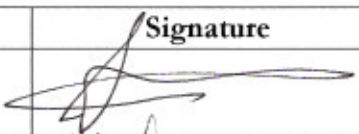

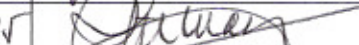



E.M.V.I.	Protocol Amendment	Trial code:	AMA-1_1_03
European Malaria Vaccine Initiative	<i>Title: Assessment of the Safety and Immunogenicity of three Formulations of the Recombinant <i>Picbia pastoris</i> Apical Membrane Antigen 1 (PfAMA-1-FVO[25-45]), Blood-stage Malaria Vaccine in Healthy Dutch Adult Volunteers : a Phase 1, Single-Blind, Randomised, Dose-escalating, Unicentre trial.</i>	Version No.:	1
Good Clinical Practices		Effective Date:	16/05/05

1. Signatures

I have read the amendment and agree that the trial will be conducted according to the procedures described.

Function	Name	Date	Signature
Principal Investigator	Prof Robert Sauerwein	24/6/05	
Investigator	Dr Meta Roestenberg	24/06/05	
E.M.V.I. Project manager	Dr Hildur E. Blythman	24.06.05	
E.M.V.I. Director of Clinical and Regulatory Affairs	Dr Odile Leroy	22/06/05	

E.M.V.I.	Protocol Amendment	Trial code:	AMA-I_1_03
European Malaria Vaccine Initiative	<i>Title: Assessment of the Safety and Immunogenicity of three Formulations of the Recombinant <i>Pichia pastoris</i> Apical Membrane Antigen 1 (PfAMA-1-FVO[25-45]), Blood-stage Malaria Vaccine in Healthy Dutch Adult Volunteers : a Phase 1, Single-Blind, Randomised, Dose-escalating, Unicentre trial.</i>	Version No.:	1
Good Clinical Practices		Effective Date:	16/05/05

2. Justification of the amendment

The paragraphs modified by this amendment are described below. Other paragraphs remain unchanged

Page 35 and 36

7.2.2. Cellular Immune response:

2. Parameters to be measured, Method and Timing of Measurement

Cytokine production will be assayed by ELISPOT for the cytokines IL-4 and IFN γ

Change to:

Cytokine production will be assayed by ELISPOT for the cytokines IL-5 and IFN γ

Justification for the change:

- The IL-4 production of Polymorphic Blood Mononuclear Cells (PBMC's) measured in the ELISPOT is low as compared to the IL-5 production. Therefore, due to the low numbers of spots, the read-out will be less reproducible and the intra-assay variability will be higher as compared to IL-5.
- ELISPOT results from this study can easily be compared with the IFN γ /IL-5 data published by researchers of GSK[1], [2], one of the co-investigators in this study.

[1] Walsh DS, Pichyangkul S, Gettayacamin M, et al. Safety and immunogenicity of rts,s+trap malaria vaccine, formulated in the as02a adjuvant system, in infant rhesus monkeys. *Am.J.Trop.Med.Hyg.* 2004;70(5):499-509.

[2] Pichyangkul S, Gettayacamin M, Miller RS, et al. Pre-clinical evaluation of the malaria vaccine candidate *P. falciparum* MSP1(42) formulated with novel adjuvants or with alum. *Vaccine* 2004;22(29-30):3831-40.

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Good Clinical Practices		Effective Date:	16/05/05

3. Appendixes

1. Amendment List

Amendment number	Date	Protocol file name	Version	EC submission	
				Yes/ No	date
1	03/03/05	PAMAI 050303	Final_1	No	
2	16/05/05	PAMAI 050516	Final_2		

2. Amended protocol