PDVAC is an independent WHO committee of experts that provides external advice to WHO's Department on Immunization, Vaccines and Biologicals The meeting took place in the context of development of the immunization agenda for 2030, and work is underway across global and regional stakeholders to define strategic goals for the next decade.

Malaria WHO Consultation: Next Generation Malaria Vaccines and Biologicals Research and Development: Landscape Review to Inform WHO Technical Documents,

15-17 July, 2019
Geneva, Switzerland

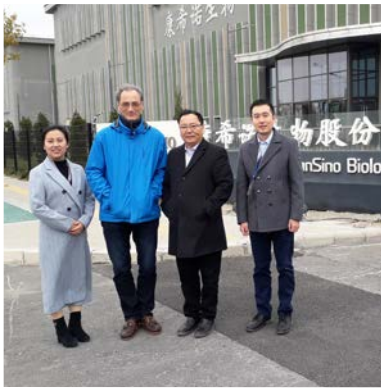
This consultation reviewed the malaria vaccine R&D landscape and fomented discussions in the Malaria Vaccine Advisory Committee (MALVAC). MALVAC provides advice to WHO on activities related to the development of malaria vaccines.

ESFRI Roadmap 2021 Information Day,
25 September, 2019
Brussels, Belgium

The "European Strategy Forum on Research Infrastructures" (ESFRI) organised this information day to inform interested parties about the evolution of the ESFRI Roadmap of European research infrastructures and to provide details about opportunities for involvement.

Meeting of the TDR Clinical Research and Development Fellowship (CRDF) Training Partner Organizations (TPOS),
10 October, 2019
Geneva, Switzerland

The meeting brought together current and previous TPOs of the TDR Clinical Research and Development Fellowship (CRDF) programme. Aim of the meeting was to discuss the results of the latest evaluation of the CRDF programme, to prepare the next round of selection of the fellows and to develop a fundraising strategy for the future selection.



EU China Vaccine Collaboration Seminar,
9-10 November, 2019
Chengdu, China

The EU Project Innovation Center (EUPIC), Chengdu, China, and EVI organised this networking event to facilitate cooperation opportunities between vaccine developers from China and Europe. Approximately fifty participants from the public and private sector participated in the event which offered the opportunity for institutional presentations and networking. Hilde Depraetere and Stefan Jungbluth from EVI co-organised and attended the event.

The WHO Immunization Practices Advisory Committee (IPAC) - Delivery Technologies Working Group (DT WG),
September – December 2019

The DT WG focuses on innovative delivery and primary container technologies and aims to address this need by informing industry about LMIC programmatic preferences and operational realities,and sensitizing the public sector to industry constraints and economic realities of investing in product development. EVI was represented on this working group by Nicola Viebig and Hilde Depraetere.

INTERNATIONAL FORA ATTENDED

2nd ENOVA Adjuvant Workshop,
21-22 January 2019, Copenhagen, Denmark and
3rd ENOVA Adjuvant Workshop,
23-24 September 2019, Belgrade, Serbia

ENOVA is a science and technology "Network on Vaccine Adjuvants", funded by COST through the EU Framework Programme Horizon 2020. Workshops organized by the consortium are a valuable opportunity to network and discuss latest technical, clinical and regulatory developments. At the 2nd ENOVA workshop, which was dedicated to Bench to Bedside – How to get your vaccine into clinical testing, Hilde Depraetere, from EVI, presented TRANSVAC2. The 3rd ENOVA Adjuvant workshop focused on Regulatory Considerations in the development of adjuvanted vaccines.

Flanders Vaccine Symposium on "A new generation of Genetically Modified (GM) vaccines: How to overcome the hurdles from bench to practice?"
19 March 2019, Brussels, Belgium.

The meeting, organized by Flanders Vaccines, explored the challenges associated with novel types of vaccines, namely GM Technology-based vaccines. A wide range of presentations covered topics related to regulatory frameworks, pre-clinical and clinical challenges, safety and effectiveness as well as environmental risk associated with GM vaccines.

ADITEC: Advanced Immunization Technologies,
30 September-2 October 2019, Siena, Italy

The meeting, organized by SCLAVO and University of Siena, brought together ADITEC partners and other experts from Europe and USA. The symposium focused on "Advanced immunization technologies" and included presentations on Vaccine Adjuvants& Delivery Systems, Vaccines at Extremes of Ages, Global Efforts to Support Vaccine R&D, System Biology and Computational Models for the Analysis of Vaccine Responses, Synergies with other EU Vaccine Projects and Biomarkers of Human Immune-response to Vaccination and of Vaccine Safety.

Vaccines for Enteric Diseases,
16-18 October, Lausanne, Switzerland

This meeting covered diverse aspects of vaccines, vaccination strategies and the development of vaccines against human enteric diseases, a major cause of morbidity and mortality worldwide.

2019 International Society for Vaccines (ISV) Annual Congress,
27-29 October, Ghent, Belgium

The ISV Annual Congress is the world's largest non-commercial scientific conference for basic and clinical researchers interested in vaccines and the underlying sciences. Hilde Depraetere presented at this meeting TRANSAVC2 and VAC2VAC projects.

BioRN Annual Conference 2019: Artificial Intelligence meets Health - from desk to bench to bedside,
11 November 2019, Heidelberg, Germany

The BioRN Annual Conference 2019 provided an overview on current and future applications of artificial intelligence and machine learning in the health sector. BioRN is the non-profit science and industry cluster of the Rhine-Main-Neckar region around Heidelberg.

2nd Vaccine Manufacturing Forum,
12-15 November 2019, Casablanca, Morocco

Africa and Middle East regions produce less than 1% of the human vaccines they use. Increasing local manufacturing capacity for vaccines is an ambitious project for these regions. This forum allowed to share best practices in the region and further understand the roadmap to local biomanufacturing and ensure a sustainable capacity for the future. Dr. Depraetere gave presentations on vaccine journey and quality and the vaccine registration process.

American Society of Tropical Medicine and Hygiene (ASTMH) 68th Annual Meeting,
20 – 24 November 2019, National Harbor, MD, USA

The ASTMH Annual Meeting is a five-day educational conference that attracts tropical medicine and global health professionals from academia, government, non-profits, philanthropy, NGOs, industry, military and private practice. The meeting attracts approximately 4,800 attendees from more than 100 countries.

Animal Testing for Vaccines – Implementing Replacement, Reduction and Refinement: Challenges and Priorities,
3-4 December, Bangkok

The meeting was dedicated to the challenges and priorities concerning the development and implementation of alternative methods to animal testing for vaccines and gathered key experts from companies, regulators and international organisations. During the conference, progress obtained during the last years in the development and regulatory acceptance of alternative methods to animal testing for batch release testing was presented, and discussions were held on what still needs to be accomplished by manufacturers and regulators to transition to non-animal based testing strategies. The meeting was co-organised by EVI, as coordinator of the VAC2VAC consortium. EVI was represented by Hilde Depraetere and Stefan Jungbluth.

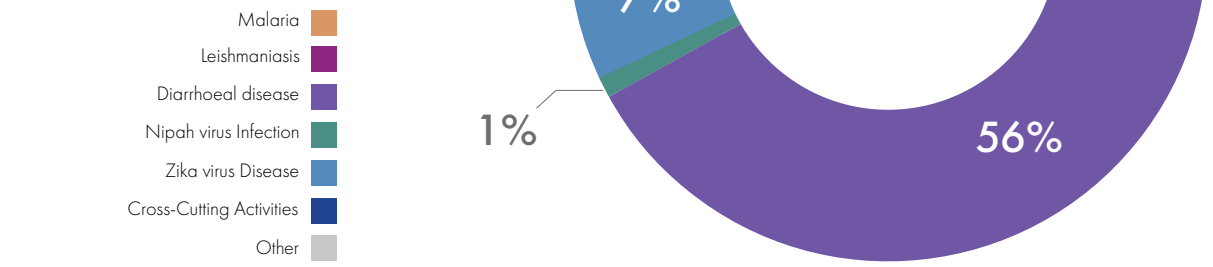
Nipah 20: Nipah Virus International Conference,
09 - 10 December 2019, Singapore

The Nipah 20, Nipah Virus International Conference in Singapore marked the 20th anniversary since the discovery of Nipah. EVI's Partner Prof. Dr. Chieko Kai, from University of Tokyo, presented the progress and challenges of developing a measles virus-vector vaccine for Nipah virus infection.

FINANCIAL PERFORMANCE REPORT 2019

EVI receives funding from national and international governmental agencies, as well as private organisations. EVI uses those funds to support a broad portfolio of projects, which help to accelerate the development and clinical assessment of vaccine candidates to promote the affordability and accessibility of vaccines, and to act as a focal point for the alignment of all major stakeholders in the area of vaccine development for diseases of poverty and emerging infectious diseases. The strategic objective is to improve the worldwide access of people in need of adequate and affordable vaccines.

EVI Expenditure per Disease 2019

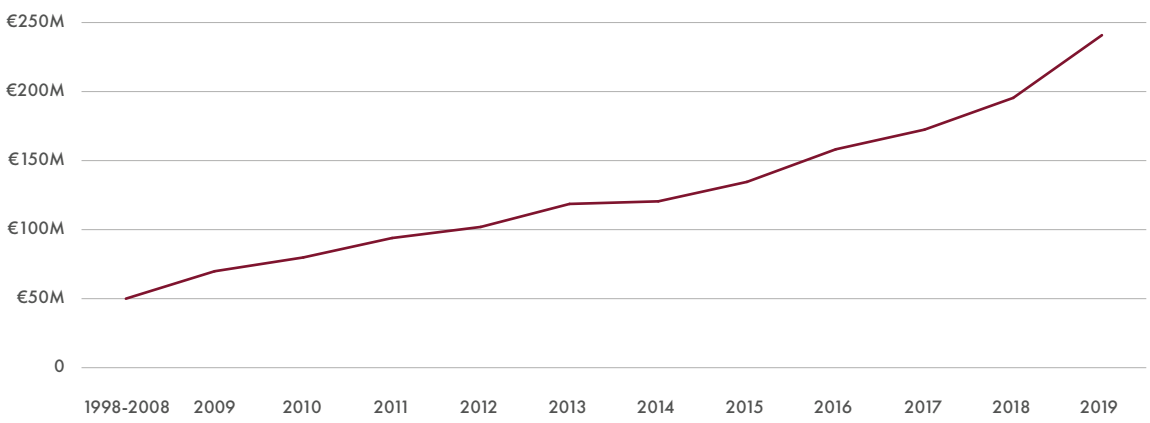


Fundraising

EVI secured additional funding in 2019 by participating in successful grant applications to two highly competitive calls for proposals from EDCTP and GHIT Fund, respectively. The two new projects will start beginning of 2020. EVI's portfolio as of 31 December 2019 consists of twelve active projects in the broad field of vaccine development and cross-cutting activities. Six projects were contractually concluded in 2019. EVI appreciates the establishment of new partnerships and valuates highly the continued support by its long-term partners and funders.

EVI's activities over the current reporting period included EU, EDCTP, CEPI, IMI and GHIT funded projects and during 2019.

A description of the projects that were active in 2019 can be found in this report.



Financial Statements 2019

Table 1. Statement of financial position as of 31 December 2019

	Notes	EUR 2019	EUR 2018
Current assets			
Cash and cash equivalents:			
Cash and banks - key accounts		4,437,924.05	5,635,110.66
Total cash and cash equivalents		**4,437,924.05**	**5,635,110.66**
Current accounts and receivables:			
Other receivables		23,244.94	12,709.61
Financial and debtor receivables		1,563.00	8,666.55
Total current accounts and receivables		24,807.94	21,376.16
Total current assets		**4,462,731.99**	**5,656,486.82**
Non-current assets			
Tangible fixed assets, net		8,605.00	11,624.00
Long term securities	2	500,000.00	-
Total non-current assets		**508,605.00**	**11,624.00**
Total assets		**4,971,336.99**	**5,668,110.82**
Current liabilities			
Creditors	3	799,156.94	121,990.82
Accrued expenses	4	434,457.16	1,647,984.76
Other liabilities	5	20,597.12	25,418.08
Deferred income	6	1,611,607.55	1,840,011.85
Total current liabilities		**2,865,818.77**	**3,635,405.51**
Equity of organisation			
Operating result		72,812.91	(198,459.21)
Operating funds		2,032,705.31	2,231,164.52
Total equity of the organisation		**2,105,518.22**	**2,032,705.31**
Total equity and liabilities		**4,971,336.99**	**5,668,110.82**

Table 2. Statement of comprehensive income for the year as of 31 December 2019

	Notes	EUR 2019	EUR 2018
Income	7		
Turnover from sales		-	812.03
Public institutional funding:	7		
Governmental & international organisations		486,151.71	2,415,705.47
EU & IMI grants		7,462,293.70	3,305,080.47
EDCTP		3,152,851.96	2,134,617.52
Total public institutional funding	7	11,101,297.37	7,855,403.46
Other income net		302,988.76	24,578.41
Total income		**11,404,286.13**	**7,880,793.90**
Social mission expenditure			
Research & vaccine development expenditure:	8		
Malaria		433,523.94	1,620,538.88
Leishmaniasis		753,864.32	2,296,034.60
Diarrhoeal diseases		6,360,059.16	0.00
Nipah virus disease		143,652.64	0.00
Zika virus Infection		760,796.68	758,939.00
Cross-Cutting activities		2,649,400.63	2,551,735.12
Advocacy & communications expenses		12,148.50	107,551.41
Total social mission expenditure		**11,113,445.87**	**7,334,799.01**
Supportive social mission expenditure	8		
Training, quality assurance and project development		4,652.45	11,053.25
Fundraising		36,418.28	178,840.98
Governance		42,220.35	32,194.02
Total supportive social mission expenditure		**83,291.08**	**222,088.25**
Non-social mission expenditure	8		
General executive administration		134,736.27	522,365.85
Total non-social mission expenditure		**134,736.27**	**522,365.85**
Total expenditure		**11,331,473.22**	**8,079,253.11**
Operating surplus / (deficit)		72,812.91	(198,459.21)
Net surplus/ (deficit) for the year prior to allocations		72,812.91	(198,459.21)
Allocation / (release) to restricted operating funds in equity		-	-
Allocation / (release) to unrestricted operating funds in equity		(72,812.91)	198,459.21
Net surplus for the year after allocations		**-**	**-**

For more detailed information about EVI's financial statements and related indicators the 2019 EVI Financial and Performance Report is available upon request (https://www.euvaccine.eu/contact-us)..

GOVERNANCE

AS OF 31 DECEMBER 2019

EVI Board

Claude Leclerc
Institut Pasteur, France (until 25.11.2019)

Clemens Kocken
Biomedical Primate Research Centre, The Netherlands

Corine Kruiswijk
Institute for Translational Vaccinology, Bilthoven (until 31.12.2019)

David Salisbury
Jenner Vaccine Foundation, United Kingdom

Marita Troye-Blomberg
Wenner Gren Institute, Stockholm University, Vice Chair (until 31.12.2019)

Martin Trillsch
Legal Council, University Clinical Centre, Heidelberg

Samuel McConkey
RCSI University of Medicine and Health Sciences, Ireland

Christiane Gerke
Institut Pasteur, France (from 25.11.2019)

EVI Board of Stakeholders

Charles de Taisne
Sanofi Pasteur, France

Diarmuid O'Donovan
Irish Health Service Executive, representing Irish Aid, Ireland

Jean-Paul H. Prieels
MaSTherCell, Belgium

Marcel Tanner
Swiss Tropical and Public Health Institute, Switzerland

Sodiomon B. Sirima
Groupe de Recherche Action en Santé, Burkina Faso

Suresh Jadhav
Serum Institute of India Pvt. Ltd., Pune

EVI Scientific Advisory Committee (SAC)

James Searl Robertson
Independent, United Kingdom

Michael Lanzer
Heidelberg University, Germany

Diana Boraschi
National Research Council, Naples, Italy

Dominique Mazier
University Pierre et Marie Curie, France

Francine Ntoumi
Université Marien Ngouabi, Republic of Congo

Johan Vekemans
World Health Organization, Switzerland

Nadia G. Tornieporth
University of Applied Sciences & Arts, Hannover, Germany

Nancy Le Cam Bouveret
Independent Consultant

Nathalie Garçon
BIOASTER Technology Research Institute, France

EVI Finance and Risk Management Committee (FRMC)

Clemens Kocken
Biomedical Primate Research Centre, Rijswijk, The Netherlands

Terry McWade
Chair of FRMC, succeeded during 2019 by Steffen Ahrens, Falk & co

Martin Trillsch
Legal Counsel, University Clinical Centre, Heidelberg, Germany

EVI Secretariat

Eliana Acosta
Project Manager

Flavia D'Alessio
Project Manager

Hilde Depraetere
Acting Executive Director (from March 2019)

Sten Larsen Finnsson
Finance and HR Director

Sandra Hauenstein
Finance Assistant

Nicolas Havelange
Consultant

Sophie Houard
Director of Vaccine Development

Stefan Jungbluth
Head of Business Development

Thorsten Kohaut
Senior Finance Officer

Odile Leroy
Executive Director (until February 2019)

Catarina Luis
Project and Communication Manager

Irina Meln
Project Manager

James Onyemata
EDCTP WHO/TDR Fellow

Monika Slezak
Project Manager

Nicola Viebig
Chief Scientific Officer

Ole F. Oleson
Executive Director

EVI welcomed Ole Olesen, PhD, as the organisation's new Executive Director as of 1st of January 2020.

"I am excited about this opportunity to work with the EVI team and their tremendous partners to discover and develop new vaccines against poverty-related diseases"

ACKNOWLEDGEMENTS

During our more than twenty years of existence, EVI has succeeded in securing the support of a large number of partners, funders, and other individuals and organisations. We would like to sincerely thank everyone for their backing and collaboration and gratefully acknowledge the financial support and donations from the following organisations

- Coalition for Epidemic Preparedness Innovations (CEPI), Norway
- Danida, Danish International Development Agency
- Irish Aid, Department of Foreign Affairs, Ireland
- Dutch Ministry of Foreign Affairs, Directorate-General for International Cooperation (DGIS), The Netherlands
- Dutch Research Council (NWO), The Netherlands
- European & Developing Countries Clinical Trials Partnership EDCTP1 and 2 Programmes, The Netherlands, with co-funding from EU Member States and other countries
- European Union (EU), Framework Programmes 6, 7, Horizon 2020, Belgium
- Federal Ministry of Education and Research (BMBF) through KfW, Germany
- Global Health Innovative Technology (GHIT) Fund, Japan
- Innovative Medicines Initiative (IMI and IMI2 Programme), Belgium
- Nobelpharma Co., Ltd., Japan
- Swedish Ministry of Foreign Affairs, Swedish International Development Cooperation Agency (Sida), Sweden
- World Health Organization - Special Programme for Research and Training in Tropical Diseases (WHO-TDR), Switzerland
- Wellcome Trust, United Kingdom
- All4Cloud
- SAP

linkedin.com/company/european-vaccine-initiative/

twitter.com/EuropeVaccine

youtube.com/channel/UC9t-3sG9x_W_hRJaNTm_4MA/videos

Subscribe to EVI's Mailing List:
www.euvaccine.eu/contact-us

European Vaccine Initiative
Universitäts Klinikum Heidelberg
Vossstrasse 2, Geb. 4040
69115 Heidelberg Germany

Email: contact.us@euvaccine.eu
Tel: +49 6221 565373