Specific support action
Contract n°: LSSP-CT-2006-018860

Final Activity Report

Final Activity Report
Version : 1
Author:
Roland Ventura

Period covered: from *01/11/2006 – 31/10/2008*
Date of preparation*: 25/01/2009*
Start date of project: *01/11/2006*
Duration: *24 months*
Project coordinator name: *Dr Odile Leroy*
Project coordinator organisation name: *Statens Serum Institut*

SIXTH FRAMEWORK PROGRAMME

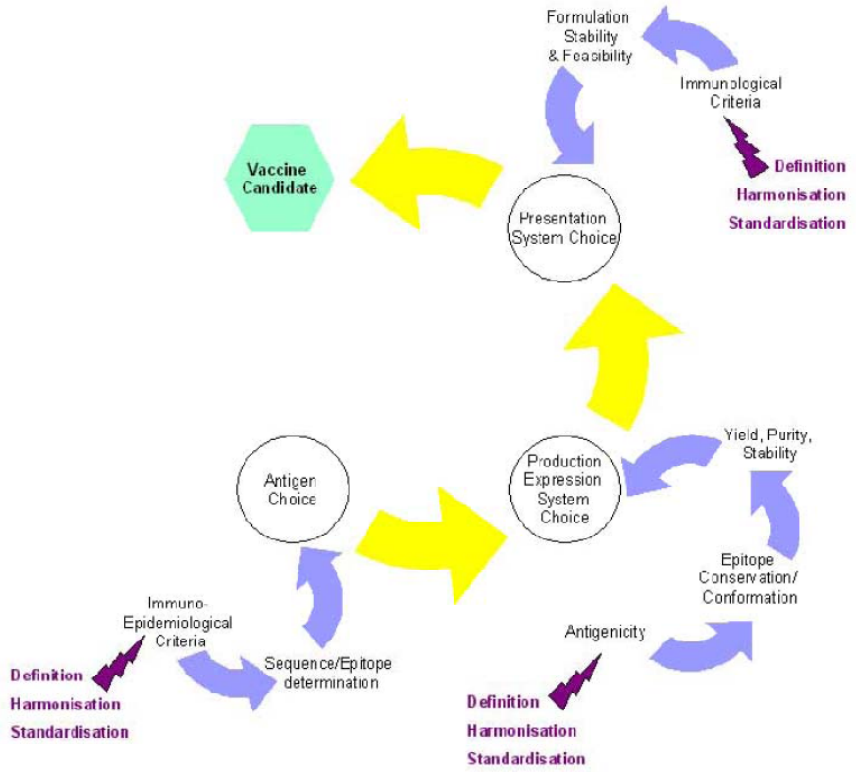
List of Abbreviations

ADCI	Antibody dependent cellular inhibition
AIA	African mmunoassay network
AMANET	African malaria network trust
AVAREF	African Vaccine Regulatory Forum
BC	Brighton Collaboration
BPRC	Biomedical primate research centre
EC	European community
ED	Executive director
ELISA	Enzyme linked immunosorbent assay
EMVDA	European malaria vaccine developers association
EMVI	European malaria vaccine initiative
EudraCT	European clinical trials database
EURHAVAC	European network for harmonisation of malaria vaccine development
FDA IND	Food drug administration investigational new drug application
FDA	Food drug administration
GIA	Growth inhibition assay
GIM	Growth inhibition assay in presence or absence of monocytes
GLURP	Glutamate-rich protein
GMP	Good manufacturing practice
IgG	Immunoglobulin G
IPH	Scientific institute of public health
IVR	Initiative for vaccine research
MVI	Malaria vaccine initiative
NIAID	National institute of allergy and infectious disease
NIBSC	National institute for biological st
NIH	National institutes of health
NIMR	National institute of medical research
OPTIMALVAC	Initiative on optimising malaria vaccine lab assays evaluation
RTD	Research and technological development
SME	Small and medium enterprise
SSI	Statens Serum Institut
UEDIN	University of Edinburgh
USAID	United States aid
WEHI	The Walter and Eliza hall institute of medical research
WHO	World heath organisation
WRAIR	Walter Reed army institute or research

Table of Contents

Executive summary

Basic research in the field of malaria parasitology has allowed several research groups to discover numerous malaria antigens that may be considered for formulation as potential vaccine candidates. From this initial stage of vaccine development, a finite set of well defined guidelines are missing which support and guide the development of experimental vaccines towards a safe, efficacious, affordable and widely available malaria vaccine. Consequently, the global portfolio of experimental malaria vaccines is very unbalanced, as shown by the status of the commonly studied MSP1 and CSP antigens. In 2004, among the 90 ongoing malaria vaccine projects, these two antigens represent 40% of the global portfolio, and 56% of the projects in phase I clinical trials. Thus, the limited research funding available for malaria vaccine development is dispersed over several similar projects and handled by different groups without concert or collaboration resulting in a questionable cascade of phase I clinical trials. This problem is further compounded as poor clinical design provides non-comparable results due to the lack of harmonisation on design, methodology and evaluation criteria. This fragmentation is continually increasing, and is currently a major issue for global and European malaria vaccine development. Therefore, we are working in collaboration with the World Health Organisation and the malaria vaccine community to concentrate on formulating decision making processes for supporting the development of more innovative and rationale-based vaccines that are carefully guided through design and production into clinical trials and so are not hampered by inexperience or competition.



The first stage of this project was completed in collaboration with WHO/IVR and the EC-funded project EMVDA. A workshop was planned in order to bring together a group of experts involved in malaria vaccine development from the vaccine industry, SMEs, academics, and regulatory agencies. Fourteen experts were invited to participate in a two day workshop entitled, "Decision making processes in malaria vaccine development" which was held in Copenhagen in February 2008. The level of interest from the malaria vaccine community was high and a second workshop was then organised to address issues regarding safety in clinical trials.

In collaboration with the WHO, the second workshop focused on the design of a strategic clinical development plan and was held in Brussels on the 21st- 22nd October 2008. Members of the malaria vaccine development community, the vaccine industry, SMEs, academics, regulatory agencies and clinical trials specialists were invited. Twenty-four experts attended a two day workshop entitled "Safety Harmonisation in Pre-Licensure Clinical Trials".

The third objective on assay development and standardisation was pursued in collaboration with EMVDA and WHO on both humoral and functional immunological assays at the Siena workshop.

The successful completion of this project has lead to the creation and dissemination of a set of decision making algorithms and reports that provide the basis of guidelines for malaria vaccine development, thus supporting the creation of an efficacious and affordable malaria vaccine. Workshop reports have been posted on EMVI's publically-accessible website and one has been submitted for publication in a peer-reviewed journal. In addition, the output from this project has significantly strengthened two other EC-funded projects; INYVAX and OPTIMLAVAC. In addition, EURHAVAC has built strong links between European and US groups working towards a malaria vaccine.

Project website: www.emvi.org/eurhavac

Project Execution

Summary of Project Objectives:
Organise and implement three workshops to deliver a series of reports/guidelines/recommendations and efficiently disseminate the findings.

Contractors Involved:
The European Malaria Vaccine Initiative (EMVI)
EMVI is a non profit organisation funded by the European Commission and several EU donors, and was founded in 1998. The specific objective of EMVI is to bridge the conceptual and operational gaps between experimental vaccine candidates developed at the bench, through further validation of bench testing, to small-scale GMP production and clinical testing. EMVI provides both the funding and expertise required to take an experimental vaccine candidate efficiently from the bench into clinical trials. EMVI has extensive experience in the coordination of large vaccine development and EC-funded projects and collaborates with a large number of international groups working in malaria research and vaccine development. Within EURHAVAC alone, EMVI has collaborated with over 30 different organisations to complete the project's objectives.

Summary of Work Performed:
The EURHAVAC project brought together and synergised numerous groups of global experts and organisations, from a diverse range of disciplines, in order to address the current challenges facing the development of a safe and effective malaria vaccine. The main achievements of EURHAVAC were to orchestrate and guide three workshops focusing on:

Copenhagen Workshop
Developing a set of criteria to allow the assessment/evaluation of new experimental malaria vaccines and to propose how decisions should be made on whether or not to continue their development into clinical trials.

Brussels Workshop
To report on safety assessment in pre-licensure clinical trials, highlighting weaknesses and areas in need of review.

Siena Workshop
To report on the standardisation and harmonisation of assays commonly used in the development of experimental malaria vaccines and to identify exactly what is needed to advance the field.

In addition, the project disseminated the findings of each workshop in an open and accessible manner, endeavouring to reach as wide an audience as possible.

Summary end results and degree to which objectives were reached

All three workshops were successfully organised and completed with a high level of engagement and interest from the vaccine development community. Three reports are now publically available and have been fed into larger ongoing EC-funded projects which are engaging the EURHAVAC recommendations and applying then in a practical way. The achievements of EURHAVAC have provided a strong foundation for larger initiatives to build upon (initiatives holding adequate funding to practically implement the findings of the EURHAVAC workshops). For example, the EC-funded OPTIMALVAC project has taken the recommendations from the Siena workshop and is now initiating the practical laboratory work to develop harmonised laboratory assays. EURHAVAC has also engaged various organisations not previously involved in the EU malaria vaccine development field (e.g. US FDA) and formed strong collaborations with numerous groups inside and outside of Europe, thus further supporting the development of a safe and efficacious malaria vaccine on a wider scale.

Methodologies and approaches employed

The reports produced by EURHAVAC were complied during a series of meetings. A panel of experts was first assembled to discuss and agree upon items for a draft agenda, to identify potential speakers for the workshops, and to prepare a provisional list of delegates to be invited to participate. Using these recommendations the EURHAVAC secretariat then compiled the agenda and invited speakers and participants. All delegates and speakers were invited to comment on the agenda. The secretariat then organised all of the necessary travel and accommodation for the experts to attend the meeting. In addition, the secretariat minuted the discussions which took place at each meeting and subsequently prepared draft reports. Experts were invited to comment on the draft reports before they were made publically available by posting on EMVI's website, as well as dissemination by publication or presentation.

In addition, the secretariat engaged numerous groups (e.g. AMANET, Brighton Collaboration) working in areas relevant to EURHAVAC's aims. This allowed EURHAVAC to avoid duplicating the efforts already completed and enabled the development of collaborations to strengthen and support EURHAVAC's influence.

Achievements of the project in relation to the state-of-the-art

The Brussels workshop, which reported on safety assessment in pre-licensure clinical trials, was the first known workshop discussing safety in malaria clinical trials. At the time, the Siena workshop was the most advanced effort to standardise and harmonise various malaria vaccine assays and the findings have now fed into the OPTIMALVAC EC-funded project which is supporting the laboratory development of assays and reagents as recommended at the Siena workshop. The Copenhagen workshop provided a report detailing a set of criteria that can be used to assess the quality of an experimental vaccine candidate allowing decision to be made on whether or not to continue its development through the vaccine pipeline. This is currently the most advanced and detailed set of recommendations of its kind and is currently being applied to the EC-funded EMVDA project.

Impact of the project on its industry or research sector

The workshops provided the establishment of a collaborative environment encompassing EMVDA, MVI, NIH, USAID, EMEA, US FDA, US CDC, EC, industry, academia and WHO. Prior to the workshops, there had been extensive collaboration and contact with other organisations resulting in the strengthening of EURHAVAC's position and mission.

Another significant achievement of EURHAVAC has been in laying excellent foundations for the EC-funded INYVAX and OPTIMALVAC projects. Not only has EURHAVAC highlighted and clarified the technical issues that need to be addressed but it has also inspired and motivated many of the EURHAVAC workshop participants to become involved in the INYVAX and OPTIMALVAC projects (at no cost additional to either projects). Thus EURHAVAC has successfully synergised with INYVAX and OPTIMALVAC, strengthening both projects and further united experts from cross disciplinary groups. In addition, the clarification of many issues by the EURHAVAC workshops has allowed both projects to initiate activities much more efficiently than would have occurred otherwise. The selection criteria from the Copenhagen workshop are currently being applied to the EC-funded project EMVDA, in order to allow the selection for funding of the most superior experimental vaccine candidates to enter into further development.

EURHAVAC has also been a pioneer in the establishment of links between European and US FDA/US CDC efforts to standardise and harmonise within the malaria vaccine field. Two of the three workshops involved the US CDC and US FDA.

Project Logo

Website: www.emvi.org/eurhavac

The Copenhagen Workshop Experts

The Brussels Workshop Experts

Final plan for using and disseminating the knowledge

Section 1 - Exploitable knowledge and its use:

This project has not generated any knowledge having a potential for industrial or commercial application in research activities or for developing, creating or marketing a product or process or for creating or providing a service. The main philosophy of this project was to make all findings freely and publically accessible rather than to create something which could be exploited. However, the report from the Copenhagen workshop describes a process that can be used to allow decision making as to whether to continue the pre-clinical development (with eventual advancement to clinical assessment) of an experimental vaccine candidate. The Siena workshop report describes the necessary steps for the development of standardised and harmonised assays for use in malaria vaccine development, and the Brussels report recommends the steps needed to ensure that safety is harmonised in malaria clinical trials.

Section 2 – Dissemination of knowledge

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
Feb 2008	Report (Copenhagen)	Research/Industry	Global	Malaria Research Community	WHO
Dec 2007	Report (Siena)	Research/Industry	Global	Malaria Research Community	WHO
Oct 2008	Report (Brussels)	Research/Industry	Global	Malaria Research Community	WHO
Dec 2008	Presentation to MVFG	Malaria Vaccine Funders Group	Europe, USA & Africa	Entire MVFG group	MVFG*
Various	Oral presentations to EMVI's collaborators	Various	Various	Various	EMVI's many collaborators
Ongoing	Project web-site (www.eurhavac.org/eurhavac)	Research/Industry/General Public	Global	Global	N/A

*WHO, PATH MVI, the Bill & Melinda Gates Foundation, the Wellcome Trust, the European and Developing Countries Clinical Trials Partnership (EDCTP), the European Malaria Vaccine Initiative (EMVI), the European Commission (Directorate General for Research), the United States National Institute for Allergy and Infectious Diseases (NIAID), and the United States Agency for International Development (USAID) form part of a malaria vaccine funders' group, with the WHO Initiative for Vaccine Research as its focal point.

The recommendations from the Copenhagen workshop have been submitted for publication in Trends in Parasitology. The reports of the Brussels and Siena workshops have been published on the EMVI website (www.emvi.org). Many aspects of the EURHAVAC findings have been presented to numerous groups in Europe, Asia, Africa and the United States. Together, the reports provide a set of guidelines indicating strategies for overcoming current problems (Copenhagen workshop) or highlight areas that need to be improved and suggest strategies for improving them (Siena and Brussels workshops).

Another significant achievement of EURHAVAC has been in laying excellent foundations for the EC-funded INYVAX and OPTIMALVAC projects. Not only has EURHAVAC highlighted and clarified the technical issues that need to be addressed but it has also inspired and motivated many of the EURHAVAC workshop participants to become involved in the INYVAX and OPTIMALVAC projects. Thus EURHAVAC has successfully synergised expertise within the United States and Europe, strengthening both INYVAX and OPTIMALVAC projects as well as strengthening European efforts to develop malaria vaccines.

EURHAVAC has also been a pioneer in the establishment of links between European and US FDA / US CDC efforts to standardise and harmonise vaccine activities. Each of the workshops involved representatives from the

US CDC and/or US FDA. These interactions have resulted in continuing collaborations allowing European US efforts to synergise for the benefit of European malaria vaccine development.