ANNUAL REPORT 2021

European Vaccine Initiative

Contents

Message from the Chairman and Executive Director

The COVID-19 pandemic continued its rampage throughout 2021 and has heavily impacted global health priorities and research activities in infectious diseases at large. This has also affected EVI, which has engaged and contributed whole-heartedly to the global search for solutions against the pandemic, while also keeping focused on our long-term mission of developing affordable vaccines for the poorest people on the planet.

The beginning of 2021 saw the roll-out of the highly effective and safe mRNA vaccines against SARS-CoV-2. Developed in record time and using a new technology, these vaccines attracted massive attention and reminded everybody of the importance and huge potential of vaccines in combatting deadly diseases. Despite the many operational challenges caused by COVID-19, the heightened focus on vaccines has made it possible for EVI to engage in a number of new and ambitious projects during the last year.

A new grant from GHIT has allowed EVI to resume its support to the development of a placental malaria vaccine, a condition that annually affects more than 100,000 women in resource-poor settings and an area that EVI has pioneered. With generous funding from IMI2, the Inno4Vac project with over 40 partners from industry, academia, biotech and public health organisations was launched by EVI in September. Inno4Vac, which aims to develop and refine new research tools for vaccinology, ranging from organ-on-chips, human challenge models to optimisation of manufacturing methods, constitutes the largest single project that EVI has coordinated so far. PrIMAVeRa, also launched during 2021 represents a particularly interesting new project, where EVI coordinates a consortium that aims at developing a model for predicting the impact of vaccines in combatting anti-microbial resistance (AMR). This is the first time that EVI engages in a large-scale project in AMR, a hugely important area for global public health.

Supporting the global effort to combat COVID-19, EVI has in 2021 contributed to the formation of the VACCELERATE EU-wide vaccine trial network. VACCELERATE, which is led by University Hospital Cologne, will act as a single-entry point for vaccine developers, who are looking to carry out vaccine trials across Europe, and EVI plays a key role in the network as co-leading the immune monitoring activities. Through the TRANSVAC2 infrastructure, a variety of services from antigen discovery to preclinical and clinical trial support, has enabled SMEs and public institutions to speed-up their developments of COVID-19 vaccine candidates.

As an organisation, EVI has also evolved and adapted to the challenges of the coming years. During 2021 we have prepared a change in our legal status from a European Economic Interest Grouping (EEIG) to a non-profit Association under German law. This change will be completed during 2022 and will allow EVI to engage in a wider range of activities, as well as collaborating with a broader range of stakeholders. To reflect this, a new Strategic Business Plan from EVI, covering the period from 2021 to 2025 has been prepared and published, describing our goals and ambitions for the coming years.

Looking back on 2021, the COVID-19 pandemic has continued to inflict pain and suffering on the world, as well as major disruptions on research and global public health. In this environment it has become evident that vaccines are some of the most powerful weapons against infectious diseases. By the end of 2021, EVI has a broader project portfolio than ever before, and a larger network than ever before. This is undisputed evidence that EVI and like-minded organisations provide an essential contribution to global public health.

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

2021 IN HIGHLIGHTS

New projects:

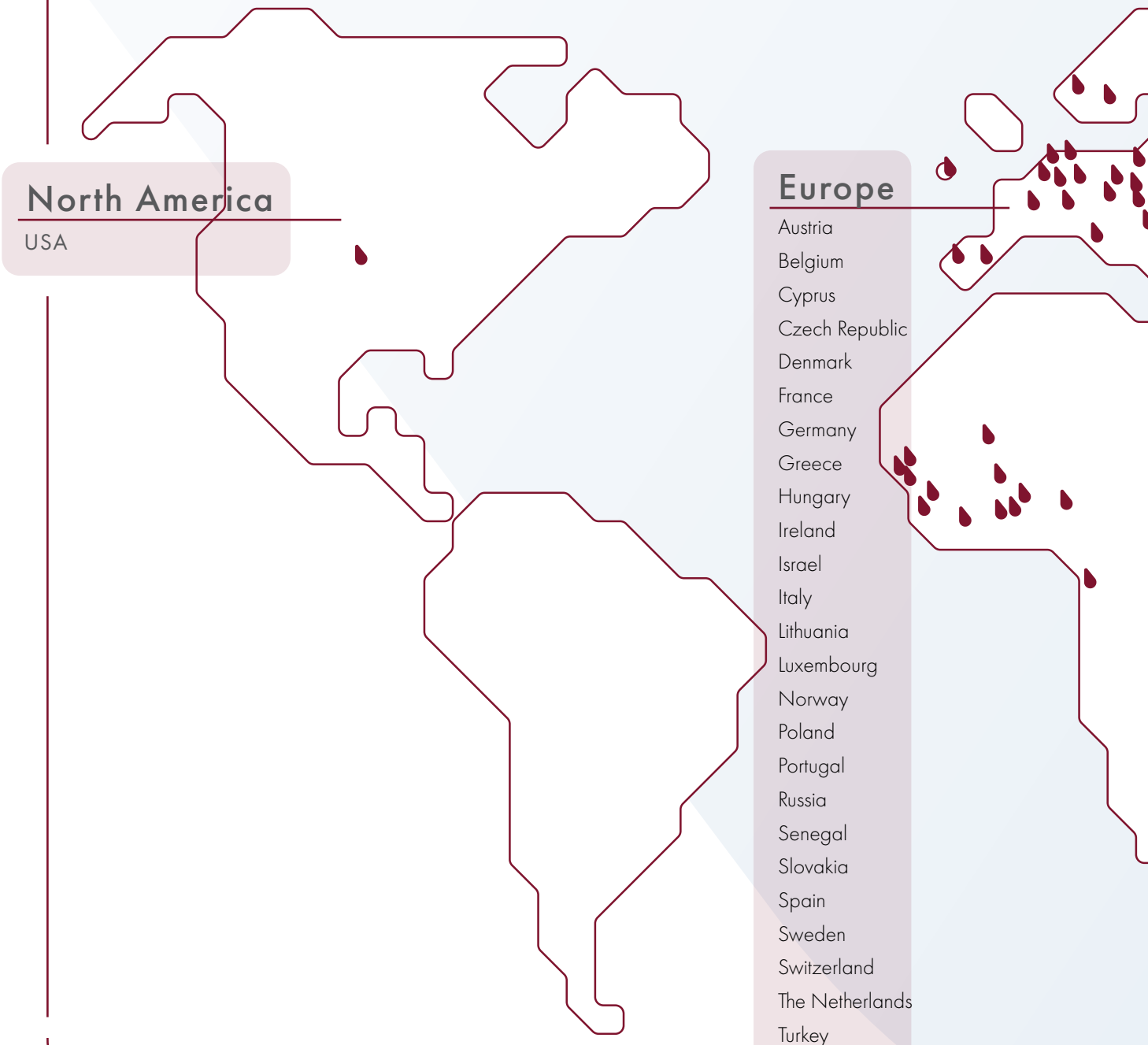
PrIMAVeRa
VACCELERATE
Inno4Vac
MVPE-CC
VAC4PM
WANETAM 3

Finalised Projects:

PfRipr5
SENET

Global partners

After more than two decades, EVI has grown into a network of more than 200 partners across the globe, brought together by our pursuit of safe, effective and affordable vaccines developed through collaboration.



North America

USA

Europe

Austria
Belgium
Cyprus
Czech Republic
Denmark
France
Germany
Greece
Hungary
Ireland
Israel
Italy
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Norway
Poland
Portugal
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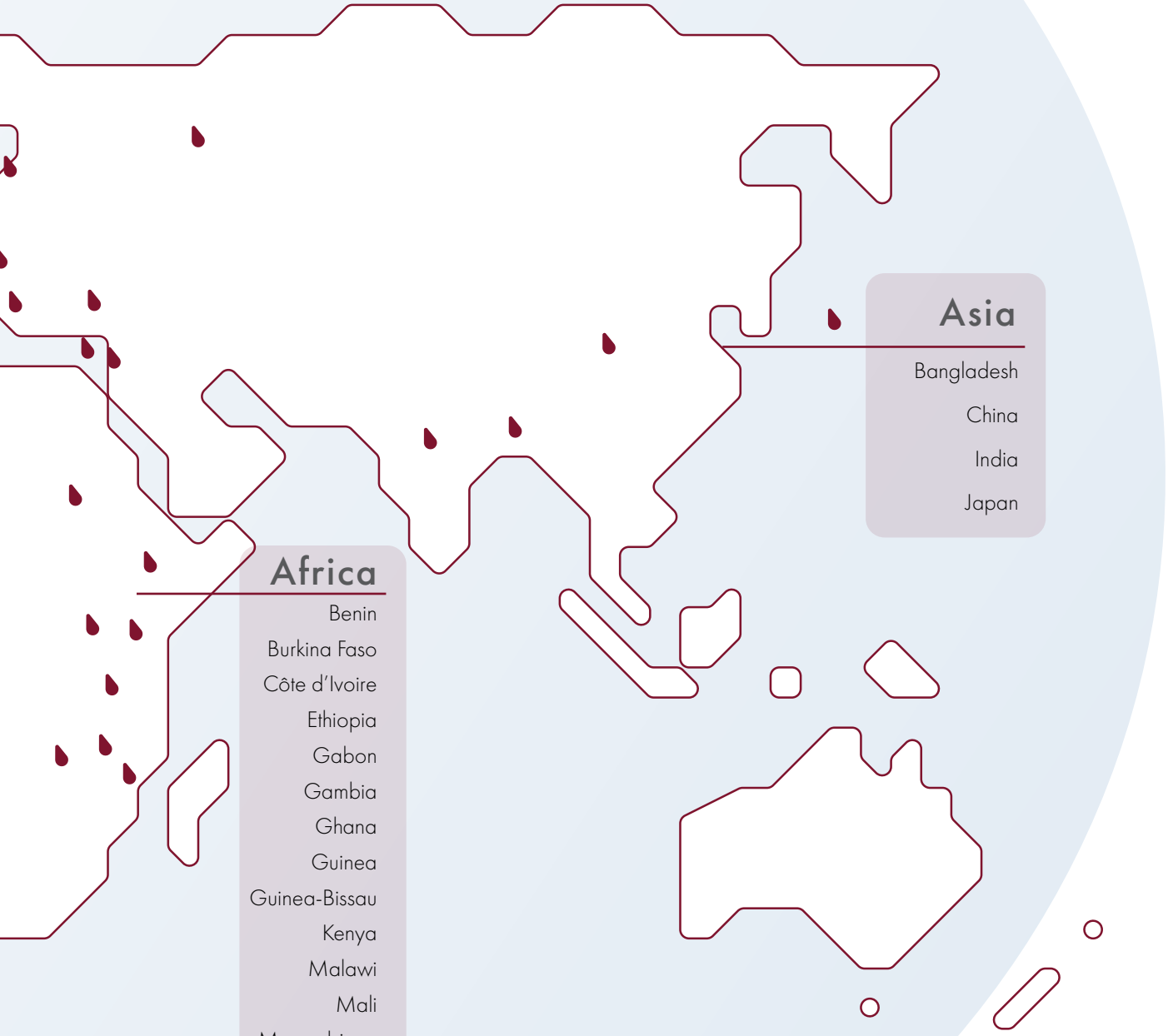


Asia

Bangladesh
China
India
Japan

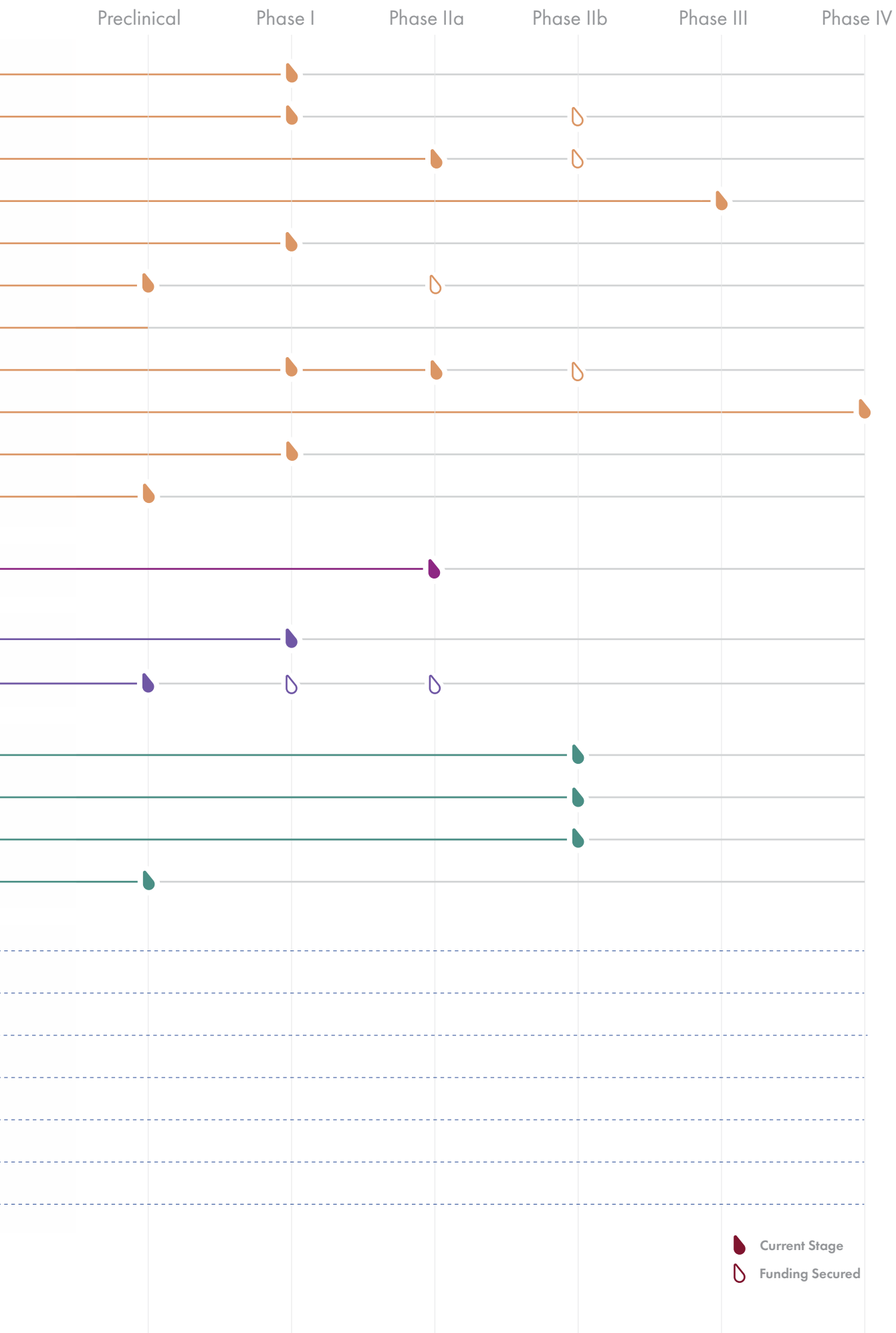
Africa

Benin
Burkina Faso
Côte d'Ivoire
Ethiopia
Gabon
Gambia
Ghana
Guinea
Guinea-Bissau
Kenya
Malawi
Mali
Mozambique
Nigeria
Senegal
Sierra Leone
Sudan
Tanzania
Togo
Uganda
Zambia

PIPELINE IN 2021

Area	Projects	Candidates
MALARIA	MMVC; MIMVaC-Africa	PfRH5
		Pfs25
		ME-TRAP
		R21
	SEmalvac2	FBK-SE36/CpG
	SEmalvac4; MIMVac-Africa	NPC-SE36/CpG
	PfRipr5	PfRipr5
	MIMVaC-Africa	PfSPZ-CVac
	MVPE-CC	RTS,S*
	VAC4PM	PRIMVAC
		PAMVAC-CLP
LEISHMANIASIS	PREV_PKDL	ChAd63-KH
DIARRHOEAL DISEASES	SHIGETECVAX	ShigETEC
	ShigaOraVax	ShigOraVax
EMERGING EPIDEMICS	VACCELERATE (COVID-19)	BNT162b2**
		mRNA-1273**
		ChAdOx-1-S**
	CEPI-Nipah	MV-Nipah
CROSS-CUTTING ACTIVITIES	TRANSVAC-DS	
	TRANSVAC2	
	VAC2VAC	
	SENET	
	PrIMAVeRa	
	Inno4Vac	
	WANETAM 3	

* WHO-recommended malaria vaccine
** Approved vaccine assessed for alternative administration schedules


Preclinical
Phase I
Phase IIa
Phase IIb
Phase III
Phase IV
Current Stage
Funding Secured

Malaria

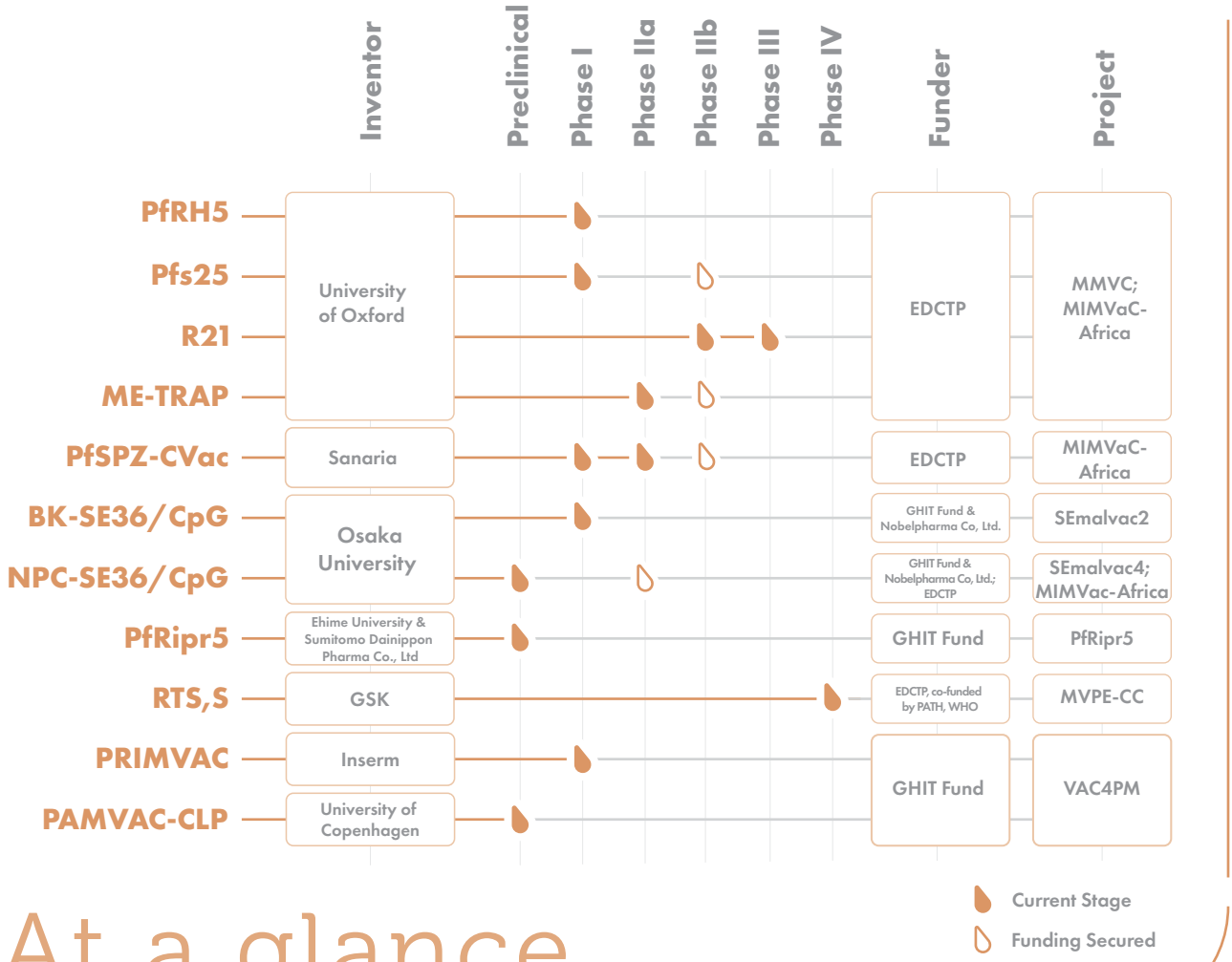
95%
of all cases
occur in Africa

80%
of all deaths occur
in children under 5

1/2
nearly half of the world's
population is at risk

627,000
malaria deaths
worldwide (in 2020)

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. Malaria is caused by five species of *Plasmodium* single-cell parasites, among which *P. falciparum* is responsible for most deaths. *P. falciparum* is the most prevalent malaria parasite in the WHO African Region, accounting for 95% of malaria cases in 2020. 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. Disruption to malaria prevention, diagnosis and treatment during the COVID-19 pandemic, led to an increase in malaria burden in most moderate and high transmission countries, especially in sub-Saharan Africa (WHO World Malaria Report 2021). 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. The world's most advanced malaria vaccine, RTS,S/AS01, was recently recommended by WHO for widespread use among children in sub-Saharan Africa and in other regions with moderate to high *P. falciparum* malaria transmission following its pilot implementation in three African countries (Malawi, Ghana, Kenya). However, RTS,S/AS01 only confers partial protection waning over some months as antibody levels rapidly decline after vaccination. Therefore, more efforts are needed for the development of a second-generation malaria vaccine with greater efficacy and longevity in target populations.

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 antigenic polymorphism, the intricate immunological interplay between the host and the parasite, heterogeneity in human immune response depending for example 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 Immunisation).

Malaria infection during pregnancy can lead to the development of placental malaria (PM), accounts for an estimated 200,000 infant deaths annually, 819,000 children with low birthweight and is predicted to contribute to nine maternal deaths per 100,000 live births. PM causes adverse pregnancy outcomes, including anaemia and hypertension in first-time pregnant women, and low birth weight due to premature delivery and foetal growth restriction, which are associated with a higher risk of foetal and neonate morbidity and mortality. An effective vaccine would be an attractive tool to control PM on its own or to complement the existing yet imperfect tools. The assessment of safety and efficacy of PM vaccines is challenged by the selection of the appropriate clinical trial design as well as the ethical and regulatory complexities.

Diverse approaches for better vaccines

Development of asexual blood-stage malaria

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 malaria, a suitable expression system and expression conditions have been identified and optimised for larger scale production. The PfRipr5 antigen has also been formulated with four different adjuvants, and rabbits or rats were immunised with the PfRipr5 protein alone or adjuvanted. Antibody titres were measured by ELISA and the functional activity of the immune response was assessed in *in vitro* growth inhibition assay. **Two formulations met the target threshold inducing ELISA titers above 105 and 60% growth inhibitory activity, allowing their selection for future clinical development.** With these promising results, the project ended mid-2021. EVI was 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 not requiring strict tertiary structures to elicit protective antibodies. A recombinant form of SERA5 N-terminal domain (SE36) was formulated with aluminium hydroxide gel to yield the BK-SE36 vaccine. The safety and immunogenicity of the BK-SE36 vaccine was demonstrated in phase I trials conducted in Japan and in Uganda and, with the involvement and under the coordination of EVI during the SEmalvac project, in 1 to 5 years old children in Burkina Faso. To improve its immunogenicity, in the SEmalvac2 project coordinated by EVI, the vaccine was further adjuvanted with CpG TLR9 ligand (BK-SE36/CpG) and tested in adults and children aged 5 to 10 years and 1 to 2 years in Burkina Faso. The data of the trial were analysed in 2021 and **results indicated that the safety profile was comparable to the control rabies vaccine. The vaccine was immunogenic, a third dose boosted the responses,** and the youngest cohort (1-2 years old children) showed the more robust response with higher anti-SE36 IgG antibody titres. Antibodies bonded to intrinsically unstructured regions confirming that strict conformational epitopes of SE36 are not required to elicit an immune response. Trends towards reduced risk for malaria incidences were seen only in the 5 to 10 years old children cohort with the other cohorts having less reported malaria cases during the study. The project will end in January 2022.

The SEmalvac4 project coordinated by EVI pursues the clinical development of the SE36 vaccine toward the preparation of a phase IIb trial with the manufacture and preclinical testing of a new vaccine batch (named NPC-SE36/CpG) and the preparation of the protocol and the selection of clinical trial sites. In 2021, new batches of vaccine antigen and CpG adjuvant have been successfully manufactured. Physicochemical and immunological properties were similar to the previous BK-SE36 vaccine product allowing to proceed to clinical use without the need of conducting general toxicity study. Phase 2b protocol synopsis and clinical site assessment questionnaire have been drafted. Two additional objectives have been added to the project. One is to assess, in collaboration with University of Copenhagen and AdaptVac, the potential of a SE36-cVLP formulation where a capsid-virus like particle (cVLP) has been added as backbone to improve immunogenicity, cross-reactivity and longevity of the induced immune response. Recombinant cVLP-SE36 have been prepared and immunogenicity studies will be carried in 2022. The second additional objective is to conduct a follow up sero-epidemiology study to assess the persistence of the anti-SE36 antibodies in the 5-10 year-old participants of the BK-SE36/CpG phase Ib trial. Protocol and study documentation have submitted to the Burkinabe national ethics committee in December 2021.

Comparing approaches

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

The MIMVaC-Africa consortium 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.

The five 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 adjuvanted with CpG. Candidate vaccines will first be tested in phase I/II trials using controlled human malaria infection (CHMI) platforms at the University Hospital Tübingen (Germany) and the Ifakara Health Institute (Tanzania) for pre-erythrocytic and blood-stage vaccine candidates, respectively (started in 2021). The most promising candidate(s) from these trials will proceed for further development into a multi-centre phase II trial conducted in healthy African children under natural malaria exposure in Burkina Faso, Gabon and Mozambique (start planned for 2023). In preparation for the phase II trial, a baseline sero-epidemiological study in the three African (phase II) trial sites will be undertaken to assess the incidence of malaria in children, to identify the most effective antimalarial drug for use in a pre-vaccination radical cure strategy, and to measure the immune responses to vaccine antigens (started in 2021).

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. During the first and second year (2020-2021) of the project clinical trial preparations and start were significantly delayed due to the COVID-19 pandemic that also affected the GMP manufacturing of vaccine lots. The trial protocol for the CHMI study in Germany was fully developed and documentation prepared for ethics and regulatory submissions (planned start during Q2/Q3 2022). In Tanzania, the CHMI trial package (protocol and informed consent) was close to finalization (planned start during Q3/Q4 2022). The phase IIb trial protocol drafting was progressing and the quality assurance stakeholders (auditors) have been selected by EVI. The baseline malaria epidemiology study was completed in Burkina Faso, while the Gabon and Mozambique sites were nearly ready to initiate their studies. The delay of clinical trials also affected networking activities led by EVI. Training capacities and needs have been mapped and the relief of COVID-19 restrictions will enhance the capacity building and networking activities in 2022.

4 in 1, multi-component vaccine

The Multi-Stage Malaria Vaccine Consortium (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. In 2021, the MMVC clinical trials continued to progress successfully, although delays were caused due to the COVID-19 pandemic. Two phase I trials were started in Tanzania: a phase Ib safety and immunogenicity assessment of the blood-stage vaccine RH5.1/Matrix-M in adults and infants (ClinicalTrials.gov Identifier: NCT04318002), and a phase Ib study assessing safety, immunogenicity and *ex vivo* efficacy of the transmission-blocking vaccine Pfs25-IMX313/Matrix-M in adults and children (ClinicalTrials.gov Identifier: NCT04271306). Three further trials, including a phase Ib multi-stage trial with RH5.2 and R21 vaccines in Matrix-M were in preparation stage. Most notably, published results of a phase II trial in Burkina Faso (ClinicalTrials.gov Identifier: NCT03896724) demonstrated high-level efficacy of **R21/Matrix-M** of 77% over 12-months of follow-up in children, making it **the first vaccine to achieve the WHO-specified 75 % efficacy goal.**

In parallel, MMVC is building 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. Capacity has been strengthened at IRSS-DRO in Burkina Faso where the direct

membrane feeding assay (DMFA) at large scale was successfully validated and is now also implemented and used at KHRC in Ghana, CERMEL in Gabon and MRTC in Mali. This will allow field efficacy testing of transmission blocking vaccines. Three African PhD and one MSc student have successfully continued their trainings and made good progress on their trial-related research activities. A second African MSc student has commenced training in 2021. Despite networking and training activities still being hampered by the pandemic in 2021, two virtual courses - one on "Vaccinology in Africa" held by UOXF (England) and one on the immunobiology of parasites (Afribop) held by KWTRP (Kenya) - allowed the training of PhD students, postdocs and other staff from the different partner sites.

The first WHO-recommended Malaria vaccine

MVPE-CC to further strengthen evidence for widespread use of RTS,S/AS01

RTS,S/AS01 (GSK) is the first malaria vaccine to receive a positive scientific opinion from the European Medicines Agency (in 2015) and being recommended by WHO (in 2021) for broad use among children in sub-Saharan Africa and in other regions with moderate to high P. falciparum malaria transmission. The ongoing vaccine implementation in Ghana, Kenya and Malawi is accompanied by an independent Malaria Vaccine Pilot Evaluation (MVPE). Embedded in MVPE, the MVPE-CC project is using case-control studies that take advantage of the community-based mortality surveillance and hospital-based disease surveillance systems that have been established as part of MVPE. The main objectives of MVPE-CC are to assess safety signals observed in the phase 3 trial of the vaccine, to estimate vaccine effectiveness in preventing malaria in children, to assess the incremental benefit of receiving a 4th vaccine dose, and to strengthen capacity in African countries to monitor the effectiveness of malaria vaccines after their introduction. **The findings of MVPE-CC will be instrumental for wider use of RTS,S/AS01 at global and country level, inform policy decisions, and will help to maximise acceptability, uptake and impact of the vaccine.**

The project has started in April 2021, a governance system has been established, study protocols, standard operating procedures, and data management tools were developed and ethical approvals successfully obtained. The data collection began between October to November 2021 - within the catchment area of 18 sentinel hospitals across the three participating countries - and progressed well until the end of the year. EVI is part of the project management team and has closely worked with KHRC as a co-lead on the project management work package of the study, also aiming to transfer capacity between EVI and KHRC in this area.

Placental Malaria

Clinical development of placental malaria vaccine candidates (VAC4PM)

PM is caused by parasite-infected red blood cells adhering to the placental receptor Chondroitin Sulfate A (CSA), and their subsequent accumulation in the placenta. Primigravid women are highly susceptible to develop severe clinical outcomes following *P. falciparum* infection. However, the prevalence of PM sharply decreases with successive pregnancies, demonstrating that protective immunity can be naturally acquired. These observations raised the hope of developing a vaccine that could reduce the incidence and severity of PM, protecting the mother and unborn child early on in pregnancy. The variant surface antigen that mediates adhesion of the infected erythrocyte to CSA (VAR2CSA) is the leading candidate for a PM vaccine.

The GHIT-funded VAC4PM project started in October 2021 and builds on the success of previous pre-clinical and first-in-human clinical studies conducted in Europe and Africa with two VAR2CSA-derived PM vaccine candidates: PAMVAC and PRIMVAC. These two PM vaccine candidates use similar but complementary approaches and consist of a single recombinant protein encompassing the placental binding region of VAR2CSA. Results from clinical trials demonstrated that **PAMVAC and PRIMVAC vaccine candidates are safe, well-tolerated and induce good homologous immune responses.** The preclinical and phase I clinical trial results for PAMVAC and PRIMVAC are highly encouraging and confirm the feasibility of developing a PM vaccine through further clinical testing. However, prior to embarking on costly, large-scale phase II clinical trials, it is essential to optimise cross-reactivity against different VAR2CSA variants and further evaluate the longevity of the immune response.

The VAC4PM project seeks to further characterise the longevity of the PRIMVAC-induced immune response, as well as the capacity of the vaccine to boost and broaden a naturally acquired immune response. Another aspect of the project is to undertake the pre-clinical development of PAMVAC-CLP. PAMVAC-CLP is an improved version of PAMVAC, where a capsid-like particle (CLP) will be added as backbone, potentially improving immunogenicity, cross-reactivity and longevity of the induced immune response.

Leishmaniasis

There are over

20

Leishmania parasite species

Poverty increases the risk for leishmaniasis

700,000 -1,000,000

new cases occur annually

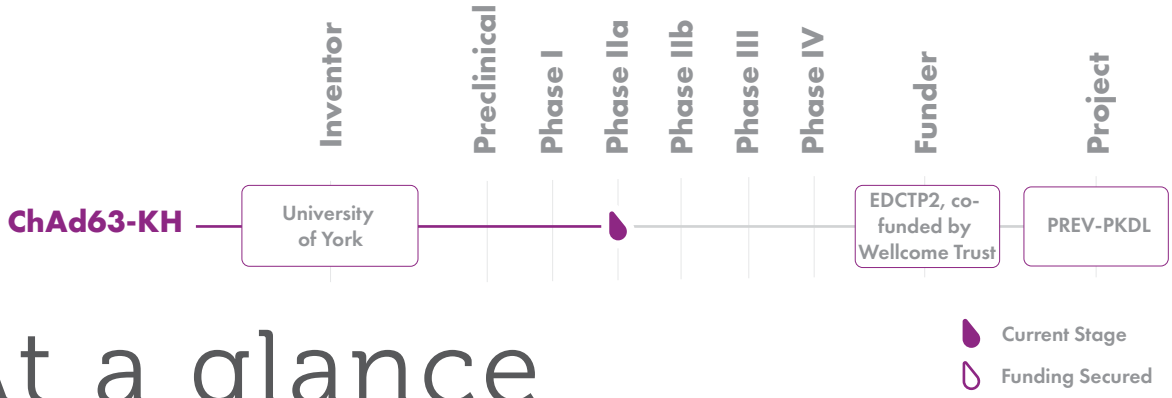
Post kala-azar dermal leishmaniasis (PKDL) appears in

5-10%

of patients that suffered from VL

No vaccine for leishmaniasis is available

Leishmaniasis vaccine candidates



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 2021, 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. 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 consequent to the COVID-19 pandemic. Nevertheless, required ethical and regulatory approvals were secured by all sites by end of 2021. 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 but was completed by end of 2021. Despite the pandemic situation, the team continued to hold a weekly virtual training session.

Diarrhoeal Diseases

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

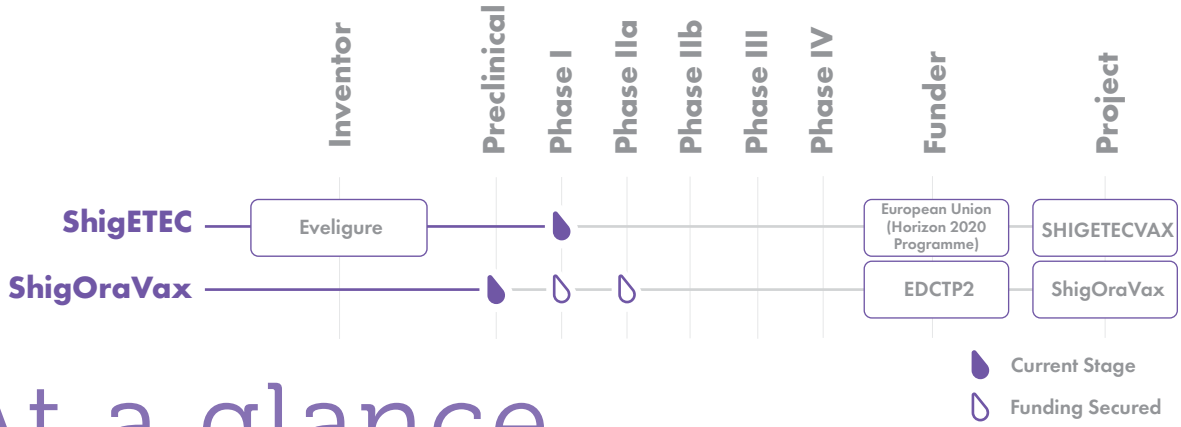
Most of cases occur in South Asia and sub-Saharan Africa regions

525,000
deaths annually

1.7 billion
cases each year

Leading cause of malnutrition in children under five

Diarrhoeal vaccine 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 regions 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 current approaches are too complex and costly to provide an adequate solution for Low- and Middle- Income Countries (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.

Stopping the cycle of diarrhoeal diseases

Early clinical development of oral vaccines

ShigOraVax

The original plans of the project were based on a tetravalent whole cell inactivated oral *Shigella* vaccine 'ShigOraVax', containing *Shigella flexneri* serotypes 2a, 3a, and 6, as well as *Shigella sonnei*. It was planned to develop the proposed *Shigella* vaccine candidate up to mid clinical stage. Specific objectives of this project included (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. In the year 2021, the original plans have changed as the vaccine was not made available and a new candidate vaccine was identified to replace the original candidate. Now it is intended to conduct with this new vaccine candidate a phase Ia/b clinical trial in European and African adults followed by an age de-escalating phase IIa trial in Burkina Faso. **During the year 2021, specific epidemiologic data were 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 will be completed in 2022. The results of this study will be used for sample size calculation of future efficacy trials.

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, 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.

In 2021, the first-in-human Phase Ia clinical trial to assess safety and tolerability of ShigETEC was conducted at the University of Debrecen, Hungary. The study was conducted in two stages; stage 1 as a single, dose escalating study and stage 2 as a multi-dose study using the optimal dose defined in stage 1. Taken together, the **safety and immunogenicity results confirmed the selection of a safe and likely effective dose and vaccination schedule to use in further clinical development of ShigETEC**, including the Phase Ib study in Bangladesh to start as soon as the manufacture of a new clinical batch is completed. The sero-epidemiology study was conducted in Bangladesh where samples were collected at study-defined timelines. Sample processing and analyses have been initiated and will be completed during the 2nd reporting period.

Overall, the SHIGETECVAX project has progressed according to the objectives and tasks despite the impact of the COVID-19 pandemic leading to delays in some of the activities.

EVI is coordinating the project and overseeing the communication and ethics related activities.

Emerging infectious diseases

COVID-19 VIRUS KEY FIGURES

5.44 million
deaths confirmed in 2021

36.7 million
cases in 2021

5%
of people infected develop critical symptoms

Vaccines were developed in record time

NIPAH VIRUS KEY FIGURES

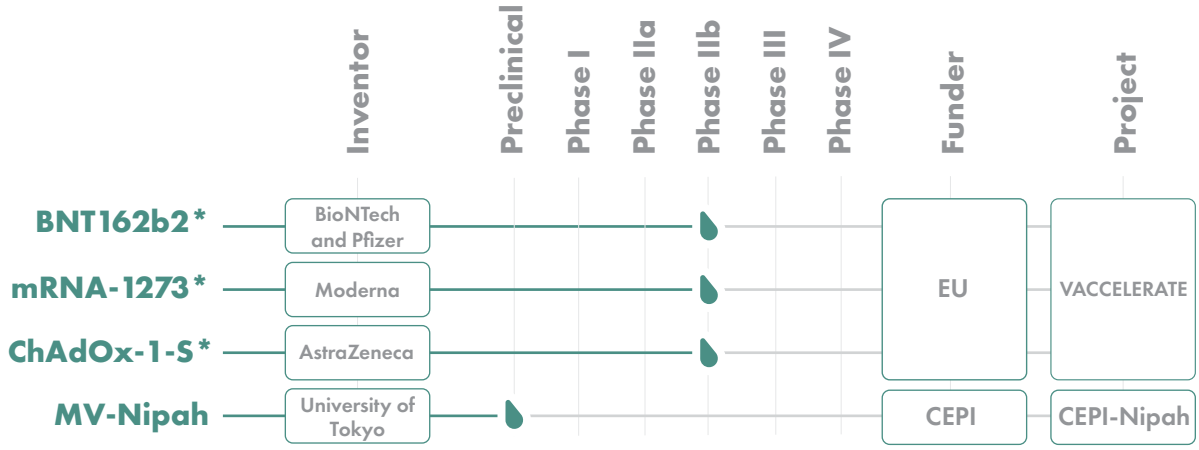
2 Billion
people at risk

40-75%
estimated case fatality rate

Nipah virus represents a high pandemic threat

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

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, is difficult to predict.
WHO provides a list of diseases and pathogens that are prioritised for R&D in public health emergency contexts. At present, there are 10 priority diseases: COVID-19, Crimean-Congo haemorrhagic fever, Ebola virus disease and Marburg virus disease, Lassa fever, Middle East respiratory syndrome coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS), Nipah and henipaviral diseases, Rift Valley fever, Zika and "Disease X". EVI has focused its efforts on COVID-19, Nipah and Zika virus.

Coronavirus disease (COVID-19) has reminded the world of the impact that emerging and pandemic-prone pathogens can have in society. COVID-19 is a highly contagious infectious disease caused by the SARS-CoV-2 virus and first identified in 2019. The virus spreads through small liquid particles when infected person breathes, coughs, sneezes or speaks. COVID-19 affects different people in different ways. Severe symptoms include shortness of breath, loss of speech or mobility, or confusion, respiratory failure, shock, and multiorgan dysfunction. Over ten variants of the virus have been identified, reflecting the ability of the virus to mutate and adapt. Although vaccines have been shown to reduce COVID-19 symptoms and serious illness, their ability to prevent coronavirus transmission is unclear.

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

Although, safe and effective vaccines against COVID-19 were developed and made available in record time, major challenges remain when tackling the pandemic. **The current vaccines are remarkably effective protecting against severe disease, however their impact on preventing the spread of the disease is limited.** The approved vaccines efficacy against new COVID-19 variants is also variable, so a second generation of vaccines that address cross-variant protection is urgently required.

Moreover, additional clinical trials are critical to further understand how specific population groups (*e.g.*, elderly, immunocompromised patients, children, infants, pregnant and lactating people) respond to the currently approved vaccines, as well as to optimise and test administration schedules.

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

Tackling (re)emerging diseases and outbreaks

VACCELERATE

VACCELERATE is a new European Union's Horizon 2020 funded project that aims at becoming the single entry-point for phase 2 & 3 vaccine trials for COVID-19 vaccines in europe. One of VACCELERATE's main goals is to accelerate and increase the quality of vaccine development during pandemics by establishing a pan-European clinical trial platform, enhancing capacity mapping and building on clinical trial sites, providing easy access to all citizens-volunteers including underserved minorities and interconnect them with the trial sites, as well as privileged access to vaccine researchers. Beyond the COVID-19 pandemic, it will be an established pandemic preparedness network, ready to face emerging future pandemics, as well as a pivot in Europe's capacity to develop vaccines.

During 2021, the registry for clinical trial volunteers has started to be set up across different European countries. It will create and provide **the first transnational registry of volunteers for participation in future trials, a standardised way of collecting data, as well as foster community engagement, enhance vaccine trial equity and diversity in Europe.** The volunteer registry will accelerate the recruitment of participants for COVID-19 vaccination trials, thereby avoiding unnecessary delay. In 2021, VACCELERATE started the preparations for three phase II clinical trials to further test the approved mRNA vaccines and optimise their administration to young children, elderly as well as the general population.

EVI co-leads Work Package 8 on Immune Monitoring, which aims to identify a core set of immune assays to be validated and used across the VACCELERATE network in order to ensure standardised testing of all samples collected in the clinical trials. In 2021, high priority assays for measuring both the humoral immune response and the cellular immune response were identified within VACCELERATE and standardised protocols and associated standard operating procedures (SOP's) were prepared and made available to the scientific community at large.

EVI is also deeply involved in the Communication and Outreach activities. In this context, EVI developed an 'Inventory and gap analysis report of existing public outreach material' to identify and tackle existing gaps in public information material on COVID-19 vaccine trials in Europe, with special emphasis on identifying informational, promotional and educational material for underserved groups. This information is freely available in EVI website, and a publication is under preparation.

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 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 2021, a confirmation run batch of the vaccine has been successfully produced using the established process and 6 months and in use stabilities studies have been completed. The vaccine batch has been used in proof-of-concept study to confirm efficacy of the vaccine candidate in the hamster model.

ZIKAVAX

Since 2016, EVI has been involved in the development of a Zika vaccine candidate (MV-ZIKV), a recombinant measles-based (MV) viral vectored vaccine for prophylaxis of Zika virus infection that was discovered by the Austrian biotech company Themis. The EVI-led project, ZIKAVAX, aimed to demonstrate safety and immunogenicity of MV-ZIKV in adult volunteers in a phase Ia clinical trial. During the project, both mouse and non-human primate (NHP) challenge models were further standardised, refined, and made available to researchers in the field, which will be highly relevant to evaluate Zika virus vaccines, treatments, or to better understand immune responses, due to the lack of relevant animal models. Following promising results in pre-clinical animal models, the selected vaccine candidate, **MV-ZIKA-RSP, was shown to be well tolerated in a phase I clinical trial in healthy adults** and to induce an immune responses that provides confidence that a vaccine against Zika virus disease can be developed

Cross-cutting activities

EVI coordinates and promotes a number of projects that address disease-overarching issues that are transversal to vaccine R&D in general. These collaborative endeavours between industry partners and other key actors in the R&D ecosystem, such as academic institutions, small and medium enterprises, regulatory authorities and others, 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
Timeline: 01 May 2017- 30 April 2023
Funder: European Union (Horizon 2020 Programme)

TRANSVAC2, European Vaccine Research and Development Infrastructure project, is a joint effort of leading European research groups and SMEs 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.

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 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 2021, TRANSVAC2 launched three calls for applications for TNA services, including a continued effort to support COVID-19 vaccine R&D. **A total of 11 services were awarded to eight research groups from SMEs and public institutions, to help speed-up the vaccines development for Helicobacter pylori, Influenza, Poliomyelitis, Tuberculosis and Chlamydia, Hepatitis C and COVID-19.**

Moreover, **three calls for vaccinology training modules were launched as well, receiving over 100 applications.** Six training modules took place in the last year, with nearly 40 participants attending courses on Clinical vaccine development and biomanufacturing, Human and veterinary vaccinology, Process development and scale-up of viral and protein vaccines, GMP requirements and assay development and validation.

As part of the JRA, methods and platforms developed in various JRA programs were used to support numerous vaccine research projects. Utilised JRA-derived services included adjuvant profiling services, cross-linking mass spectrometry techniques, and platforms for cytokine/chemokine analysis, transcriptomics/ next-generation sequencing, and computational modelling.

To ensure the long-term sustainability of the infrastructure, TRANSVAC2 Board of Stakeholders, including representatives of industry associations, other research infrastructures/networks and biotechnology clusters, continued to engage in laying the groundwork for a permanent TRANSVAC2 infrastructure. Moreover, to strengthen collaboration across European initiatives, TRANSVAC2 established a memorandum of understanding with BactiVac, the Bacterial Vaccines Network.

A workshop on harmonisation of animal studies across different species was held, as an open forum, led by a group of ten invited expert panel members, to discuss the needs and challenges in harmonisation of animal model study design (incl. COVID-19, Influenza and Tuberculosis), immunological assays across different animal species as well as the needs for specific reference standards and reagents.

TRANSVAC-DS

Target: Vaccine R&D infrastructure
Timeline: 01 June 2020- 30 November 2022
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

In order to explore different options for the potential establishment of a sustainable vaccine infrastructure, four different business model options for its overall design were developed and assessed. One of these models that offers the advantage of tapping two different streams of revenues was subsequently selected for the further infrastructure design. A detailed five-year business plan including an implementation plan for this infrastructure model are currently being developed. The ultimate positioning of the vaccine infrastructure will be informed by a gaps and needs assessment of current vaccine R&D that was previously performed by the project partners and will allow to align the infrastructure as close as possible to the needs of the user community.

Vaccine batch to vaccine batch comparison by consistency testing

VAC2VAC

Target: Batch to Batch Control Testing
Timeline: 01 March 2016- 28 February 2022
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 nonanimal 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

With a total duration of 6 years, the project has allowed the validation of two *in vitro* assays the monocyte activation test (MAT) and the Tetanus Neurotoxin (TeNT) LC-MS/MS assay.

The MAT has been transferred to industry, validated, approved by the competent regulatory authorities and implemented in industry as a replacement of the Rabbit Pyrogen Test. A proposal to revise Ph. Eur. monograph 1375 on tick-borne encephalitis virus (TBEV) by replacing the RPT with the MAT was submitted, acknowledged and included in the more extensive revision of all monographs to replace the RPT. Also, novel biomarkers for TBEV vaccine potency testing were identified, including a link between type I interferon expression upon stimulation of human PBMC with inactivated TBEV and Ig production by B cells (doi.org/10.1371/journal.ppat.1009505).

The TeNT LC-MS/MS is an antibody free method that is able to identify and quantify the amount of TeNT present in the bacterial medium during the different production time points.

In addition, seven ELISA assays have been qualified. Among them, the Diphtheria and Tetanus, and TBEV ELISAs have been transferred to the industry partners for further product-specific optimisation and validation. **Furthermore, 11 *in vitro* assays have reached proof of principle, which have been transferred to industry partners (to be applied to four veterinary vaccines and three human vaccines).**

Overall, the project has produced 21 peer-reviewed open access publications so far. More publications are expected beyond the end of the project.

VAC2VAC has not only been very successful in the development of new assays. During the VAC2VAC project, over 13 young scientists were able to further their education and refine their skills through graduate degree and internships at consortium members.

Implementation of the sustainability plan: Monoclonal antibodies available at the NIBSC catalogue

After being identified as critical reagents, an agreement has been made within the VAC2VAC consortium allowing for VAC2VAC partner NIBSC to be entrusted to manage the handling, distribution, and future production of monoclonal antibodies needed in DTaP ELISA and Luminex assays developed in VAC2VAC. Depositor agreements between NIBSC and other owners of the monoclonal antibodies (GSK, Sanofi, and Intravacc B.V) have been signed whereby depositors agree to supply the material and hybridoma information to NIBSC. NIBSC will make the monoclonal antibodies available to the public subject to a handling fee to cover operational costs and future replacement of antibody batches.

Work on regulatory acceptance of the consistency approach

Awareness of VAC2VAC is quickly growing due to a coordinated approach with global organisations, the Bangkok meeting (doi.org/10.1016/j.biologicals.2020.07.010) and participation at congresses and workshops. Stakeholders' webinar meetings led to wide outreach to stakeholders and regulatory authorities (NC3Rs, WHO, EDQM, USDA, FDA, OIE, ICH/VICH and national regulatory authorities from 22 countries). A significant outcome was the acceptance of the need for global harmonisation of *in vitro* batch control in a consistency approach.

West African Network of Excellence for Tuberculosis, AIDS and Malaria

WANETAM 3

Target: Capacity Building for Malaria, Tuberculosis and AIDS
Timeline: 01 August 2021 - 31 July 2024
Funder: The European & Developing Countries Clinical Trials Partnership (EDCTP)

The West Africa Network of Excellence for TB, AIDS, and Malaria (WANETAM) has evolved and developed from the first EDCTP grant in 2009-2013 to the consolidation phase in 2016-2019 (WANETAM-2). The overall goal of WANETAM is to strengthen the WANETAM network through building of regional, national, institutional, and individual capacities to conduct clinical trials in line with the International Conference on Harmonization guidelines for Good Clinical Practice (ICH-GCP).

WANETAM-3 will build on the activities of the disease-defined work packages (WPs): TB, Malaria, HIV, Neglected Tropical Diseases, Emerging Infections response and preparedness, and the inclusion of the Cross-Cutting Trainings to strengthen capacity of individuals in specialised skills needed in clinical research and the capacity of supporting infrastructure.

The WPs will consolidate the project's mission to achieve sustainable capacity and multi-institutional collaboration in clinical research through activities that premise on: i) Strategic project-based training to build research leadership; ii) Hands-on operational and clinical studies that inform clinical trial plans and prevention; iii) Resource and platform infrastructure development; iv) Surveillance to build evidence-base for clinical trials; v) Diagnosis to support intervention; and vi) Building on quality assurance and expanding laboratory accreditation. Each WP is led by one of the institutions with advanced capabilities in that disease area of research. The rest of the members in a WP area are the sister sites. The competency trainings as well as the cross-cutting activities are built around the gaps existing in the sister sites. EVI is involved in WP6: Cross-Cutting Training and Platform Building.

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

During the final year of the SENET project, the partners continued their efforts to engage with researchers, policy makers and intermediaries from both European and Chinese side. Three more stakeholder meetings were organised: one further policy dialogue, one expert meeting, and one multi-stakeholder meeting. In parallel to these meetings, a final consultation through interviews with selected stakeholders and an online survey were conducted to complement the information so far collected.

The results and major findings of SENET were presented and discussed during the Sino-European Health Collaboration Week on the 29 November 2021 that was organised by the partners. **Major final output of SENET was a roadmap including recommendations and action plan published by the consortium at the end of the project.**

Predicting the Impact of Monoclonal Antibodies & Vaccines on Antimicrobial Resistance

PrIMAVeRa

Target: Antimicrobial Resistance
Timeline: 01 November 2021 to 31 October 2026
Funder: Innovative Medicines Initiative 2 (IMI2) and European and Federation of Pharmaceutical Industries and Associations (EFPIA)

PrIMAVeRa (Predicting the Impact of Monoclonal Antibodies & Vaccines on Antimicrobial Resistance) is an ambitious project with the goal of developing an open-source, web-based platform combining mathematical models with a comprehensive epidemiological repository (*i.e.*, with data referring to health and economic outcomes). This platform aims to enable policymakers to reach data-driven decisions regarding the prioritisation of specific vaccines and monoclonal antibodies (mAbs), informing the strategic allocation of limited resources.

Key achievements

Since the start of the project on 1 November 2021, the PrIMAVeRa consortium successfully completed its main deliverable for the first two months. The kick-off meeting took place on 25 November 2021 and drew approximately 56 attendees from 19 partner organisations. The meeting consisted of 16 Agenda items in 3 sessions, which covered an introduction of partners, the vision of the project, a scientific overview of PrIMAVeRa, overviews of the different work packages and their activities for the first six months of the project, and three special presentations from individuals outside the consortium. Dr Tek-Ang Lim gave a presentation regarding the IMI perspective and the Initiative's expectations of the consortium throughout the project lifetime, Prof Anders Karlén gave an overview of the AMR Accelerator and COMBINE, which will collaborate with and aid the PrIMAVeRa consortium, and Dr Mateusz Hasso-Agopsowicz of the World Health Organisation gave a keynote lecture articulating the role of vaccines in preventing AMR and highlighting gaps upon which the PrIMAVeRa project could potentially focus. Internal meetings amongst work packages and steering committee meetings have been conducted to plan the way forward.

Innovations to accelerate vaccine development and manufacture

Inno4Vac

Target: Innovations for Vaccine R&D
Timeline: 01 September 2021 to 28 February 2027
Funder: Innovative Medicines Initiative 2 (IMI2) and European and Federation of Pharmaceutical Industries and Associations (EFPIA)

Inno4Vac is a public-private partnership that addresses scientific bottlenecks in vaccine development.

It proposes to develop predictive biological and mathematical models of vaccine performance and bio-manufacturing. Artificial intelligence combined with big data and computational modelling will be used to build an open-access and cloud-based platform for *in silico* vaccine efficacy assessment and development. Controlled human infection models and cell-based human *in vitro* 3D models will be developed to enable early evaluation of vaccine efficacy and prediction of immune protection.

Finally, for vaccine bio-manufacturing the goal is to establish an open source *in silico* simulation platform for guiding the production of vaccine candidates and associated stability testing.

Key achievements

The Inno4vac kick-off meeting was organised and held virtually on 28 and 29 September 2021 and drew more than 150 attendees. The meeting presented an excellent opportunity to align ideas and to strengthen interpersonal relationships within the consortium, which is essential to ensure effective communication and the success of the project. Inno4Vac website was launched on 30 November 2021. The Inno4Vac project strategy involves dissemination of information–guaranteeing optimal sharing of generated knowledge with target audiences and the general public. The design and technical implementation of the website were carried out by the Communications and Management team at European Vaccine Initiative (EVI) in alignment with Consortium partners' input.

The open call for proposals standard operating procedure (SOP) was approved 14 January 2022, which is critical to ensure, during the course of Inno4Vac project, there is the possibility to access to state-of-the-art technologies that may become available after the start of the project and could support the development of new platforms and tools and/or to have access to expertise that is not present in the consortium. **Open calls for proposals will enable new partners to join the consortium for carrying out additional activities on top of those already planned, increasing the chances of a successful project outcome**.

The Data Management Plan (DMP) was finalised and approved on 28 February 2022. The DMP describes the data management life cycle for the data to be collected, processed and/or generated by the Inno4Vac project, with the aim to make the research data findable, accessible, interoperable, and reusable (FAIR). It will also specify how it will be curated and preserved, with details such as ethical, privacy, and security issues.

Subtopic 2 CHIMICHURRI consortium members have attended two scientific workshops organised and held on 24-25 November 2021 and 25 January 2022 for Flu and RSV-B strain selection, and Immunoassays with active participants bringing their expertise together to align on the best approach and requirements for two out of three challenge strain selection activities, as well as immunoassays harmonisation and development.

TRAINING

Training at EVI

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 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).

Since 2015, EVI offers exceptional emerging researchers and key members of clinical trial research teams from LMICs first-hand experience working with vaccine research projects, as a hosting institution of the EDCTP Clinical Research and Development Fellowship Scheme and the WHO/TDR Special Programme on Tropical Diseases Research.

Fellows typically spend a year working as a full-time, paid fellow programme to senior EVI Project Managers in an experienced multi-cultural environment.

Since the beginning of EVI's involvement in this fellowship programme, nine researchers from sub-Saharan Africa and one from Latin America with different educational backgrounds and working experiences have been hosted by EVI. In July 2021, EVI hosted three new fellows: Dr Japhet Anim, former Clinical Trials Coordinator from Kintampo Health Research Centre (KHRC), Ghana; Dr Moses Phiri, Lecturer and Researcher at the University of Zambia's School of Medicine, in the Department of Pathology and Microbiology, Zambia; and Dr Amanda Wanyana, Medical Doctor/Researcher at the Uganda Virus Research Institute- International AIDS Vaccine Initiative (UVRI-IAVI), Uganda. Below are their reflections on their fellowship experience and the program's ongoing support throughout their clinical trials and project management skill development journeys.

Moreover, this year EVI welcomed Mandeep Kaur, Heidelberg University M.A health and society in South Asia student, as our first trainee.

EDCTP/TDR Fellows' experience at EVI

Japhet Anim

"The training experience gained at EVI can be described as awesome, unparalleled, and especially well-tailored at this stage of my career. My supervisors and mentors took a keen interest in my training, providing me with guidance and encouraging personal responsibility and creativity, which ensured the achievement of fellowship-related deliverables and my overall study objectives.

At EVI, I participated in project management activities such tracking study progress, tracking, and structuring deliverable reports and the development of study related and communication material under the supervision of experienced project leaders. I had the opportunity to participate in proposal writing and grant preparation.

EVI is partnering with my home organisation, KHRC, in some of the projects to which I was allocated. This ensured continuous interaction with my home organisation during the fellowship and will foster the link with EVI even beyond the fellowship timelines. I participated in a series of seminars and courses either from EVI internal resources or from external experts and partners. These included courses on project management, GMP, grant writing and vaccinology, among others.

The skills and competencies gained in project management and the practical aspects of managing vaccine development through the fellowship at EVI will be very useful in my career development and impactful in my home organisation. Thanks to EVI, EDCTP2/TDR, and KHRC for this training opportunity."

Masauso Moses Phiri

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

I had hands-on experience in managing several vaccine research projects, such as developing a vaccine candidate for Shigella and *E. coli* (ETEC), investigating a new asexual blood-stage malaria vaccine candidate, COVID-19 related clinical trial work, and innovation for vaccine development projects. These projects enabled me to learn how to work collaboratively with different partners in the consortium while achieving the same objectives. I was also part of the proposal development and grant writing for Grant Calls. I worked closely with other scientists and the Head of Business Development at EVI to develop and submit these proposals. Through the TRANSVAC2 project, managed by EVI, I had the opportunity to take several vaccine-related trainings, such as Requirement for GMP production of vaccines, Process Development and scale-up of protein vaccines, and Statistics of Vaccinology. We also had several seminars and training relating to project management and vaccinology.

The fellowship at EVI has enabled me to create new networks, which could go a long way in collaborative research. I also learnt how to better apply for funding for projects and to better manage projects where I am the principal investigator. The staff at EVI were great in making me feel welcome and part of the team."

Training experience at EVI

Amanda Wanyana

"It goes without saying that my one-year fellowship at EVI has been one of the most unforgettable experiences on my career journey. Traveling to a new continent and adjusting to a new culture and work ethic presented more questions than answers. Surprisingly, **this transition happened relatively fast and smoothly for me, all thanks to a very warm, dynamic, and experienced multi-cultural team that I found at EVI.**

Coming from a background that was mostly clinical, the learning curve in terms of professional development has been very steep. **I have been exposed to different aspects of vaccine development and project management within reputable international consortia working on grand scientific innovations.**

The hands-on training approach has been very efficient and productive in broadening my skill set by presenting new challenges daily. Networking with people from diverse professional and cultural backgrounds has been very enriching. I am forever indebted to the EVI administration for availing the opportunity as a host institution and to the WHO/TDR Special Programme on Tropical Diseases Research for making this research fellowship possible through funding. This experience has opened my mind up to new possibilities. I look forward to passing on new knowledge and skills to my Ugandan colleagues at my home institution, UVRI-IAVI."

Mandeep Kaur

"Since starting my traineeship in EVI's communications team in May 2021, I have tremendously grown professionally. From writing Twitter and LinkedIn communications to writing large final reports, **I experienced many different aspects of the responsibilities in the communications team.**

I got the opportunity to work on the VACCELERATE project, where I got a chance to analyse and collect public outreach material from all European countries on COVID-19 public health and COVID-19 clinical trial information and perform a gap analysis. Along with this, I had the opportunity to help create a database of the existing online information in different languages and then compile the results into a report, combining them with recommendations to reach underserved groups.

I was also involved in the TRANSVAC project, for which I created communications for LinkedIn and Twitter and learned social media communication strategies. I also got an opportunity to assist in the **coordination and administration of international applications** for the TRANSVAC2 training modules.

I would like to thank Prof. Ole Oleson and Dr Irina Meln for giving me the opportunity to be part of EVI. I would like to thank my mentors, Catarina Luís, and Romina Di Marzo, for making me feel welcome in the team from the start and for making my learning journey enjoyable and easy. Thank you so much for your wisdom and experience. They always encouraged and appreciated me to give my best and let me be part of an amazing team. Under their guidance, I have learned a lot and I look forward to taking the next steps in my career."

Financial performance report 2021

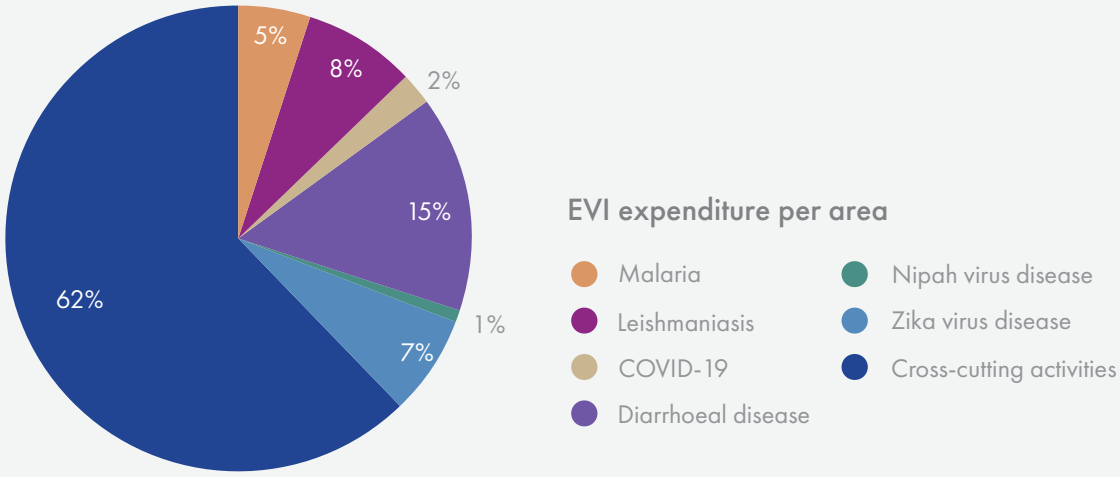
The year 2021 has, from a financial perspective, consolidated EVI. The year brought more funding to EVI in terms of more cross-cutting activities and participation in a COVID-19 follow-up project.

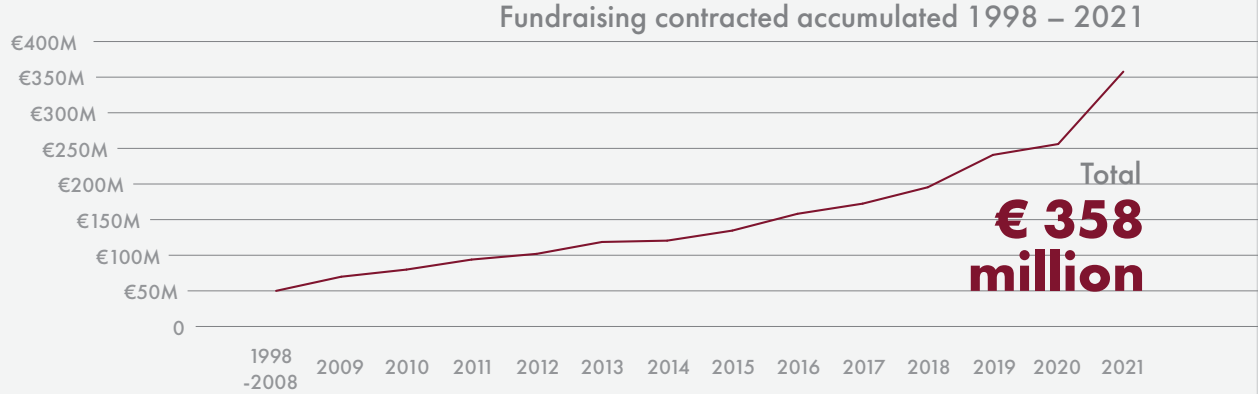
EVI managed to reduce last years' deficit (although not unusual for a non-profit). It's continually important for EVI to show a strong solvency and equity position for the organisation. Both positions were strengthened in 2021. EVI's financially strong position might be compromised by the on-going conflict in Ukraine, economic sanctions, and inflation hikes. 2022 will might be challenging year to achieve all the contractual commitments planned by utilising the normal costs/quality procurement model of EVI. In 2021 cross-cutting activities represented 62% of expenditure followed by diarrhoeal diseases and malaria. COVID-19 represented 2% as stand-alone funding under the project VACCELERATE

Fundraising

EVI's project portfolio, as of 31 December 2021, consisted of 19 active projects (including a project granted to start in 2022) in the broad field of translational vaccine R&D, transnational access services, capacity building and, of course, vaccine development. The total value of all active grants including co-funding/in-kind contributions amounted to € 203 million of which € 19.7 million are for EVI secretariat. 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.

Several new projects were initiated during 2021, including Inno4Vac, one of the largest projects ever funded by IMI2 in the vaccine space and is a joint industrial project with several pharmaceutical companies. Another public-private collaborative project called PrIMAVeRa also kicked-off in 2021





Statement of comprehensive income for the year as of 31 December 2021

	EUR 2021	EUR 2020
Income		
Turnover from sales	**26,458.22**	**16,187.51**
Public institutional funding:		
GHIT & Governmental & international organisations	394,516.15	1,778,297.94
European Union & IMI grants	5,635,180.67	4,659,459.69
EDCTP	2,130,983.12	1,132,387.77
Total public institutional funding	**8,160,679.94**	**7,570,145.40**
Other income net	738,389.37	128,506.94
Total income	**8,925,527.53**	**7,714,839.85**
Social mission expenditure		
Research & vaccine development expenditure:		
Malaria	464,008.97	1,762,419.96
Leishmaniasis	676,323.13	897,300.85
Covid19	138,920.11	0.00
Diarrhoeal diseases	1,346,660.92	147,660.63
Nipah virus disease	112,434.62	154,880.42
Zika virus disease	636,073.38	641,819.92
Cross-Cutting activities	5,489,124.94	3,966,768.65
Advocacy & communications expenses	11.127,24	19,781.60
Total social mission expenditure	**8,874,673,31**	**7,590,632.03**
Supportive social mission expenditure		
Training, quality assurance and project development	1,621.06	5,614.38
Fundraising	9,117.50	34,744.30
Governance	10,607.79	39,672.65
Total supportive social mission expenditure	**21,346.35**	**80,031.33**
Non-social mission expenditure		
General executive administration	62.829,31	126,463.43
Total non-social mission expenditure	**62.829,31**	**126,463.43**
Total expenditure	**8.958.848,97**	**7,797,126.79**
Operating surplus / (deficit)	(33.321,44)	(82,286.94)

Statement of financial position as of 31 December 2021

	EUR 2021	EUR 2020
Current assets		
Cash and cash equivalents:		
Cash and banks - key accounts	5,476,114.49	3,267,887.45
Total cash and cash equivalents	5,476,114.49	3,267,887.45
Current accounts and receivables:		
Other receivables	7,915.73	7,343.87
Financial and debtor receivables	2,458.22	3,375.00
Total current accounts and receivables	**10,373.95**	**10,718.87**
Total current assets	**5,486,488.44**	**3,278,606.32**
Non-current assets		
Tangible fixed assets, net	5,474.00	6,715.00
Long term securities	1,000,000.00	1,000,000.00
Total non-current assets	**1,005,474.00**	**1,006,715.00**
Total assets	**6,491,962.44**	**4,285,321.32**
Current liabilities		
Creditors	106,119.46	98,500.57
Accrued expenses	313,899.77	234,406.01
Other liabilities	29,974.44	38,973.62
Deferred income	4,052,058.93	1,890,209.84
Total current liabilities	**4,502,052.60**	**2,262,090.04**
Equity of organisation		
Operating result	(33,321.44)	(82,286.94)
Operating funds	2,023,231.28	2,105,518.22
Total equity of the organisation	**1,989,909.84**	**2,023,231.28**
Total equity and liabilities	**6,491,962.44**	**4,285,321.32**

For more detailed information about EVI's financial statements and related indicators the 2021, EVI Financial and Performance Report is available upon request (www.euvaccine.eu/contact-us).

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EDCTP WHO/TDR Fellow

Japhet Anim
TDR Fellow

Mandeep Kaur
Trainee

Acknowledgments

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- All4Cloud
- Austrian Federal Ministry of Science and Research, Austria
- Boehringer Ingelheim Animal Health, France, previously known Merial Boehringer Ingelheim (BI), Germany
- Centre National de la Recherche Scientifique (CNRS), France
- Centre National de Recherche et de Formation sur le Paludisme (CNRFP), Burkina Faso
- Co-funding was kindly provided by the following organisations:
- Coalition for Epidemic Preparedness Innovations (CEPI), Norway
- Danida, Denmark's development cooperation, Denmark
- Danish National Advanced Technology Foundation, 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, Belgium
- Federal Ministry of Education and Research (BMBF) through KfW, Germany
- Global Health Innovative Technologies (GHIT) Fund, Japan
- GSK Biologicals (GSKBio), Belgium
- Innovative Medicines Initiative (IMI), Belgium
- Inserm, France
- Institut National de la Transfusion Sanguine (INTS), France
- Intervet International B.V., also known as MSD Animal Health, Netherlands
- Minor donations and support though marketing and communications
- NIH – NIAID, United States of America
- Nobelpharma Co., Ltd., Japan
- Research Institute for Microbial Diseases (RIMD), Japan
- Sanofi Pasteur, France
- SAP
- Sumitomo Dainippon Pharma Co., Ltd, Japan
- Swedish Ministry of Foreign Affairs, Swedish International Development Cooperation Agency (Sida), Sweden
- Takeda Pharmaceuticals International AG, Switzerland.
- University of Copenhagen, Denmark
- University of Oxford, United Kingdom
- Wellcome Trust, United Kingdom
- World Health Organization - Special Programme for Research and Training in Tropical Diseases (WHO-TDR), Switzerland
- Zoetis Belgium SA (Zoetis), Belgium

Partners

EVI thanks all its collaborators that support our common goal of developing malaria vaccines.

SEmalvac2

Institut de Recherche en Sciences de la Santé (IRSS)	Burkina Faso
Medical Center for Translational Research, 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

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Ifakara Health Institute Trust	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
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London School of Hygiene and Tropical Medicine (LSHTM)	United Kingdom
Novavax AB	Sweden
University of Oxford	United Kingdom
Serum Institute of India Pvt. Ltd.	India
University of Sierra Leone	Sierra Leone

MIMVaC-Africa

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Eberhard Karls Universität Tübingen	Germany
University of Oxford	UK
Leiden University Medical Center (LUMC)	The Netherlands

Luxembourg Institute of Health	Luxembourg
Osaka University	Japan
Centre de Recherches Médicales de Lambaréné (CERMEL)	Gabon
Fundação Manhiça	Mozambique
Ifakara Health Institute (IHI)	Tanzania

MVPE-CC

Kintampo Health Research Centre (KHRC)	Ghana
Kenya Medical Research Institute (KEMRI)	Kenya
London School of Hygiene and Tropical Medicine (LSHTM)	United Kingdom
PATH	United States of America (USA)
University of Malawi, College of Medicine	Malawi
African Research Collaboration for Health Limited Kenya	Kenya

VAC4PM

Ehime University	Japan
Institut national de la santé et de la recherche médicale (Inserm)	France
University of Copenhagen	Denmark
Groupe de Recherche Action en Santé (GRAS)	Burkina Faso
Noguchi Memorial Institute for Medical Research (NMIMR)	Ghana
Institut de recherche pour le développement (IRD)	France

EVI thanks all its collaborators that support our common goal of developing Leishmaniasis vaccines.

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

EVI thanks all its collaborators that support our common goal of developing Diarrhoeal Diseases vaccines.

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
Leiden University Medical Center (LUMC)	The Netherlands
University of Gothenburg	Sweden

EVI thanks all its collaborators that support our common goal of developing emerging diseases vaccines.

VACCELERATE

Biomedical Research Center of the Slovak Academy of Sciences	Slovakia
Centro Hospitalar Universitário do Porto	Portugal
Collaborative Center for Clinical Epidemiology and Outcomes Research (CLEO)	Greece
European Clinical Research Infrastructure Network (ECRIN)	France
European University Cyprus	Cyprus
Hacettepe University	Turquey
Institut National de la Santé et de la Recherche Médicale (Inserm)	France
Instituto de Salut Carlos III	Spain
Karolinska Institutet	Sweden
Masaryk University, Faculty of Medicine	Czech Republic
Medical University of Bialystok	Poland
Medical University of Vienna	Austria
Ministry of Health	Israel
National University of Ireland Galway	Ireland
Országos Korányi Pulmonológiai Intézet (OKPI)	Hungary
Region Hovedstaden	Denmark
Region Stockholm, Karolinska University Hospital	Sweden
Servicio Madrileño de Salud	Spain
Université de Paris	France
University College Dublin, National University of Ireland	Ireland
University Hospital Cologne	Germany
University Medical Center Utrecht	Netherlands
University of Antwerp	Belgium
University of Belgrade (MFUB), Faculty of Medicine	Serbia
University of Bergen	Norway
University of Bern	Switzerland
University of Verona	Italy
Vilnius University Hospital Santaros klinikos	Lithuania

CEPI-Nipah

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

EVI thanks all its collaborators that support our cross-cutting activities, with a common goal to advance vaccine development beyond individual vaccine candidates, including harmonisation efforts, capacity strengthening, vaccine infrastructure, quality control, manufacturing and process innovations.

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	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
Intravacc	The Netherlands
Instituto de Biologia Experimental e Tecnológica (iBET)	Portugal
Instruct Academic Services Limited	United Kingdom
Leiden University	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	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	Italy
Vaccine Formulation Institute	United Kingdom
Wageningen Bioveterinary Research, Wageningen University & Research	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 alternatives (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
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	The Netherlands
London School of Hygiene and Tropical Medicine (LSHTM)	United Kingdom
Medicines & Healthcare products Regulatory Agency	United Kingdom
Sciensano	Belgium
Sclavo Vaccine Association	Italy
Statens Serum Institut (SSI)	Denmark
University of Siena	Italy
Vaccine Formulation Institute (VFI)	Switzerland
Wageningen Bioveterinary Research, Wageningen University & Research	The Netherlands

VAC2VAC

Bavarian Nordic	Denmark
Biomedical Primate Research Centre (BPRC)	The Netherlands
Boehringer Ingelheim	Germany
Boehringer Ingelheim Animal Health France	France
College ter Beoordeling van Geneesmiddelen (CBG/ MEB)	The Netherlands
European Commission, Joint Research Centre (JRC)	Italy
GSK Biologicals	Belgium
Intravacc	The Netherlands
International Alliance for Biological Standardization · for Europe (IABS-EU)	France
Istituto Superiore di Sanità	Italy
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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
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University of Applied Sciences Utrecht	The Netherlands
University of Utrecht	The Netherlands
Zoetis Belgium SA	Belgium

WANETAM 3

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Centre National Hospitalier de Pneumo - Phtisiologie	Benin
College of Medicine - University of Ibadan	Nigeria
Fondation mondiale Recherche et Prévention Sida	Côte d'Ivoire
Fondation pour la Recherche Scientifique (FORS)	Benin
Forschungszentrum Borstel Leibniz-Zentrum fur Medizin und Biowissenschaften (FZB)	Germany
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Hôpital National (DONKA)	Guinea
Institut de Recherche pour le Développement (IRD)	France
Institut National de Santé Publique	Burkina Faso
Institut Pasteur de Dakar	Senegal
Institute of Human Virology Nigeria	Nigeria
Jos University Teaching Hospital	Nigeria
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Nigerian Institute of Medical Research (NIMR)	Nigeria
Réseau Africain de Recherche sur le SIDA	Senegal
Universidade Nova de Lisboa (NOVA)	Portugal
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Beijing University of Chinese Medicine	China
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China National Center for Biotechnology Development	China
China National Health Development Research Center	China
GAC	France
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Steinbeis 2i GmbH	Germany

PrIMAVeRa

Ares Genetics GmbH	Austria
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Eberhard Karls Universität Tübingen	Germany
GlaxoSmithKline Biologicals SA (GSK)	Belgium
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Institut Pasteur	France
Institute of Health Carlos III	Spain

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University of Geneva	Switzerland
University of Oxford	United Kingdom
University of Verona	Italy

Inno4Vac

2-control ApS	Denmark
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Enpicom BV	The Netherlands
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Goeteborgs Universitet	Sweden
Helmholtz Center for Infection Research GmbH (HZI)	Germany
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Klinikum der Universität zu Köln	Germany
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Lund University, Department of Chemical Engineering	Sweden
MCT Bioseparation	Denmark
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Sanofi Pasteur SA	France
Sciensano	Belgium
Sclavo Vaccines Association	Italy
Stichting Centre for Human Drug Research (CHDR)	The Netherlands
Stiftung Tierärztliche Hochschule Hannover	Germany
Takeda Pharmaceuticals International AG	Switzerland
Technical University of Denmark (DTU)	Denmark
The University of Nottingham	United Kingdom
Universita Degli Studi di Siena	Italy
Universitätsklinikum Jena	Germany

Universiteit Utrecht	The Netherlands
Universitetet I Bergen	Norway
Universitetet I Oslo	Norway
University College London (UCL)	United Kingdom
University Medical Center Groningen (UMCG)	The Netherlands
University of Oxford	United Kingdom
Viroclinics Biosciences BV	The Netherlands
VisMederi SRL	Italy

List of Project Publications:

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.

VAC4PM

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TRANSVAC2

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Dijkman, K., Aguilo, N., Boot, C., Hofman, S. O., Sombroek, C. C., Vervenne, R. A., ... & Verreck, F. A. (2021). Pulmonary MTBVAC vaccination induces immune signatures previously correlated with prevention of tuberculosis infection. Cell Reports Medicine, 2(1), 100187.

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Brouwer, P. J., Brinkkemper, M., Maisonnasse, P., Dereuddre-Bosquet, N., Grobben, M., Claireaux, M., ... & Sanders, R. W. (2021). Two-component spike nanoparticle vaccine protects macaques from SARS-CoV-2 infection. Cell, 184(5), 1188-1200.

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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
MVPE-CC	EDCTP	The Malaria Vaccine Pilot Evaluation-Case Control (MVPE-CC) Project	01 April 2021- 30 June 2024
VAC4PM	GHIT Fund	Clinical development of placental malaria vaccine candidates	25 October 2021 to 30 September 2023
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 – 31 December 2025
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
VACCELERATE	European Union (Horizon 2020 Programme)	European Corona Vaccine Trial Accelerator Platform	28 January 2021 - 27 January 2024
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
TRANSVAC2	European Union (Horizon 2020 Programme)	European Vaccine Research and Development Infrastructure	01 May 2017 – 30 April 2023
TRANSVAC-DS	European Union (Horizon 2020 Programme)	Design study for a European vaccine infrastructure	01 June 2020 – 30 November 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
WANETAM 3	EDCTP	West African Network for TB, AIDS and Malaria	01 August 2021- 31 July 2024
PrIMAVeRa	Innovative Medicines Initiative (IMI) and European Federation of Pharmaceutical Industries and Associations (EFPIA)	Predicting the Impact of Monoclonal Antibodies & Vaccines on Antimicrobial Resistance	01 November 2021 - 31 October 2026
Inno4Vac	Innovative Medicines Initiative (IMI) and European Federation of Pharmaceutical Industries and Associations (EFPIA)	Innovations to accelerate vaccine development and manufacture	01 September 2021 - 28 February 2027

Report Sources

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Malaria

Key Figures:
WHO - Malaria Key Facts (April 2022) - https://www.who.int/news-room/fact-sheets/detail/malaria

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Leishmaniasis

Key Figures:
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