ANNUAL REPORT 2020

European Vaccine Initiative

CONTENTS

Message from the Chairman and Executive Director

The start of 2020 was marked by welcoming Dr. Ole F. Olesen as the new Executive Director of the European Vaccine Initiative (EVI), starting January 1st. Bringing extensive experience on research and product development from industry, academia and the European public sector, Dr Olesen's arrival marks a renewed and strengthened commitment to pursue and fulfill EVI's mission and values.

At the beginning of 2020, a new and fatal respiratory pathogen SARS-CoV-2 began to emerge in Asia and Europe and later spread across the globe to create the worst pandemic in recent memory. Throughout the year, EVI's operations have also been severely impacted by COVID-19, and we have continuously adapted our work and activities to a constantly evolving situation. From an early point, EVI engaged fully in the search for solutions against the pandemic, while keeping our overall mission in mind: to discover, develop and deliver effective and affordable vaccines for global health.

To support the global effort to accelerate the development of a vaccine against SARS-CoV-2, EVI launched in April 2020 a specific call through the TRANSVAC2 infrastructure, and funded by the European Commission, for applications focused on the development of novel COVID-19 vaccines. Provision of variety of TRANSVAC2 services, from antigen discovery to preclinical and clinical trial support, enabled SMEs and public institutions to speed-up their developments of COVID-19 vaccine candidates.

EVI also participated in the formation of a new EU-wide vaccine trial network called VACCELERATE. The VACCELERATE network, led by University Hospital Cologne, will act as a single-entry point for vaccine developers, who are looking to carry out vaccine trials acdross Europe. The consortium will work closely with the European Medicines Agency (EMA) to enable clinical trials for COVID-19 vaccines and prepare Europe for other emerging infectious diseases in the future. The first clinical trials of VACCELERATE will start in 2021 and primarily focus on the effect and duration of a third dose vaccination against COVID-19.

While EVI has actively contributed to confronting the pandemic, many of EVI's regular activities have been negatively impacted. Several projects have incurred disruptions and clinical trials have been delayed as scientists, clinicians, and health care workers have been affected or drawn into the COVID-19 response globally.

In spite of these challenges, a number of important achievements were accomplished in 2020. The PRIMALVAC project published the results a first-in-human clinical trial demonstrating that adjuvanted PRIMVAC, a candidate vaccine against placental malaria, was safe and well tolerated in malaria naive women from Europe, as well as in women who were naturally exposed to Plasmodium falciparum and nulligravid in Burkina Faso. Future development plans will be implemented in 2021. In the ZIKAVAX project, a phase I clinical trial that was initiated in Austria in mid-2019 was completed by the end of 2020. Data from the phase I clinical trial revealed that the lead vaccine candidate (MV-ZIKA-RSP) against ZIKA was well tolerated and induced immune responses that are currently further evaluated. A ZIKA challenge model in non-human primates (NHPs), highly relevant for the selection of vaccine candidates, was also developed, with potential high impact for future Zika virus research. Finally, the SEmalvac project came to an end in 2020, and an interim analysis report assessing the safety and the immunogenicity of the BK-SE36/CpG vaccine candidate 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.

EVI has initiated three new collaborative projects in 2020, two of which have EVI as the coordinating organ-

isation. These three projects, with a total budget of 17.2 Mio EUR, were funded by EDCTP2 (MIMVaC-Africa), the GHIT Fund (SEmalvac4) and Horizon 2020 (TRANSVAC-DS). While SEmalvac4 is dedicated to further developing of a blood stage malaria vaccine candidate into Phase II, MIMVaC-Africa is focused on implementing a comprehensive comparative study of no less than 5 different malaria vaccine candidates. TRANSVAC-DS focuses on paving the way for an independent and sustainable Vaccine R&D European Infrastructure, thus consolidating EVI's position in this important disease area.

Looking back on 2020, the COVID-19 pandemic has ravaged the world and left 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. This is a valuable lesson lesson as we set the course for the upcoming years of EVI's work.

On behalf of EVI, we would like to thank our friends and supporters, the entire EVI team, our collaborators around the world, our funders and partners, and the participants in clinical trials.

Dr Clemens Kocken,
Chairman of the EVI Board;
Dr Ole F. Olesen,
Executive Director

2020 IN HIGHLIGHTS

New projects

MIMVaC-Africa

SEmalvac4

TRANSVAC-DS

Finalised Projects:

SEmalvac

Zikavax

The path forward: new strategic plan

During 2020, EVI was laying the foundation for the forthcoming 5 years by renewing its commitment and broadening its scope to tackle vaccine development for global health. In the 2021-2025 Strategic Business Plan EVI's vision and mission echo this commitment and set the stage for the road ahead.

Our vision

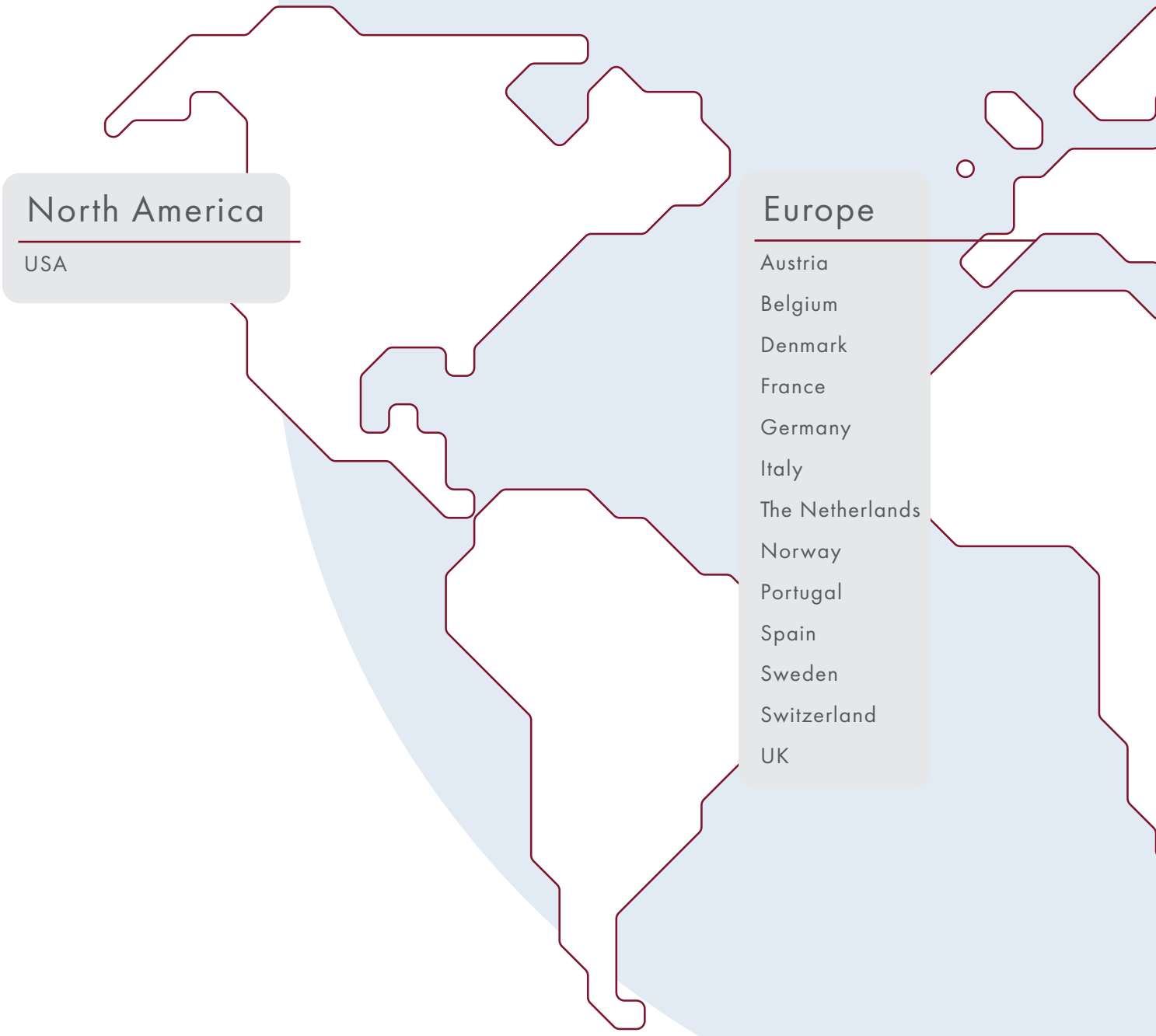
A world where vaccines create health and equity for all people

Our mission

To develop new, safe, effective, and affordable vaccines for global health

Global partners

After more than two decades, EVI has grown into a network of more than 150 partners across the globe, brought together by our pursuit of safe, effective and affordable vaccines developed through collaboration.

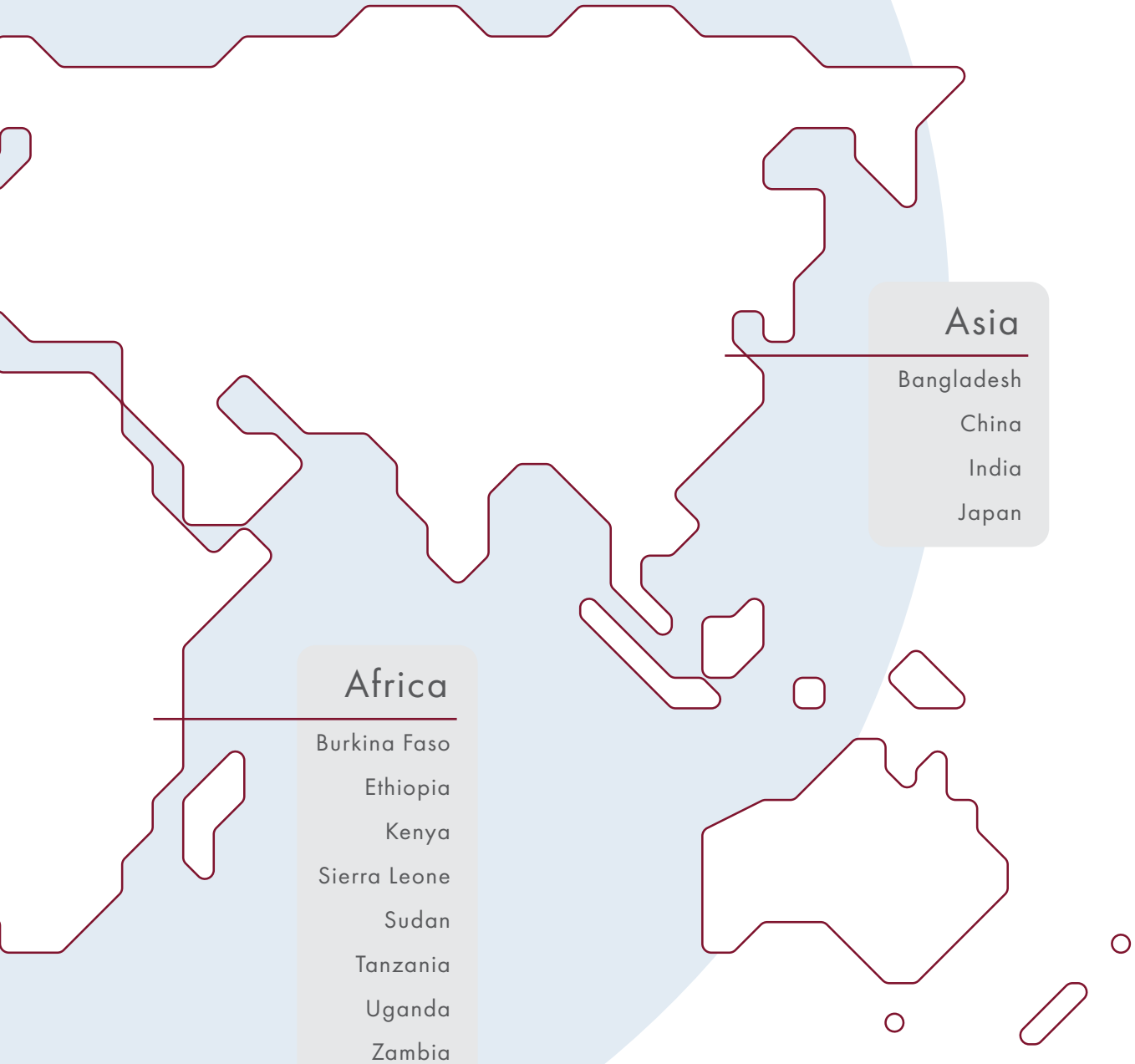


North America

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

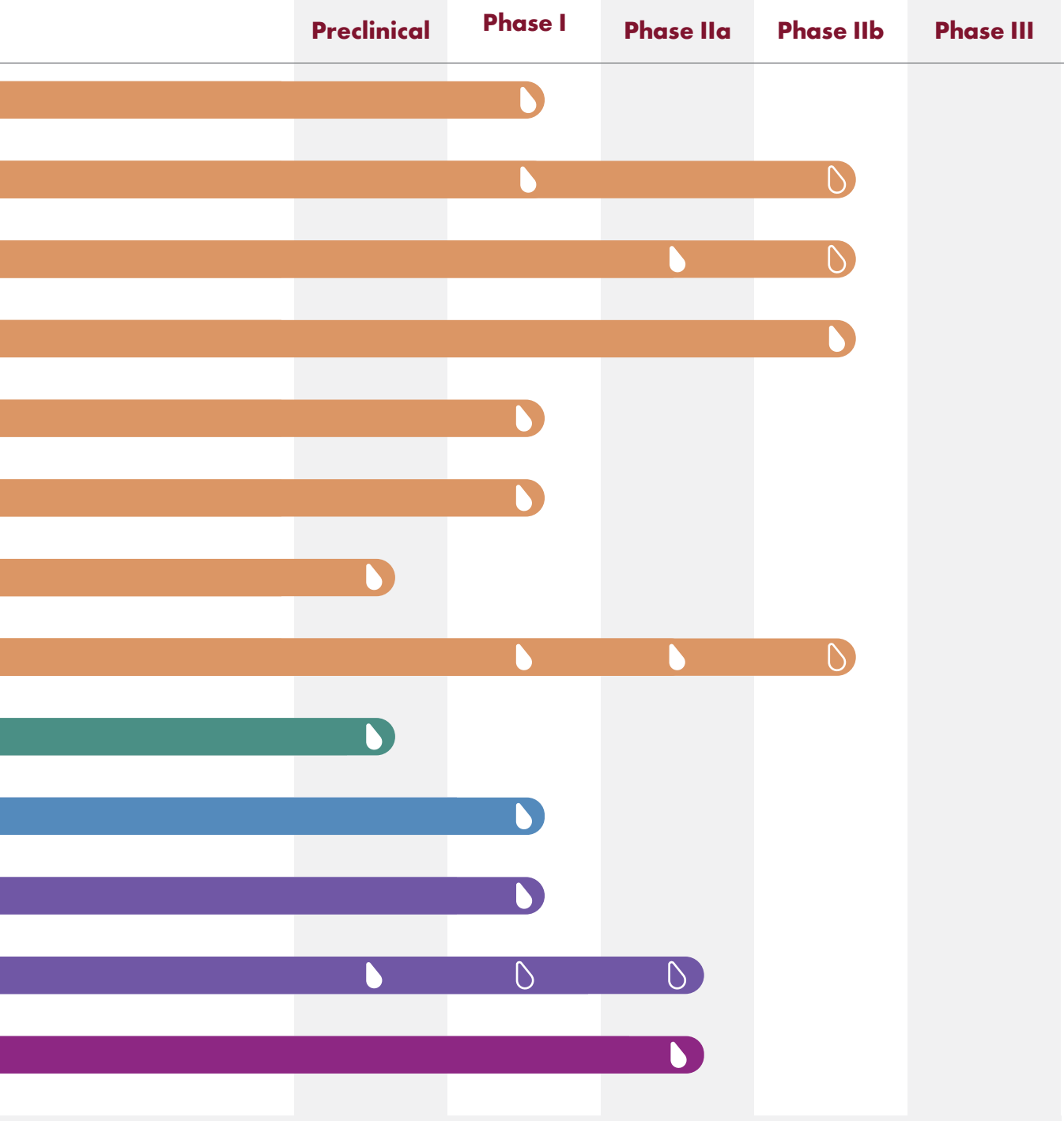
Tanzania

Uganda

Zambia

PIPELINE IN 2020

Area	Projects	Candidates
MALARIA	MMVC/ MIMVaC-Africa	PfRH5
		Pfs25
		ME-TRAP
		R21
	SEmalvac2	BK-SE36/Cpg
	SEmalvac4 / MIMVaC-Africa	NPC-SE36/CpG
	PfRipr5	PfRipr5
	PfSPZ-CVac	PfSPZ-CVac
NIPAH VIRUS	CEPI-Nipah	MV-Nipah
ZIKA VIRUS	ZIKAVAX	MV-ZIKA RSP
DIARRHOEAL DISEASE	SHIGETECVAX	ShigETEC
	ShigOraVax	ShigOraVax
LEISHMANIASIS	PREV_PKDL	ChAd63-KH
CROSS-CUTTING ACTIVITIES	TRANSVAC-DS	
	TRANSVAC2	
	VAC2VAC	
	FLUCOP	
	SENET	



Current Stage

Funding secured

Malaria

Malaria is caused by four species of single-cell parasites, Plasmodium *Plasmodium falciparum* is responsible for most deaths

67% of all deaths occur in children <5

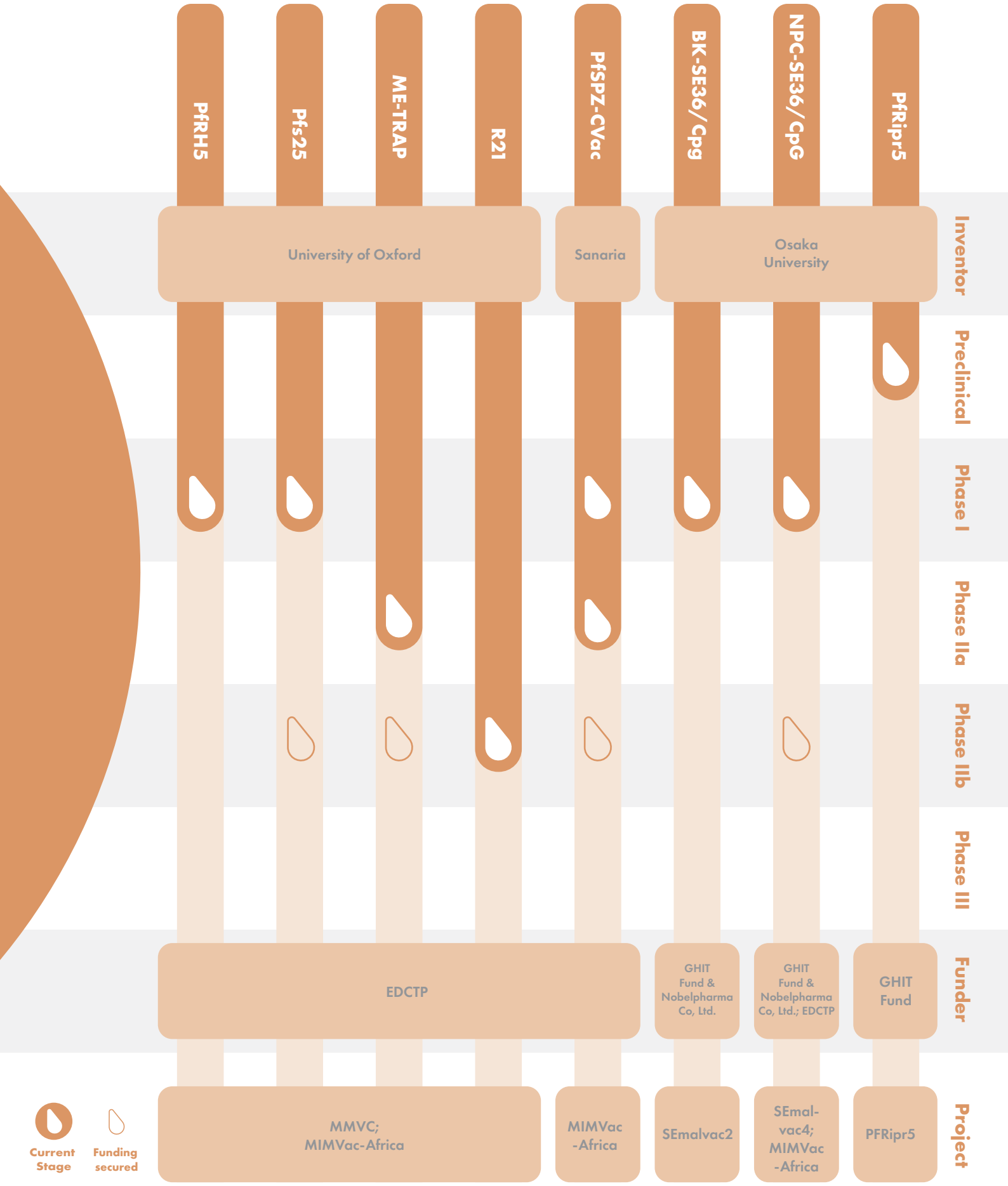
93% of all cases occur in Africa

44% of the worlds population is at risk

409,000 malaria deaths worldwide

Sources: World Malaria Report 2020 - https://www.who.int/publications/i/item/9789240015791

Malaria Vaccine Candidates



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 94% of malaria cases in 2019. Over the past couple of decades, a significant reduction in transmission rates and malaria incidence was observed due to the implementation of malaria control measures such as insecticide treated bed nets, indoor residual spraying and seasonal malaria chemoprevention (SMC) programs. 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 eliminate and ultimately eradicate malaria.

Vaccines, the challenges ahead

The enormous complexity of the P. falciparum parasite and variability in the infections is a major challenge for vaccine development. These challenges include the parasite polymorphism, the immunological interplay between the host and the parasite, heterogeneity in human immune response depending e.g. on the type of human leukocyte antigen (HLA), genetic traits such as haemoglobin type and red cell polymorphisms. The response to a malaria infection will vary in view of the antigenic repertoire and host, frequency of exposure, age, access to treatment, and presence of co-morbidities. In addition, to achieve sufficient coverage, the vaccine should be deployed through existing immunisation programs (such as the Expanded Programme on Immunization).

Placental malaria is affecting a particularly vulnerable demographic group, pregnant women, manifesting as severe disease and anaemia in the mother, and accounting for 50,000 maternal and 200,000 neonatal deaths annually. The assessment of safety and efficacy of placental malaria vaccines is challenged by the selection of the appropriate clinical trial design as well as the ethical and egulatory complexities.

© Riccardo Mayer/Shutterstock

Diverse approaches for better vaccines

Development of asexual blood-stage malaria vaccine candidates:

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. To advance this new blood-stage vaccine candidate, by the end of 2020 a suitable expression system and expression conditions have been identified and optimised for larger scale production. The PfRipr5 antigen has also been formulated with three different adjuvants that are either licensed or have been previously used in humans. Results so far indicate acceptable compatibility of the PfRipr5 with all three tested adjuvants. Finally, rabbits were immunized with the PfRipr5 protein alone and formulated with the three adjuvants, allowing the selection of the formulation for clinical development by Mid-2021. EVI is responsible for project oversight and the formulation development.

SEmalvac2 and SEmalvac4

Serine repeat antigen-5 (SERA5) is indispensable during blood-stage growth and is suggested to be involved in parasite egress and in parasite immune evasion. SERA5 may 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 the BK-SE36 vaccine. The safety and immunogenicity of the BK-SE36 vaccine was demonstrated in phase Ia trials conducted in healthy adults in Japan and phase Ib trials in Uganda and, with the involvement and under the coordination of EVI, in Burkina Faso. To improve its immunogenicity, the vaccine was further adjuvanted with CpG TLR9 ligand (BK-SE36/CpG). BK-SE36/CpG vaccine has also been tested in adults and children aged 5 to 10 years and 1 to 2 years living in Burkina Faso. In April 2020, the clinical team at IRSS successfully completed the active phase of the trial despite the COVD-19 pandemic. The data of the trial were collected and, with the support of EVI's team, the statistical and integrated clinical study report is under preparation.

An offshoot of the project started in 2020 with the SEmalvac4 project coordinated by EVI that pursues the clinical development toward the preparation of a Phase IIb trial with the manufacture and preclinical testing of a new vaccine batch (named NPC-SE36/CpG) and, with the support of EVI, the preparation of the protocol and the selection of clinical trial sites.

Comparing Approaches:

MIMVaC-Africa, a multilateral initiative to foster the clinical development of effective malaria vaccine candidates in Africa

The MIMVaC-Africa consortium is a large interdisciplinary consortium with leading vaccine developers, clinical trial experts and malaria researchers.

The project aims to evaluate pre-erythrocytic and blood-stage vaccine candidates for safety, immunogenicity and efficacy against experimental and later natural challenge with P. falciparum, and to identify the most promising candidates for further clinical development in phase III trials.
Vaccine candidates for assessment in the MIMVAC-Africa program include: i) the pre-erythrocytic vaccine candidates: R21 adjuvanted with Matrix-M, chemically attenuated whole sporozoite vaccine PfSPZ-CVac, and vectored ME-TRAP; and ii) the blood-stage candidates: PfRH5 adjuvanted with Matrix-M and NPC-SE36.

The comparative testing of the vaccine candidates is embedded in activities to build and strengthen the capacity of African research institutions to evaluate candidate malaria vaccines using the controlled human infection model and adopt state-of-the-art technologies for assessing immune correlates of protection. The project started in early 2020, at the time where the COVID-19 pandemic gathered pace. The first year of the project was therefore mainly dedicated to preparatory work and virtual networking activities to pave the road for a start of the clinical trial activities in the second year of the project. EVI is leading the work package on Quality Assurance and Networking.

4 in 1, Multi-component vaccine: MMVC

The lifecycle of the malaria parasite is complex, and a highly efficacious vaccine is most likely required to target more than one of the parasite's lifecycle stages. The Multi-Stage Malaria Vaccine Consortium (MMVC) is targeting such a multi-component, multistage approach based on antigens that have shown promise in clinical trials assessing the single components: 1) R21/Matrix M, 2) viral vectored ME-TRAP, 3) 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 is undertaking a tightly coordinated series of lead-in trials in the first years of the project building towards a phase IIb multi-stage vaccine efficacy trial in West and East African infants in the last years of the project. 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 latter trial has shown that R21/Matrix M appears safe and very immunogenic in African children, and shows promising high-level efficacy with vaccine efficacy remaining at 77% at one year in the group of children receiving 5 µg R21/25 µg Matrix M.

In parallel, MMVC will build new capacity to test the ability of the combination vaccine and/or its transmission-blocking component. EVI is leading the work package 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, and one African MSc student has commenced training in 2020. Networking and training activities have been initiated but were hampered by the pandemic in 2020.

© Ben White/Unsplash

Leishmaniasis

There are over **20** Leishmania parasite species

Poverty increases the risk for leishmaniasis

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

1 Billion of the world's population is at risk

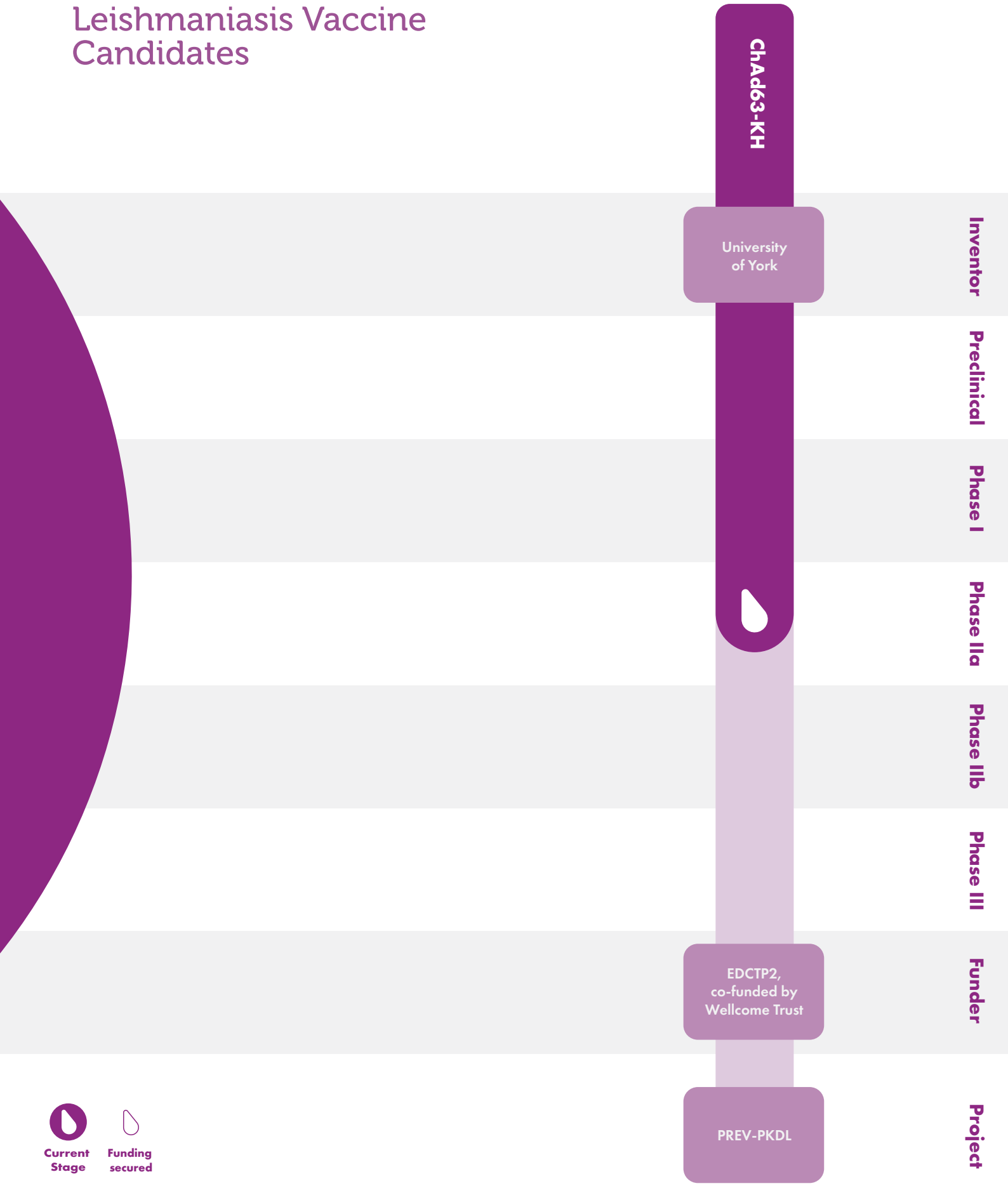
Post kala-azar dermal leishmaniasis (PKDL) appears in **5%-10%** of patients that suffered from VL

No vaccine for leishmaniasis is available

Sources:

https://www.who.int/news-room/fact-sheets/detail/leishmaniasis
Leishmaniasis: Complexity at the Host-Pathogen Interface. Kaye, P and Scott, P, Nature Reviews Microbiology 2011 Jul 11;9(8):604-15.
Post-kala-azar dermal leishmaniasis in the Sudan: clinical presentation and differential diagnosis. Zijlstra E.E. et al.,. Trans R Soc Trop Med Hyg. 2001 Apr;95 Suppl 1:S59-76.

Leishmaniasis Vaccine Candidates



Current Stage

Funding secured

At a glance

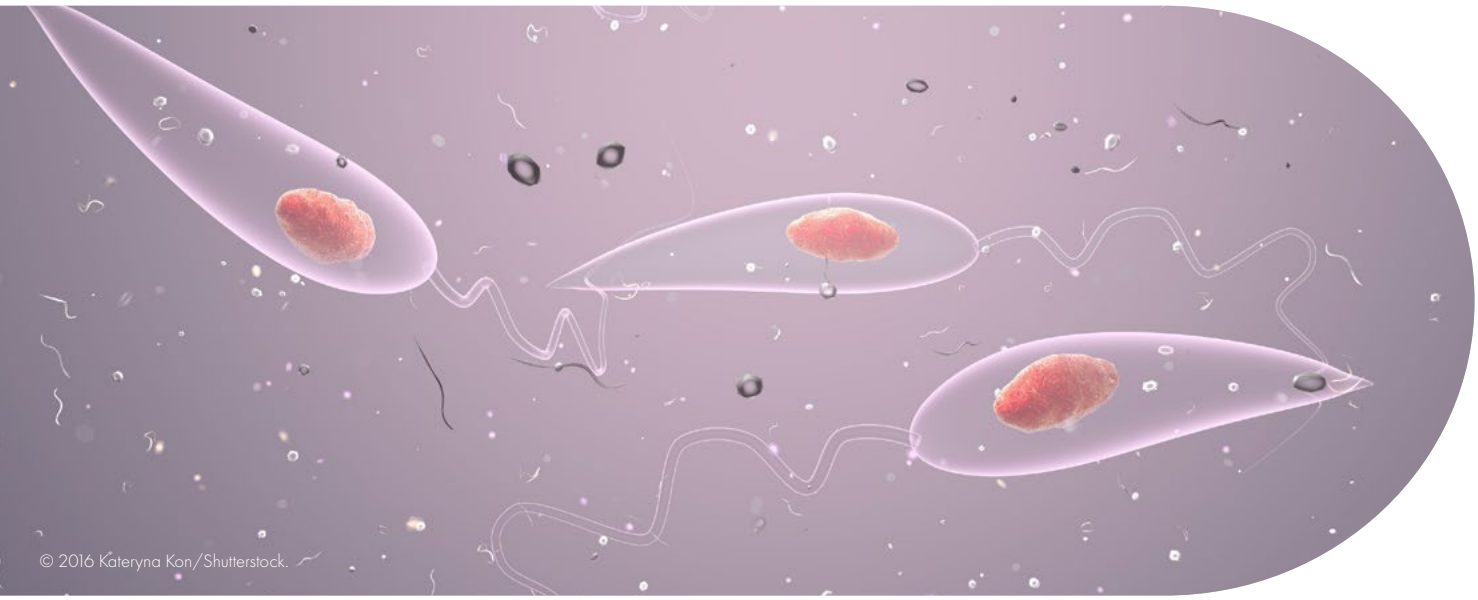
Leishmaniasis is classified as one of the "most neglected diseases" due to the limited resources invested in diagnosis, treatment, and control, and its strong association with poverty. Leishmaniases are caused by protozoan Leishmania parasites, transmitted by the bites of infected female phlebotomine sandflies. 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 reservoirs of Leishmania parasites.

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.

Vaccines, the challenges ahead

The development of vaccines has been hampered by significant antigenic diversity, as well as the fact that parasites have a digenetic life cycle in at least two hosts, which includes sandfly vector and human, but also animal reservoirs.

Another significant challenge for the development of a vaccine concerns the immune reactions against leishmaniasis, which are highly complex. And while these may accelerate cure, some responses aggravate the disease. The type of response elicited depends on the particular stage of the disease, species of the infectious agent and host immune status. Therefore, it is crucial to understand these pathophysiological and immunological complexities for the development of a safe and effective vaccine.



Fighting neglected diseases with vaccines

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

PREV_PKDL

The PREV_PKDL project aims to evaluate the safety and efficacy of ChAd63-KH as a vaccine for prevention of PKDL in clinically cured VL patients. The ChAd63-KH vaccine developed at University of York is designed to target the induction CD8+ T cells immune response. The vaccine was shown to be safe and immunogenic as a prime-only single dose vaccine in a phase I trial conducted in UK.

Additionally, 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) to better understand the disease as well as drug and vaccine responses. PREV_PKDL also supports 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.

In 2020, the work towards the Phase II Randomised Controlled Trial in Sudan, has focused on discussing the manufacture of a new clinical batch and preparing the clinical trial. However political instability in Sudan seriously impacted the communication flow and the work progress. Generic and site-specific protocols and participants' documents for the multidimensional, multiparameter phenotyping research study have been prepared with EVI support and submitted to the relevant ethics committees in Kenya, Uganda, Ethiopia, Sudan and United Kingdom.

The review process encountered significant difficulties due to the COVID-19 pandemic. For the establishment of flow cytometry, five Beckham Coulter flow cytometers were purchased and four were delivered and installed at their final destination. The delivery in Kenya was postponed due to the COVID-19 situation. Nevertheless, despite the pandemic situation, the team managed to continue to hold a weekly virtual training session.

© Adrien Taylor/Unsplash

Diarrhoeal Diseasses

2nd leading cause of death in children under five years old.

The majority of child deaths due to diarrhoea occur in **sub-Saharan Africa** and **South Asia**

525 000 child deaths annually

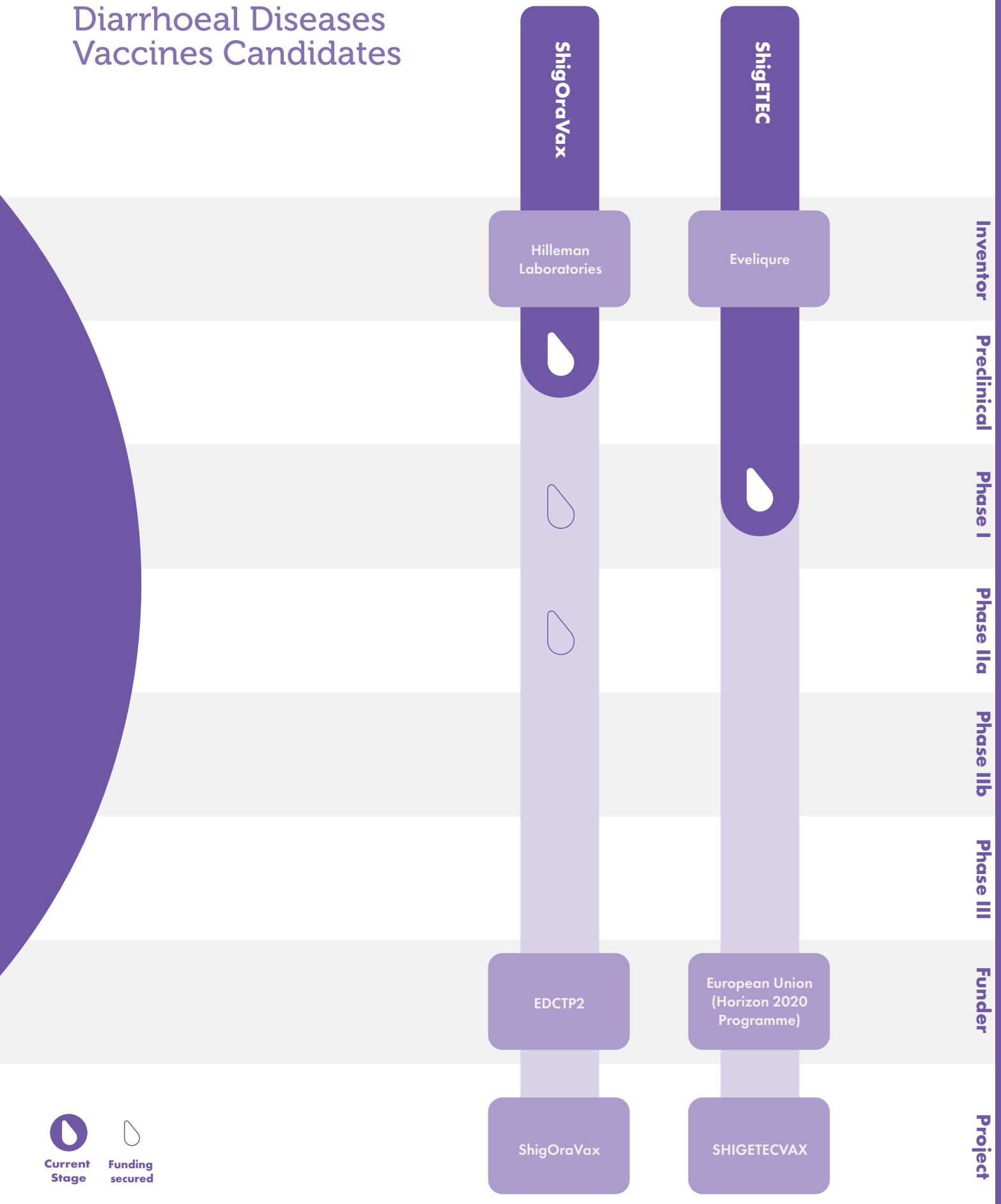
1 Billion of the world's population is at risk

1.7 Billion cases each year

1 in 10 childhood deaths

Sources:
https://www.who.int/news-room/fact-sheets/detail/diarrhoeal-disease
hhttps://www.unicef.de/blob/127260/728c481d8b-323fe15e58244179f11087/one-is-too-many-report-data.pdf

Diarrhoeal Diseases Vaccines Candidates



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. 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. The African and Southeast Asian region have the highest percentage of Enterotoxigenic E. coli (ETEC) episodes, while most Shigella cases occur in Africa, Eastern Mediterranean and Southern Asia. 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, physical stunting, 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 resistant strains of ETEC and Shigella the development of vaccines is becoming increasingly imperative.

Vaccines, the challenges ahead

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.

The absence of defined correlates of protective immunity along with the lack of good small animal models that fully recapitulate the disease, represent additional challenges to the development of a safe and effective vaccine. As Shigella and ETEC are antigenically diverse pathogens, the vaccine should provide broad coverage.

The potential of inadvertently inducing reactive arthritis; the perception that other interventions (including water and sanitation) are more appropriate; and insufficient funding to accelerate and complete the clinical development also pose major challenges in the path forward towards a vaccine against Shigella and ETEC.

© Jacob Kelvinj/Pexels

Stopping the Cycle of Diarrhoeal Disease

Early clinical development of oral vaccines

ShigOravax

The ShigOraVax project aims at advancing the clinical development of an oral Shigella vaccine called 'ShigOraVax' against three serotypes of Shigella flexneri (2a, 3a, and 6) as well as Shigella sonnei, through (i) the 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. In 2020, the work has focused on the preparation of the phase Ia/Ib trial in The Netherlands and Burkina Faso with the support of EVI.

The immunological assays to assess the immune response to the ShigOraVax vaccine in the clinical trials planned have been established at the University of Gothenburg and will be validated with samples from patients with recent confirmed Shigellosis. Capacity building at the African sites was ensured by online trainings organised by CIDRZ and GRAS teams as travel was restricted due to the COVID-19 pandemic and by the selection of PhD and Master students.
Specific epidemiologic data will also be generated on the incidence of Shigella disease in Burkina Faso and Zambia among children under five. This study has received ethical approval from both countries (NCT04312906) and the recruitment is underway.

The results of this project will strengthen the vaccine pipeline against a major diarrhoeal disease and making it available for late-stage clinical development.

SHIGETECVAX

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. 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, this vaccine candidate will target minor and highly conserved antigens that are shared among different types of Shigella and ETEC.

In 2020, the development of immunoassays, required for assessment of the clinical samples, has been advanced, and most of the assays were fully developed by the end of the year. The GMP manufacture of the ShigETEC vaccine candidate was completed and the European phase I clinical trial was successfully initiated at the clinical trial site in Hungary. The study aims to determine the safety, maximum tolerable dose and interval of oral administration of the ShigETEC vaccine. Results from the Phase 1a clinical trial will allow to select the optimal ShigETEC dosing and interval of administration for further evaluation in a Phase 1b clinical trial in endemic populations in Bangladesh. Results will be available in 2021.

Additionally, icddr,b initiated a sero-epidemiology study to assess naturally acquired immunity to Shigella and ETEC in adult (18-45 years) and paediatric (up to 5 years) patients compared to healthy adult controls (18-45 years) in Bangladesh. Recruitment will be completed in 2021.
EVI is coordinating the project and overseeing the communication and ethics related activities.

Emerging Infectious Diseases

Zika Virus

87 countries reported mosquito-borne Zika infection

An increased risk of **neurologic complications** is associated with Zika virus infection in adults and children.

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

Sources:
https://www.who.int/news-room/fact-sheets/detail/zika-virus
https://www.who.int/publications/m/item/zika-epidemiology-update
https://doi.org/10.1186/s12916-016-0660-0
https:/doi.org/10.1186/s12916-016-0660-0

Nipah virus

Outbreaks in Malaysia, Bangladesh, Singapore, India and Philippines

2 billion people at risk

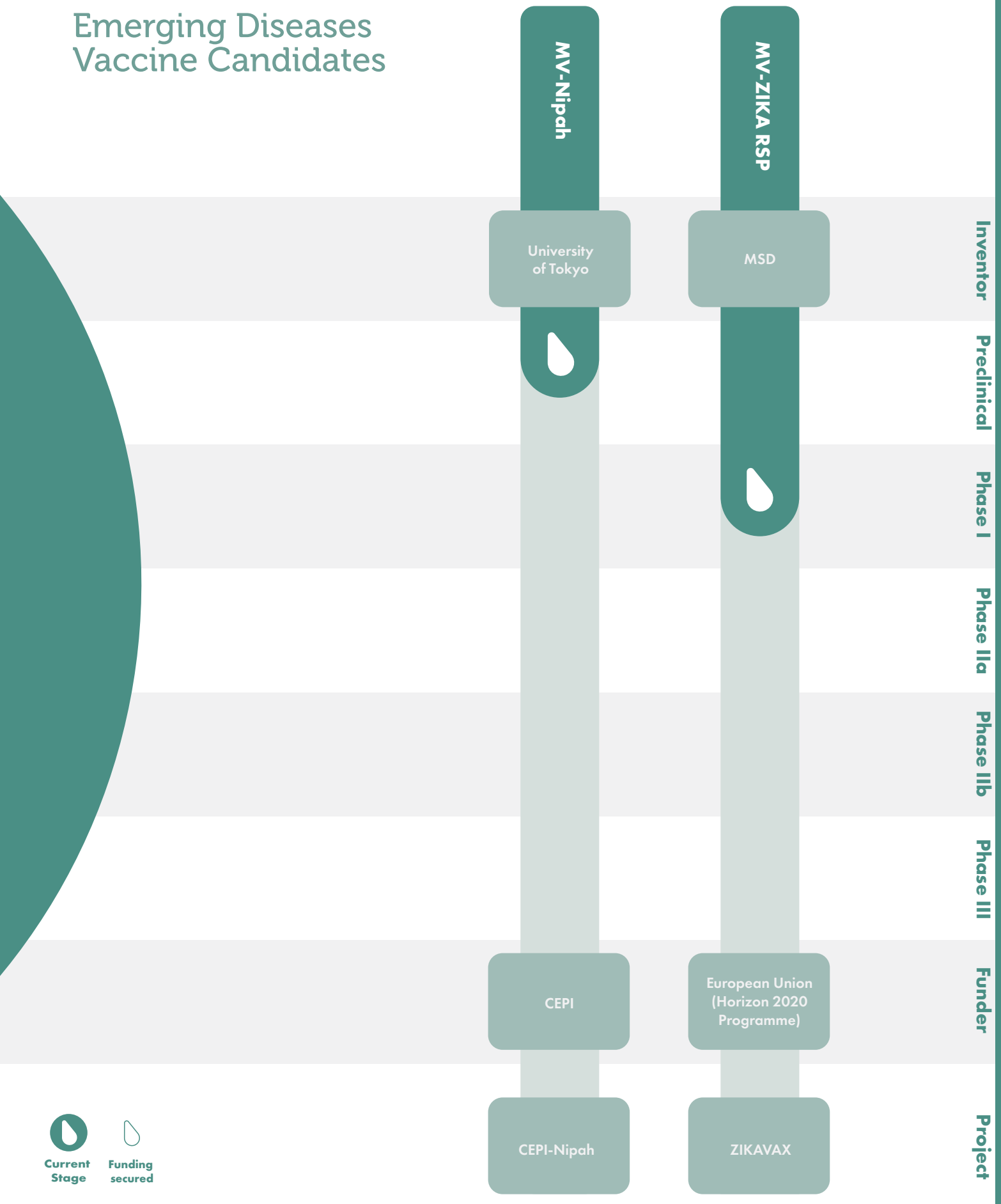
40% to 100% estimated case fatality rate

There is **no treatment or vaccine available** for either people or animals

Nipah virus represents a **high pandemic threat**

Sources:
https://www.who.int/news-room/fact-sheets/detail/nipah-virus
Nipah virus disease: A rare and intractable disease Intractable Rare Dis Res. 2019 Feb; 8(1): 1–8. 8 doi:10.5582/ird 2018.01130
Nipah virus infection: A review Epidemiol Infect. 2019; 147: e95.

Emerging Diseases Vaccine Candidates



At a glance

An emerging infectious disease (EID) is one that either has appeared and affected a population for the first time, or has existed previously but is rapidly spreading, either in terms of the number of people getting infected, or to new geographical areas. Many EIDs are zoonotic in origin. Often humans may have little or no natural immunity to EIDs, so their impact, on health, society, and the economy, are difficult to predict.

Examples of EIDs are infections caused by the Zika and Nipah viruses where EVI has focused some of its efforts.
Zika virus is a mosquito-borne flavivirus. The virus is transmitted through the bite of an infected Aedes mosquito, in tropical and subtropical regions, but also from mother to foetus during pregnancy, through sexual contact, transfusion of blood and blood products, and organ transplantation. Symptoms are usually mild and often do not require any specific treatment. However, Zika virus infection during pregnancy causes poor pregnancy outcomes e.g., preterm births, foetal loss and is also indicated as a cause of microcephaly and other congenital abnormalities in the developing foetus and new-born, collectively termed as congenital Zika syndrome (CZS). The Zika virus has also been associated with increased risk of Guillain-Barre syndrome. The provision of long-term care for affected children and families poses a real threat to healthcare systems and communities, especially in resource constraint settings. Although infections worldwide are not too prevalent, there is need to continue vigilance in the diagnosis and prevention of this virus. Currently, there is no therapy available to treat or prevent Zika virus infection. Vector control s in the environment and protection against human bites remain the key preventative measures.

Nipah virus (NiV) is a zoonotic virus, of the family Paramyxoviridae, genus Henipavirus for which the primary reservoirs are fruit bats (genus Pteropus). 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 75%, making it 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 bat species are found. There is a risk it could also be spread to areas where fruit bats do not live via transmission from infected animals to humans and from human to human. It is spread through contact with infected body fluids of humans and animals. Human infections range from asymptomatic infection to acute respiratory infection (mild, severe), and fatal encephalitis. Encephalitis and seizures occur in severe cases, progressing to coma within 24 to 48 hours. The incubation period (interval from infection to the onset of symptoms) is believed to range from 4 to 14 days. However, an incubation period up to 45 days has been reported. Most people who survive acute encephalitis make a full recovery, but long-term neurologic conditions have been reported in survivors.

Nipah virus has the biological potential to be a truly global threat. There are no known treatments and vaccines for Nipah virus. Research is ongoing for the development of a vaccine.

Vaccines, the challenges ahead

Vaccine development for the Zika virus faces several challenges, including the lack of an established correlate of protection (in children, adults, and the foetus), current unpredictability and lack of outbreaks, the large number of subclinical infections, the marked variability in clinical manifestations during symptomatic illness, the need to test multiple vulnerable populations, the uncertain effects of prior immunity to ZIKV or other flaviviruses (i.e., DENV), and the lack of animal models that recapitulate important features of human disease.

Although there are also ongoing efforts to develop a vaccine against Nipah virus, there remain challenges in determining the correlates of protection, choice of assays for serum neutralizing antibodies and the characterisation of animal challenge models.

Tackling (re)emerging diseases and outbreaks

Development of vaccines based on measles

ZIKAVAX

The ZIKAVAX project aimed at developing a safe, effective, and affordable preventive vaccine against Zika virus infection. To achieve this goal, ZIKAVAX used 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. The ultimate goal of ZIKAVAX was the demonstration of safety and immunogenicity of a recombinant measles-Zika vaccine candidate (MV-ZIKV) in adult volunteers in a phase Ia clinical trial.
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 RSP. Immunogenicity and protective efficacy of MV-ZIKA RSP was further demonstrated in a non-human primate challenge model for Zika virus infection. The established ZIKV mouse and NHP challenge models will be used to further evaluate additional ZIKV vaccine candidates, treatment options, or to better decipher the immune responses induced by vaccines or natural viral infections.

Profiting from the knowledge acquired on manufacturing its MV-based Chikungunya vaccine candidate (MV-CHIK), Themis (now part of MSD) GMP manufactured and released the selected MV-ZIKA RSP vaccine candidate. A first-in-man phase I clinical trial was conducted in Austria to investigate the safety and immunogenicity of MV-ZIKA-RSP. The clinical trial data indicates that the MV-ZIKA-RSP vaccine candidate was well tolerated and induced immune responses that are currently further evaluated. The clinical study was registered in the public platform clinicaltrials.gov (NCT04033068) where data will be available by the end of 2021.

EVI was the coordinator of the project and was instrumental in overseeing harmonization activities across animal and human studies as well as partner sites.

CEPI-Nipah

The CEPI-funded Nipah vaccine candidate is a live attenuated measles vector-based vaccine containing the Nipah-virus G gene (Malaysia strain). The recombinant MV-NiV vaccine candidate was developed at The Institute of Medical Science, University of Tokyo, and has shown to induce humoral responses in a preclinical study. In addition, the vaccine protected against lethal Nipah virus infection in hamster and non-human primate models. In 2020, work has been undertaken to establish robust process development and manufacturing at Batavia Biosciences for the MV-NiV vaccine. A scientific advice request meeting was held to discuss and receive recommendations on the further clinical development of the vaccine. The proof-of-concept study to confirm efficacy of the vaccine candidate in the hamster model is under preparation and is expected to take place in 2021.

Sources:
World Health Organization. Regional Office for South-East Asia. ([2014])". A brief guide to emerging infectious diseases and zoonoses. WHO Regional Office for South-East Asia. https://apps.who.int/iris/handle/10665/204722

https://www.who.int/news-room/fact-sheets/detail/nipah-virus

https://www.mayoclinicproceedings.org/article/S0025-6196(19)30483-5/fulltext

https://media.tghn.org/medialibrary/2021/02/

Cross-cutting activities

In addition to the different activities that EVI undertakes to advance the development of vaccines for specific diseases, EVI also coordinates a number of projects that address vaccine R&D in general. These collaborative endeavours between key actors in the R&D ecosystem such as industry, academic institutions, biotech, NGO's and regulatory authorities have proven efficient vehicles for driving innovation in pharmaceutical research, with wide-spread and transformative impact on vaccine development.

European infrastructure for the development of human and veterinary vaccines

TRANSVAC2

Target: Vaccine R&D infrastructure
Funder: European Union (Horizon 2020 Programme)

TRANSVAC2, European Vaccine Research and Development Infrastructure project, 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 (TNA), (ii) Joint Research Activities (JRA) 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 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 2020, in support of the global effort against SARS-COVID-19, TRANSVAC2 launched specific call for applications for the development of COVID-19 vaccines. A total of 31 services were awarded to eight research groups from SMEs and public institutions, to help speed-up the COVID-19 vaccines development pipeline. A variety of TRANSVAC2 services, from antigen discovery to preclinical and clinical trial support, were performed through the year. To uphold this fast and COVID-19 focused vaccine R&D support, the EU provided, in agreement with Member States, additional top-up funds worth 4 Mio EUR.

Besides the COVID-19 related activities, three calls were launched in 2020 for TNA services where 9 projects requesting 14 services were granted.

Moreover, two calls for training modules were launched as well, however due to COVID-19 restrictions the courses, both in fundamental and applied vaccinology, courses were postponed and are planned to take place in 2021.
As part of the JRA, the development of a human whole-blood assay using Luminex bead arrays to assess the potency of cytokine/chemokine responses has been completed and will be made available as a new TNA service in the upcoming year.

To reach wider public, TRANSVAC2 established a collaboration with another EC-funded project VetBioNet to harmonize the sample sharing process, established in the previous year.

A webinar on "Regulatory information for veterinary vaccine development in the EU and where to find it" was successfully held in collaboration with ENOVA - European Network of Vaccine Adjuvants - and COST - European Cooperation in Science and Technology.

Additionally, two workshops were planned, one jointly with VetBioNet on "Aerosol administration, devices and methods used in respiratory infection studies" and one on "Follow-up of physiology and pathology by telemetry in animal science" jointly with CEA-IDMT. Unfortunately, both workshops were postponed due to in an effort to reduce the impact and spread of SARS-CoV-2.

TRANSVAC-DS

Target: Vaccine R&D infrastructure
Funder: European Union (Horizon 2020 Programme)

TRANSVAC-DS, Design Study for a European Vaccine Infrastructure, builds on the outstanding accomplishments of TRANSVAC and during the two-year project duration will further prepare and advance the establishment of a sustainable European vaccine infrastructure. A feasibility study will be conducted and -for the business model selected through this process- detailed business and implementation plans will be prepared for a permanent and sustainable vaccine infrastructure of direct relevance to and benefit for Europe and further afield.

Key achievements:

A detailed gaps and needs analysis was conducted whose findings will support the ultimate positioning of a sustainable vaccine infrastructure. Three different business model options were developed and assessed and compared with each other. One of the business models was chosen based on an evaluation framework that had been developed. For the selected model, the preparation of a full five-year business plan and related implementation plan was started.

Vaccine batch to vaccine batch comparison by consistency testing

VAC2VAC

Target: Batch to Batch Control Testing
Funder: Innovative Medicines Initiative 2 (IMI2) and European and Federation of Pharmaceutical Industries and Associations (EFPIA)

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, MAT) was optimized, validated and transferred to the industry partner, who adapted the method to GMP standard within the Quality Control laboratory. Method B as described in the European Pharmacopoeia (version 9.2) was validated by the industry partner and a variation was submitted by end of 2019. MAT as replacement of the Rabbit Pyrogen Test for vaccine routine testing has been implemented by the industry partner after the approval by European regulatory authorities. The Italian Pharmacopeia delegation presented a request to the G15 of Ph. Eur. to replace the rabbit pyrogen test foreseen in the monograph 1375 Tick-born encephalitis vaccines (inactivated).

The development and validation of a new and reliable antibody free targeted LC-MS/MS method that is able to identify and quantify the amount of Tetanus neurotoxin (TeNT) present in the bacterial medium during the different production time points up to the harvesting of the TeNT just prior to further upstream purification and detoxification was completed. The method was validated according to ICH guidelines and by the application of the total error approach. Six ELISAs and one multiplex assay have

©Edward Jenner/Pexels

been qualified and are ready for validation: three TBEV ELISA, a Clostridium chauvoei ELISA, a Diphtheria ELISA, a Tetanus (human and veterinary) ELISA and a DTaP multiplex assay. Nine in vitro assays accomplished the discovery/optimization phase.

Work on Pre-validation of selected methods

VAC2VAC focuses on vaccines released under an in vivo based control strategy (CS) and develops methods to be used under a consistency approach-based CS not involving animal tests. Discussion on how to move from the current CS to a consistency approach-based CS started in year 4 of the project and was continued with VAC2VAC internal and external experts during year 5. Elements of such a CS and potential problems have been identified and will be presented with possible solutions in a White Paper.

Three ELISA methods for potency testing of TBEV vaccines have been selected to enter the validation phase. Planning of a collaborative study has been completed and will be conducted in year 6.

Work on Regulatory acceptance of the consistency approach

Global awareness about VAC2VAC is quickly growing thanks to a coordinated approach with international organizations, the Bangkok meeting (10.1016/j.biologicals.2020.07.010) and the participation of consortium members at congresses and workshops. Through active participation at NC3Rs WHO project, outreach to EDQM, USDA, FDA, WHO SAGE, WHO, ECBS, OIE, ICH/VICH has happened and is intensified.

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

FLUCOP

Target: Harmonization/ Influenza
Funder: Innovative Medicines Initiative (IMI) and European Federation of Pharmaceutical Industries and Associations (EFPIA)

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

Based on the results from an initial pilot study, progress was made towards the standardisation of the haemagglutination inhibition (HAI) and virus neutralisation assays. HAI is the most commonly used serologic assay in influenza vaccine evaluation. Regarding the development of assays to detect Neuraminidase (NA)-specific antibody responses for evaluating influenza vaccine immunogenicity, a harmonization exercise was undertaken and a , the NA enzyme-linked lectin assay (ELLA) consensus Standard Operating Procedure (SOP) was validated in an inter-laboratory study, demonstrating that the ELLA assay is precise, linear, robust within defined limits and has good specificity. Moreover, in the past two years significant progress has been made regarding the understanding and application of cell-mediated immunity.

Strengthening international health R&I cooperation between China and the EU

SENET

Target: Policy and EU-China Collaboration
Timeline: 01 January 2019- 31 December 2021
Funder: European Union (Horizon 2020 Programme)

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

For the preparation of a roadmap and strategic recommendations that are key deliverables of SENET, several interactive online consultation meetings were organised by SENET, (i) Policy stakeholder dialogues and (ii) Research & Innovation expert group meetings. For these meetings, key stakeholders from different target groups such as researchers from the public and private sector, policy and decision makers, funders, and other groups of experts could be engaged. Further events are due in 2021. The findings of all meetings combined will eventually inform the different deliverables mentioned above that will be published towards the end of 2021.

©Kindel Media/Pexels

TRAINING

Training at EVI

EVI is dedicated to strengthening public health and vaccine research capacities in the fight against diseases of poverty and emerging infectious diseases.

Within EVI's research projects, training is included as an integral part offered in form of webinars, short modular training courses or long-term training of MSc and PhD students.

EDCTP/TDR Fellowships - Training at EVI

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 to develop and implement appropriate solutions. In 2015, EVI 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 and mid-career researchers from LMICs to acquire skills in clinical research and development through placements in pharmaceutical companies and PDPs.

The goal of this 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. This is done through thematic internal trainings by experienced staff members of EVI, hands-on engagement within research projects at EVI and also through attending online and physical trainings offered by partners of EVI. EVI's mentoring approach encourages the trainees to take personal responsibility of project tasks and stimulates individual creativity, while still offering the required assistance and guidance. The mentorship is continued by EVI upon return and re-integration of the fellows to their home institution. This mentorship has also included ithe organisation of joint training sessions between former fellows and staff at EVI.

Since the beginning of EVI's involvement in this fellowship programme, seven researchers from sub-Saharan Africa and one from Latin America with different educational backgrounds and working experiences have been hosted by EVI. In 2020, EVI hosted a young Nigerian researcher, Dr James Onyemata from the Institute of Human Virology, Nigeria and Dr Robert A. Shey from the Molecular and Cell Biology Laboratory, University of Buea. Following these positive experiences, EVI is pleased to host three African trainees in 2021.

Fellows' profiles and their experience at EVI

Robert Adamu Shey

The fellowship at EVI has been a uniquely exciting experience. I had the opportunity to learn about various concepts on vaccinology including product development, preclinical and clinical development, and vaccine-related project management.

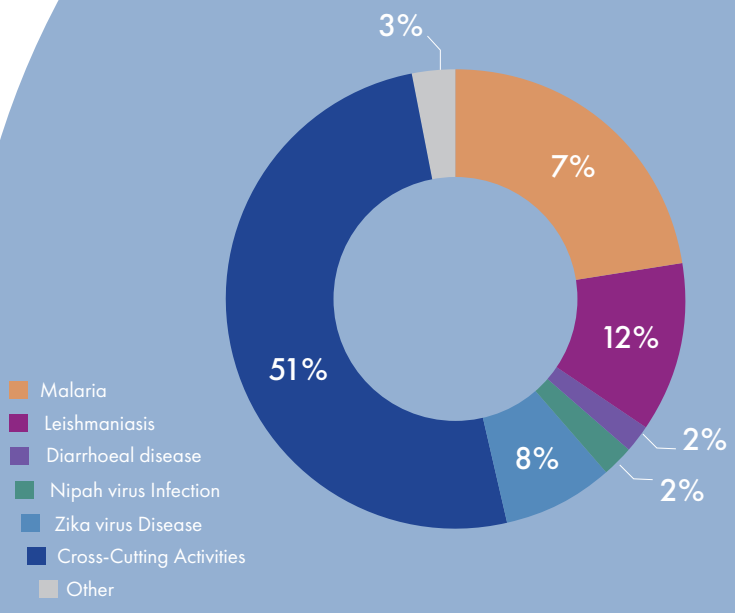
I also had the opportunity to serve a project manager for a project on the preclinical development of a novel malaria vaccine candidate – having the opportunity to interact with sponsors, funders and different research teams. This created a unique platform not only for learning but to create new networks which could go a long way to facilitate my establishment as principal investigator. The entire EVI staff was very supportive and made every experience at EVI very exciting despite the COVID-19 pandemic. The program enabled me to gain lots of theoretical knowledge and practical experience. This has helped me win my first grant as a principal investigator. I also used the opportunity to submit a project on the development of novel vaccine candidate for onchocerciasis for the TRANSVAC2 Service applications in collaboration with my supervisors and this was granted. For my re-entry, I am implementing an 11-month course that includes amongst others, modules on ethics in human and animal research, project management, vaccinology, data management and others. The overall goal is to strategize to improve on the quality of research output from early-career researchers at my home institution.

Financial performance report 2020

The year 2020 was heavily affected by SARS 2. The disease named Covid 19 was and still is raging throughout the world. EVI had a massive delay in several projects from 3 to 12 months but also saw the emergence of new projects to combat the pandemic. Consequently, the funding landscape and use hereof remain unchanged, EVI receives funding from national and international governmental agencies, as well as private organisations. EVI uses those funds to finance a broad portfolio of projects, which help to accelerate the development and clinical assessment of vaccine candidates for diseases of poverty and emerging infectious diseases, to promote the affordability and accessibility of those vaccines, and to act as a focal point to enhance 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 globally.

The pandemic certainly emphasized the need of EVI to play a bigger role.

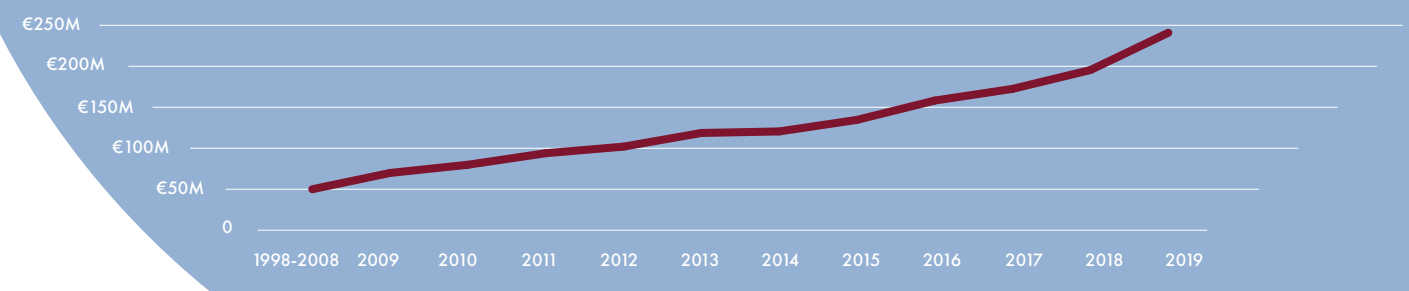
EVI EXPENDITURE PER DISEASE



Fundraising

EVI's project portfolio as of 31 December 2020 consists of fifteen active projects in the broad field of translational vaccine R&D, transnational access services, capacity building and of course vaccine development in general through clinical trials. EVI appreciates the establishment of new partnerships to fight the pandemic and highly valuates the continued support by its long-term partners. EVI's activities over the current reporting period were covering a broad portfolio of EU, EDCTP, CEPI, IMI and GHIT projects.

FUNDRAISING CONTRACTED ACCUMULATED 1998 – 2020



Financial Statements 2020

Statement of comprehensive income for the year ended 31 December 2020

	2020	2019
Income		
Turnover from sales	16.187,51	-
Public institutional funding:		
GHIT & Govern. & public int. organisations	1.778.297,94	486.151,71
European Union & IMI grants	4.659.459,69	7.462.293,70
European and Developing Countries Clinical Trial Partnership	1.132.387,77	3.152.851,96
Total public institutional funding	**7.570.145,40**	**11.101.297,37**
Other income net	128.506,94	302.988,76
Total income	**7.714.839,85**	**11.404.286,13**
Social mission expenditure		
Research & vaccine development expenditure:		
Malaria	**1.762.419,96**	**433.523,94**
Leishmaniasis	**897.300,85**	**753.864,32**
Diarrhoeal diseases	**147.660,63**	**6.360.059,16**
Nipah virus disease	**154.880,42**	**143.652,64**
Zika virus disease	**641.819,92**	**760.796,68**
Cross-Cutting activities	**3.966.768,65**	**2.649.400,63**
Advocacy & communications expenses	19.781,60	12.148,50
Total social mission expenditure	**7.590.632,03**	**11.113.445,87**
Supportive social mission expenditure		
Training, quality assurance and project development	5.614,38	4.652,45
Fundraising	34.744,30	36.418,28
Governance	39.672,65	42.220,35
Total supportive social mission expenditure	**80.031,33**	**83.291,08**
Non-social mission expenditure		
General executive administration	126.463,43	134.736,27
Total non-social mission expenditure	**126.463,43**	**134.736,27**
Total expenditure	**7.797.126,79**	**11.331.473,22**
Operating surplus / (loss)	(82.286,94)	72.812,91
Other income (expenses)		
Financial income, net	-	-
Total other income (expenses), net	-	-
Net surplus for the year prior to allocations	(82.286,94)	72.812,91
Allocation / (Release) to restricted operating funds in equity	-	-
Allocation / (Release) to unrestricted operating funds in equity	82.286,94	(72.812,91)
Net surplus for the year after allocations	-	-

For more detailed information about EVI's financial statements and related indicators the 2020, EVI Financial and Performance Report is available upon request (https://www.euvaccine.eu/contact-us).

GOVERNANCE

AS OF 31 DECEMBER 2020

EVI Board

Clemens Kocken
Biomedical Primate Research Centre, The Netherlands

Martin Trillsch
Legal Council, University Clinical Centre, Heidelberg

Samuel McConkey
Royal College of Surgeons in Ireland, Ireland

Christiane Gerke
Institut Pasteur, France

David Salisbury
Jenner Vaccine Foundation, United Kingdom

EVI Board of Stakeholders (BoS)

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

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

Suresh Jadhav
Serum Institute of India, India

EVI Scientific Advisory Committee (SAC)

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

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

Nancy Le Cam Bouveret
Independent Consultant

Nathalie Garçon
BIOASTER Technology Research Institute, France

EVI Secretariat

Ole Olesen
Executive Director

Hilde Depraetere
Acting Executive Director (from March 2019)

Sten Larsen Finnsson
Finance and HR Director

Sophie Houard
Director of Vaccine Development

Nicola Viebig
Chief Scientific Officer

Stefan Jungbluth
Head of Business Development

Thorsten Kohaut
Finance and HR Director

Sandra Hauenstein
Finance Assistant

Flavia D'Alessio
Project Manager

Monika Slezak
Project Manager

Catarina Luis
Project and Communication Manager

Eliana Acosta
Project Manager

Irina Meln
Project Manager

Robert Shey
Finance Assistant

Nicolas Havelange
Consultant

ACKNOWLEDGMENTS

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 and other support received from the following organisations.

Coalition for Epidemic Preparedness Innovations (CEPI), Norway
Danida, Denmark's development cooperation, Denmark
Department of Foreign Affairs, Irish Aid, Ireland
Dutch Ministry of Foreign Affairs, Directorate-General for International Cooperation (DGIS), The Netherlands
Dutch Research Council, The Netherlands
European & Developing Countries Clinical Trials Partnership (EDCTP), The Netherlands, with co-funding from EU Member States and other countries
European Union (EU), Belgium
Federal Ministry of Education and Research (BMBF) through KfW, Germany
Global Health Innovative Technologies (GHIT) Fund, Japan
Innovative Medicines Initiative (IMI), 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
Minor donations and support though marketing and communications
All4Cloud
SAP
Co-funding was kindly provided by the following organisations:
NIH – NIAID, United States of America
Research Institute for Microbial Diseases (RIMD), Japan
Centre National de Recherche et de Formation sur le Paludisme (CNRFP), Burkina Faso
University of Copenhagen, Denmark
Danish National Advanced Technology Foundation, Denmark
Inserm, France
Institut National de la Transfusion Sanguine (INTS), France
Centre National de la Recherche Scientifique (CNRS), France
Austrian Federal Ministry of Science and Research, Austria
University of Oxford, United Kingdom
Sanofi Pasteur (SP), France
Zoetis Belgium SA (Zoetis), Belgium
Boehringer Ingelheim Animal Health, France, previously known Merial Boehringer Ingelheim (BI), Germany
Intervet International B.V., also known as MSD Animal Health (MSD), Netherlands
GSK Biologicals (GSKBio), Belgium
Wellcome Trust, United Kingdom

Partners

EVI thanks all its collaborators that supports our common goals.

SEmalvac2

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

SEmalvac4

Groupe de Recherche Action en Santé (GRAS)	Burkina Faso
Nobelpharma Co, Ltd.	Japan
Research Institute for Microbial Diseases (RIMD), Osaka University	Japan

PfRipr5

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

MMVC

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

MIMVaC-Africa

Groupe de Recherche Action en Santé (GRAS)	Burkina Faso
Eberhard Karls Universität Tübingen (EKUT)	Germany
University of Oxford (UOXF)	UK
Leiden University Medical Center (LUMC)	The Netherlands
Luxembourg Institute of Health (LIH)	Luxembourg
Osaka University	Japan
Centre de Recherches Médicales de Lambaréné (CERMEL)	Gabon
Fundação Manhiça	Mozambique
Ifakara Health Institute (IHI)	Tanzania

PREV-PKDL

University of York	United Kingdom
Institute of Endemic Diseases (IEND), University of Khartoum	Sudan
University of Gondar	Ethiopia
Kenya Medical Research Institute (KEMRI)	Kenya
Makerere University	Uganda

SHIGETECVAX

Eveliqure Biotechnologies GmbH	Austria

icddr,b	Bangladesh
PATH	USA
University of Gothenburg	Sweden

ShigOraVax

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

ZIKAVAX

Commissariat à l'énergie atomique et aux énergies alternatives (CEA)	France
Institut Pasteur	France
Themis Bioscience (now part of Merck Sharp & Dohme (MSD))	Austria

CEPI-Nipah

Batavia Biosciences B.V.	The Netherlands
Stanford University School of Medicine	USA
University of Tokyo	Japan

TRANSVAC2

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
GenIbet Biopharmaceuticals S.A.	Portugal
Helmholtz Centre for Infection Research (HZI)	Germany
Institut de Recerca i Tecnologia Agroalimentàries (IRTA)	Spain
Institut National de la Recherche Agronomique (INRA)	France
Institute for Translational Vaccinology (ITV) - Intravacc	The Netherlands
Instituto de Biologia Experimental e Tecnológica (iBET)	Portugal
Instruct Academic Services Limited	United Kingdom
Leiden University (LU)	The Netherlands
Leiden University Medical Center, Dept. Infectious Diseases (LUMC)	The Netherlands
London School of Hygiene and Tropical Medicine (LSHTM)	United Kingdom
Public Health England (PHE)	United Kingdom
Sclavo Vaccine Association (SVA)	Italy
Statens Serum Institut (SSI)	Denmark
The National Institute for Biological Standards and Control (NIBSC)	United Kingdom
University of Oxford	United Kingdom
University of Siena (UNISI)	Italy
Vaccine Formulation Institute	United Kingdom
Wageningen Bioveterinary Research, Wageningen University & Research (SWR)	The Netherlands

TRANSVAC-DS

BIOASTER - Fondation de Cooperation Scientifique	France
Biomedical Primate Research Centre (BPRC)	The Netherlands
Commissariat a l'energie atomique et aux energies alternat ives (CEA/IDMIT)	France
Dutch Ministry of Health and Sport	The Netherlands
European Clinical Research Infrastructure Network (ECRIN)	France
European Infrastructure for Translational Medicine (EATRIS)	The Netherlands
European Vaccine Initiative (EVI)	Germany
Flanders Vaccines	Belgium
Fraunhofer Institute for Molecular Biology and Applied Ecology IME	Germany
GenIbet Biopharmaceuticals S.A.	Portugal
Helmholtz Centre for Infection Research (HZI)	Germany
Institut de Recerca i Tecnologia Agroalimentàries (IRTA)	Spain
Institut de Salut Carlos III	Spain
Institut national de la Recherche agronomique (INRA)	France
Instituto de Biologia Experimental e Tecnológica (iBET)	Portugal
Instruct Academic Services Limited	Italy / United Kingdom
Leiden University (LU)	The Netherlands
London School of Hygiene and Tropical Medicine (LSHTM)	United Kingdom
Medicines & Healthcare products Regulatory Agency	United Kingdom
Sciensano	Belgium
Sclavo Vaccine Association (SVA)	Italy
Statens Serum Institut (SSI)	Denmark
University of Siena (UNISI)	Italy
Vaccine Formulation Institute	United Kingdom
Wageningen Bioveterinary Research, Wageningen University & Research (SWR)	The Netherlands

VAC2VAC

Bavarian Nordic (BN)	Denmark
Biomedical Primate Research Centre (BPRC)	The Netherlands
Boehringer Ingelheim (BI)	Germany
Boehringer Ingelheim Animal Health France (BIAH FR)	France
College ter Beoordeling van Geneesmiddelen (CBG/ MEB)	The Netherlands
European Commission, Joint Research Centre (JRC)	Italy
GSK Biologicals (GSKBio)	Belgium
Institute for Translational Vaccinology (Intravacc)	The Netherlands
International Alliance for Biological Standardization · for Europe (IABS-EU)	France
Istituto Superiore di Sanità (ISS)	Italy
Merck Sharp & Dohme (MSD)	The Netherlands
National Institute for Biological Standards and Control (DH-NIBSC)	United Kingdom
National Institute for Public Health and the Environment (RIVM)	The Netherlands
Österreichische Agentur für Gesundheit und Ernährungssicherheit GmbH (Austrian Agency for Health and Food Safety: AGES)	Austria
Paul-Ehrlich Institute (PEI)	Germany
Pfizer (Pfizer)	Austria
Sanofi Pasteur (SP)	France

Sciensano (WIV-ISP)	Belgium
University Medical Center Groningen (UMCG)	The Netherlands
University of Applied Sciences Utrecht (HU)	The Netherlands
University of Utrecht (UU)	The Netherlands
Zoetis Belgium SA (Zoetis)	Belgium

FLUCOP

Abbott	The Netherlands
Artemis Bio-Support B.V.	The 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
Department of Health (MHRA)	United Kingdom
Paul-Ehrlich-Institut, Bundesinstitut Für Impfstoffe Und Biomedizinische Arzneimittel	Germany
Sanofi Pasteur	France
QUINTEN	France
Sclavo Vaccines Association	Italy
Sequirus	USA
The Chancellor, Masters and Scholars of the University of Oxford	United Kingdom
Università degli Studi di Siena	Italy
Universiteit Gen	Belgium
Universitetet i Bergen	Norway
University of Perugia	Italy
University of Surrey	United Kingdom

SENET

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 / Germany
Sociedade Portuguesa de Inovação (SPI) - Consultadoria Empresarial e Fomento da Inovação S.A.	Portugal
Steinbeis 2i GmbH (S2i)	Germany

List of Project Publications:

SEmalvac

Palacpac, N., & Horii, T. (2020). Malaria vaccines: facing unknowns. F1000Research, 9, F1000 Faculty Rev-296. https://doi.org/10.12688/f1000research.22143.1

PRIMALVAC

Sirima, S. B., Richert, L., Chêne, A., Konate, A. T., Campion, C., Dechavanne, S., Semblat, J. P., Benhamouda, N., Bahuaud, M., Loulergue, P., Ouédraogo, A., Nébié, I., Kabore, M., Kargougou, D., Barry, A., Ouattara, S. M., Boilet, V., Allais, F., Roguet, G., Havelange, N., ... Gamain, B. (2020). PRIMVAC vaccine adjuvanted with Alhydrogel or GLA-SE to prevent placental malaria: a first-in-human, randomised, double-blind, placebo-controlled study. The Lancet. Infectious diseases, 20(5), 585–597. https://doi.org/10.1016/S1473-3099(19)30739-X

MMVC

Datoo, M. S., Natama, M. H., Somé, A., Traoré, O., Rouamba, T., Bellamy, D., Yameogo, P., Valia, D., Tegneri, M., Ouedraogo, F., Soma, R., Sawadogo, S., Sorgho, F., Derra, K., Rouamba, E., Orindi, B., Ramos Lopez, F., Flaxman, A., Cappuccini, F., Kailath, R., ... Tinto, H. (2021). Efficacy of a low-dose candidate malaria vaccine, R21 in adjuvant Matrix-M, with seasonal administration to children in Burkina Faso: a randomised controlled trial. Lancet (London, England), 397(10287), 1809–1818. https://doi.org/10.1016/S0140-6736(21)00943-0

PREV_PKDL

Press release: Multinational Research Team Granted Eight Million Euros to Help Reduce Burden of Parasitic Disease in African Countries https://www.beckman.com/news/multinational-research-team-granted-eight-million-euros

Le Rutte, E. A., Coffeng, L. E., Malvolti, S., Kaye, P. M., & de Vlas, S. J. (2020). The potential impact of human visceral leishmaniasis vaccines on population incidence. PLoS neglected tropical diseases, 14(7), e0008468. https://doi.org/10.1371/journal.pntd.0008468

Expanding research capacity into neglected tropical diseases, https://pharmaphorum.com/r-d/views-analysis-r-d/expanding-research-capacity-into-neglected-tropical-diseases/

TRANSVAC2

Sisteré-Oró, M., Pedersen, G.K., Córdoba, L. et al. Influenza NG-34 T cell conserved epitope adjuvanted with CAF01 as a possible influenza vaccine candidate. Vet Res 51, 57 (2020). https://doi.org/10.1186/s13567-020-00770-4

Lucchesi, S., Nolfi, E., Pettini, E., Pastore, G., Fiorino, F., Pozzi, G., Medaglini, D., & Ciabattini, A. (2020). Computational Analysis of Multiparametric Flow Cytometric Data to Dissect B Cell Subsets in Vaccine Studies. Cytometry. Part A : the journal of the International Society for Analytical Cytology, 97(3), 259–267. https://doi.org/10.1002/cyto.a.23922

Lucchesi, S., Furini, S., Medaglini, D., & Ciabattini, A. (2020). From Bivariate to Multivariate Analysis of Cytometric Data: Overview of Computational Methods and Their Application in Vaccination Studies. Vaccines, 8(1), 138. https://doi.org/10.3390/vaccines8010138

Beyer, W., Palache, A. M., Reperant, L. A., Boulfich, M., & Osterhaus, A. (2020). Association between vaccine adjuvant effect and pre-seasonal immunity. Systematic review and meta-analysis of randomised immunogenicity trials comparing squalene-adjuvanted and aqueous inactivated influenza vaccines. Vaccine, 38(7), 1614–1622. https://doi.org/10.1016/j.vaccine.2019.12.037

Palgen, J. L., Tchitchek, N., Rodriguez-Pozo, A., Jouhault, Q., Abdelhouahab, H., Dereuddre-Bosquet, N., Contreras, V., Martinon, F., Cosma, A., Lévy, Y., Le Grand, R., & Beignon, A. S. (2020). Innate and secondary humoral responses are improved by increasing the time between MVA vaccine immunizations. NPJ vaccines, 5(1), 24. https://doi.org/10.1038/s41541-020-0175-8

Dijkman, K., Lubbers, R., Borggreven, N. V., Ottenhoff, T., Joosten, S. A., Trouw, L. A., & Verreck, F. (2020). Systemic and pulmonary C1q as biomarker of progressive disease in experimental non-human primate tuberculosis. Scientific reports, 10(1), 6290. https://doi.org/10.1038/s41598-020-63041-4

Schmidt, S. T., Christensen, D., & Perrie, Y. (2020). Applying Microfluidics for the Production of the Cationic Liposome-Based Vaccine Adjuvant CAF09b. Pharmaceutics, 12(12), 1237. https://doi.org/10.3390/pharmaceutics12121237

Ciabattini, A., Garagnani, P., Santoro, F., Rappuoli, R., Franceschi, C., & Medaglini, D. (2020). Shelter from the cytokine storm: pitfalls and prospects in the development of SARS-CoV-2 vaccines for an elderly population. Seminars in immunopathology, 42(5), 619–634. https://doi.org/10.1007/s00281-020-00821-0

Funnell, S., Dowling, W. E., Muñoz-Fontela, C., Gsell, P. S., Ingber, D. E., Hamilton, G. A., Delang, L., Rocha-Pereira, J., Kaptein, S., Dallmeier, K. H., Neyts, J., Rosenke, K., de Wit, E., Feldmann, H., Maisonnasse, P., Le Grand, R., Frieman, M. B., & Coleman, C. M. (2020). Emerging preclinical evidence does not support broad use of hydroxychloroquine in COVID-19 patients. Nature communications, 11(1), 4253. https://doi.org/10.1038/s41467-020-17907-w

Guzmán C. A. (2020). Next Generation Influenza Vaccines: Looking into the Crystal Ball. Vaccines, 8(3), 464. https://doi.org/10.3390/vaccines8030464

VAC2VAC

Michiels TJM, Tilstra W, Hamzink MRJ, de Ridder JW, Danial M, Meiring HD, Kersten GFA, Jiskoot W, Metz B. Degradomics-Based Analysis of Tetanus Toxoids as a Quality Control Assay. Vaccines. 2020; 8(4) https://doi.org/10.3390/vaccines8040712

van den Biggelaar RHGA, van Eden W, Rutten VPMG, Jansen CA. Macrophage Activation Assays to Evaluate the Immunostimulatory Capacity of Avibacterium paragallinarum in A Multivalent Poultry Vaccine. Vaccines. 2020; 8(4). https://doi.org/10.3390/vaccines8040671

van den Biggelaar RHGA, van Eden W, Rutten VPMG, Jansen CA. Nitric Oxide Production and Fc Receptor-Mediated Phagocytosis as Functional Readouts of Macrophage Activity upon Stimulation with Inactivated Poultry Vaccines In Vitro. Vaccines. 2020; 8(2). https://doi.org/10.3390/vaccines8020332

Akkermans, A., Chapsal, J. M., Coccia, E. M., Depraetere, H., Dierick, J. F., Duangkhae, P., Goel, S., Halder, M., Hendriksen, C., Levis, R., Pinyosukhee, K., Pullirsch, D., Sanyal, G., Shi, L., Sitrin, R., Smith, D., Stickings, P., Terao, E., Uhlrich, S., Viviani, L., ... Webster, J. (2020). Animal testing for vaccines. Implementing replacement, reduction and refinement: challenges and priorities. Biologicals : journal of the International Association of Biological Standardization, 68, 92–107. https://doi.org/10.1016/j.biologicals.2020.07.010

Etna, M. P., Giacomini, E., Rizzo, F., Severa, M., Ricci, D., Shaid, S., Lambrigts, D., Valentini, S., Galli Stampino, L., Alleri, L., Gaggioli, A., Von Hunolstein, C., Spreitzer, I., & Coccia, E. M. (2020). Optimization of the monocyte activation test for evaluating pyrogenicity of tick-borne encephalitis virus vaccine. ALTEX, 37(4), 532–544. https://doi.org/10.14573/altex.2002252

van den Biggelaar, R., Arkesteijn, G., Rutten, V., van Eden, W., & Jansen, C. A. (2020). In vitro Chicken Bone Marrow-Derived Dendritic Cells Comprise Subsets at Different States of Maturation. Frontiers in immunology, 11, 141. https://doi.org/10.3389/fimmu.2020.00141

Pennings, J. L., Abachin, E., Uhlrich, S., Esson, R., Mallet, L., & Vandebriel, R. J. (2020). A next generation sequencing based method for determining genetic stability in Clostridium tetani vaccine strains. Biologicals, 64, 10–14. https://doi.org/10.1016/j.biologicals.2020.02.001

FLUCOP

Beyer, W. E., Palache, A. M., Reperant, L. A., Boulfich, M., & Osterhaus, A. D. (2020). Association between vaccine adjuvant effect and pre-seasonal immunity. Systematic review and meta-analysis of randomised immunogenicity trials comparing squalene-adjuvanted and aqueous inactivated influenza vaccines. Vaccine, 38(7), 1614–1622. https://doi.org/10.1016/j.vaccine.2019.12.037

Project Index

Project	Funder	Project Title	Timeline
MMVC	EDCTP	The Multi-Stage Malaria Vaccine Consortium (MMVC)	01 April 2018 – 30 September 2023
SEmalvac2	GHIT Fund and Nobelpharma Co, Ltd.	Safety evaluation of BK-SE36/CpG in the malaria endemic population	01 November 2016 – 31 January 2022
SEmalvac4	GHIT Fund and Nobelpharma Co, Ltd.	Preparatory phase II for the malaria vaccine candidate NPC-SE36/CpG	01 April 2020 – 30 September 2022
PfRipr5	GHIT Fund	Further development of a new asexual blood-stage malaria vaccine candidate (PfRipr5)	01 April 2019 – 30 June 2020
MIMVaC-Africa	EDCTP	A multilateral initiative to foster the clinical development of effective malaria vaccine candidates in Africa (MIMVaC-Africa)	01 February 2020 – 31 January 2025
PREV-PKDL	EDCTP2, co-funded by Wellcome Trust	Clinical development of a therapeutic vaccine for prevention of post-kala azar dermal leishmaniasis	01 April 2018 – 30 June 2023
LEISHDNAVAX	GHIT Fund	Preclinical and preparation of early clinical testing of a new vaccine candidate against cutaneous leishmaniasis	01 September 2017 – 31 March 2020
SHIGETECVAX	European Union (Horizon 2020 Programme)	Early clinical development of a live, attenuated combination vaccine against Shigella and ETEC diarrhoea	01 September 2019 – 28 February 2025
ShigOraVax	EDCTP2	Early clinical development of an oral Shigella vaccine through phase II study in Africa	01 October 2019 – 31 March 2025
CEPI-NIPAH	Coalition for Epidemic Preparedness Innovations (CEPI)	Development of a Nipah measles vector vaccine (MV-NIV) to be used in outbreaks situation in children and adults exposed population.	01 March 2019 – depending on stage gate criteria
ZIKAVAX	European Union (Horizon 2020 Programme)	Fast track development of a Zika vaccine based on measles vector	01 October 2016 – 31 December 2020
TRANSVAC2	European Union (Horizon 2020 Programme)	European Vaccine Research and Development Infrastructure	01 May 2017 – 30 April 2022
TRANSVAC-DS	European Union (Horizon 2020 Programme)	Design study for a European vaccine infrastructure	01 June 2020 – 31 May 2022
VAC2VAC	Innovative Medicines Initiative (IMI) and European Federation of Pharmaceutical	Vaccine batch to vaccine batch comparison by consistency testing	01 March 2016 – 28 February 2022
FLUCOP	Innovative Medicines Initiative (IMI) and European Federation of Pharmaceutical Industries and Associations (EFPIA)	Standardization and Development of Assays for Assessment of Influenza Vaccines Correlates of Protection	01 March 2015 – 28 February 2022
SENET	European Union (Horizon 2020 Programme)	Strengthening international R&I cooperations between China and the EU	01 January 2019 – 31 December 2021

/European Vaccine Initiative (EVI)

@Europe Vaccine

European Vaccine Initiative

Subscribe to our newsletters via 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