# INITIAL INFORMATION

-7 MAY 2001 163375

Number	Subject Number	Subject Initials	Page
Person Reporting SAE	EXPERIENCE		
Serious Adverse Experience (Please print clearly)	Eye P	roblems	Specify reason(s) for considering a serious AF, Mark allerance
Onset Date and Time	24,000		[1] atal fatal [2] [Ife threatening
End Date and Time (If angoing please leave blank)	Day Month  Day Month	Yr 24hr:min	[4] results in hospitalisation (excluding
If subject died, please complete Form D	Headwed Mongoing Died	2.49.214	[s] hospitalisation prolonged [s] congenital abnormality
Experience Course	Intermitter Constant Mild	No. of	cancer  of overdose  investigator consider
Intensity (maximum)	Moderate Savere		significant hazard, contraindication, side effect or precaution
Action Taken with Respect to Investigational Drug	None  Dose reduct  Dose increat  Drug interrup  restarted  Drug stopped	sed If and If an	the SAE abete? Yes No  roudy medication was interrupted,  opped or dose reduced:  us study medication reintroduced (or dose reased)? Yes No
elationship to investigational rug	☐ Not related ☐ Unlikely ☐ Suspected (re	asonable	es, did SAE recur? Yes No Isessment e SAE is probably associated with:  Protocol design or procedures (but not to study drug)
rective Therapy Yes', record details in the  necenitant Medication section		No I	Another condition (eg, condition under study, Intercurrent illness)
s subject withdrawn due to s specific SAE ?	☐ Yes 🛛	No Pleas	Nother drug

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## INITIAL INFORMATION

A2810

				Page
Centre Number	Subject Number	Subject Initials		
SERIOUS ADVERSE	EXPERIENCE (	SAE) (cont)	5/0,	
Relevant Laboratory Da Please provide relevant a		te below	*	
Teat	Date	Value	Units	Normal Range
	Day Month Yr		- 7 11111	
	Day Month Yr		- 7 MAY	2001
	Day Month Yr			
	Day Month. Yr			
Remarks (Please provide summary if necessary)	e a brief narrative desc	ription of the SAE, atta	eching extre pages eg	. hospital discharge
30 Whorls on		e dilated by right and l	o.ls. eff at mod	Ulor. Dosy
If applicable, was rando		ION AGNOR		No Yes
Randomisation / Study M Investigator's Signature (confirming that the above	deant 6	4 1 G 3	Date O	t m A y O I
Please PRINT Name				
22-20-				



### FAX

-7 MAY 2001

То	ADRAC	34412411745444744444444444444444444444444	
Company	,	***************************************	
Fax	US 8535 8305	***************************************	
From		**************************************	
Tel		>>	
E-mail			
		Pages including cover 12	
cc			
	Clinical Trial Serious Adverse Event (local ID#		
************	2806 to 2810)	··	

SmithKline Beecham (Australia) Pty Ltd ABN 73 008 399 415 300 Frankston Road Private Mall Bag 34 Dandenong Vic 3175 Australia

Tel: 613 9213 4444 Fax 613 9706 5883 www.gsk.com

Dear Sir / Madam

The attached fax contains five cases for reporting to you in this investigator driven study.

Study: 252263/033

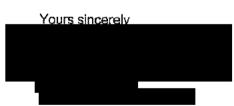
**Study Title:** A randomised, double-blind, comparative study to evaluate the safety, tolerability and effectiveness of tafenoquine and mefloquine for the prophylaxis of malaria in non-immune Australian soldiers deployed to East Timor.

Study Drug: Tafenoquine, This Study has been unblinded

Relationship to study Drug (causality): Suspected

Please note full documentation of the Safety Report has been sent to the TGA under separate cover. To follow as an attachment is a summary of the Safety Report as background information.

Should you have any enquires regarding this case, please do not hesitate to contact me on or directly on



### **CONFIDENTIAL**

### Letter to the Regulatory Authorities

## TO WHOM IT MAY CONCERN

Dear Sirs

#### Summary

The purpose of this Safety Report is to inform Regulatory Agencies, Ethics Committees and Invstigators of preliminary safety findings related to the monitoring for the effects of phospholipidosis in a Phase III Tafenoquine clinical study.

These data are from a subset of subjects (n = 33/99) in a Phase III study (Study 252263/033) investigating the safety, tolerability and effectiveness of tafenoquine in the prophylaxis of malaria in non-immune Australian soldiers deployed to East Timor.

Ophthalmological (corneal examination, visual acuity, visual field) and lung function testing (diffusing capacity of carbon monoxide –  $D_LCO$ ) data are presented on the first 33 soldiers within this subset, 26 of whom were receiving tafenoquine and 7 of whom were receiving mefloquine. After 6 months weekly dosing corneal changes (a vortex keratopathy) have been seen in 25 of 26 tafenoquine subjects, but in none of the 7 mefloquine subjects. Amsler Grid examinations suggest mild visual field changes in 4 tafenoquine subjects, but not mefloquine subjects. Minor visual acuity changes are reported across both treatment groups. All examinations were normal at baseline.

The changes considered to be clinically significant are the 4 tafenoquine subjects with Amsler Grid changes (subjects 17, 18, 22, 24 in Appendix B), and single tafenoquine subject (subject 14) with more central corneal changes in a Lasik-corrected eye and a reduction in visual acuity. These have been reported as SAEs by the Investigator.

Similar corneal changes (vortex keratopathy) have been observed with other cationic amphiphilic agents. However given the requirement to establish the reversibility of these changes off study drug, and more fully understand the associated visual field and visual acuity changes, GlaxoSmithKline have voluntarily suspended all tafenoquine dosing across both the adult and paediatric programmes.