INITIAL INFORMATION

		- 7 MAY 2001
Centre Number	Subject Subject Number Initials	Page
SERIOUS ADVERSE EXI Person Reporting SAE (Please print clearly)	PERIENCE (SAE)	
Serious Adverse Experience (Please print clearly)	Eye Problems	Specify reason(s) for considering this a serious AE. Mark all that apply. [1] fatal
		[2] life threatening
Onset Date and Time	24 APROO NA	[a] disabling/incapacitating
End Date and Time (If ongoing please leave blank)	Day Month Yr 24hr:min Day Month Yr 24hr:min	results in hospitalisation (excluding elective surgery or routine clinical procedures)
Outcome If subject died, please complete Form D	Plesolved Congoing Died	[5] hospitalisation projonged [6] congenital abnormality [7] cancer
Experience Course	Intermittent -> No. of Signature Constant episodes	[9] verdose [9] investigator considers serious or a
Intensity (maximum)	Mild Moderate Severe	significant hazard, contraindication, side effect or precaution
Action Taken with Respect to Investigational Drug	None Dose reduced Dose increased Drug Interrupted/ restarted Drug stopped	Did the SAE abate? Yes No If study medication was interrupted, otopped or dose reduced: Was study medication reintroduced (or dose increased)? Yes No If yes, did SAE recur? Yes No
Relationship to investigational Drug	Not related Untikely Suspected (reasonable possibility) Probable	Assessment The SAE is probably associated with: Protocol design or procedures (but not to study drug) Please specify
Corrective Therapy If 'Yes', record details in the 4 Concamitant Medication section	Yes 🔀 No	Another condition (eg. condition under study, intercurrent illness) Please specify
Was subject withdrawn due to this specific SAE 7	☐ Yes 🖾 No	Another drug Please specify

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INITIAL INFORMATION

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-7 MAY 2001

	Number	Subject Number	Subject initials		
SERIOUS	ADVERSE .	EXPERIENCE (S	SAE) (cont)	d Product validada yezholda)	
Relevant L	aboratory Data ride relevant ab	normal laboratory da	ta belaw		
Tes	Bt	Date	Value	Unils	Normal Range
		Day Month Yr			
		Day Month Yr			
		Day Month Yr			
		Day Month Yr			
 mild Pred 	epibeli eployment mologist	al whorlder uision sc	reened as Post deployment	pupils. Norm 6/6 6/8 but o	chorae at
If applicable	, was randomi	sation code broken	VLS LOW A		No Ves
Investigator'		cation blumbers	complete)	Date O	MAYO,() Wear
					Month tear



FAX

- 7 MAY 2001

То	ADRAC	
Company	y	
Fax	02 6232 8392	
From		
Tel		
E-mail		
Date	07-May-2001	
cc		
Subject	Clinical Trial Ser	ious Adverse Event (local ID#
	2806 to 2810)	
200.00	milita.	

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

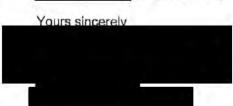
Study Title: A randomised, double-blind, comparative study to evaluate the safety, tolerability and effectiveness of tafenoquine and mefloquine for the prophylaxis of malaria in non-immune Australian soldiers deployed to East Timor.

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.

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Was subject withdrawn due to this specific SAE ?	☐ Yes 📉 Na	Another drug Please specify

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INITIAL INFORMATION MAY 2001 Page Centre Subject Subject Number Number Initials SERIOUS ADVERSE EXPERIENCE (SAE) (cont) Relevant Laboratory Data Please provide relevant abnormal laboratory data below Test Date Value Unite Normal Range Day Month Day Month Day Month Yr Day Month Remarks (Please provide a brief narrative description of the SAE, attaching extra pages eg. hospital discharge summary if necessary) 1) Soldier had red/Green cobut deficiency on pre-deployment normal examination. @ On post deployment saw waving line" on Amsler testing but unable to fully assess due to dilated pupils - requires follow up without dilation. Normal macular examination. 3) Linear epithelial whoil on coined examination @ visual accordy unchanged 6/6 6/6 to if applicable, was randomisation code broken at investigational site? Randomisation / Study Medication New Investigator's Signature: Date (confirming that the above data are accurate and complete)

Please PRINT Name

Please PRINT Name

Day Month Yest



FAX

-7 MAY 2001

То	ADRAC	umman,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,
Compan		
Fax	02 6232 8392	
From		
Tel		
E-mail		
	07-May-2001	
cc		
Subject	Clinical Trial Serio	ous Adverse Event (local ID#
	2806 to 2810)	

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Yours sincerely

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