

(System Info - 212464 FRITZ TIMOTHY 09/10/2012 11:15:36 FRITZT)

## **RECORD OF TELEPHONE CONVERSATION**

Submission Type: BLA Submission ID: 125285/0 Office: OVRR

Product:  
Influenza Vaccine

Applicant:  
Protein Sciences Corporation

Telecon Date/Time: 09-Sep-2012 12:33 PM Initiated by FDA? Yes

Telephone Number:

Communication Category(ies):  
1. Information Request

Author: TIMOTHY FRITZ

Telecon Summary:  
Clinical study sub-analyses.

FDA Participants: Timothy Fritz

Non-FDA Participants: Penny Post

Trans-BLA Group: No

Related STNs: None

Related PMCs: None

Telecon Body:

**From:** Fritz, Timothy  
**Sent:** Sunday, September 09, 2012 12:33 PM  
**To:** 'Penny Post'  
**Subject:** CBER Information Request STN 125285 (Flublok), clinical study sub-analyses

**Importance:** High

**Attachments:** Clinical study sub-analyses.pdf  
Dear Dr. Post-

CBER's review of Protein Sciences Corporation's July 17, 2012 submission (STN 125285) is ongoing and we have the following requests for additional information. Please note that PSC may use another format for the example tables provided, if preferred.

1. We have the following requests for sub-analyses of integrated safety data from PSC01 and PSC04 according to gender, race and ethnicity:
  - a. Solicited AEs
  - b. Unsolicited AEs

Summary tables might be organized according to the following examples:

**Table 1: Solicited Adverse Events by Severity, Gender, and Treatment Group – Integrated Summary PSC04 and PSC01**

Solicited Adverse Events		Gender and Treatment Group			
		Male		Female	
Total Subjects in Safety analysis group		FluBlok N=	Placebo N=	FluBlok N=	Placebo N=
	<b>Severity</b>				
<b>All Solicited Local AEs, n(%)</b>	Overall				
	Grade 3				
Injection site pain	Overall				
	Grade 3				
Injection site redness	Overall				
	Grade 3				
Injection site swelling	Overall				
	Grade 3				
Injection site bruising	Overall				
	Grade 3				
<b>All Solicited Systemic AEs, n(%)</b>	Overall				
	Grade 3				
Fever	Overall				
	Grade 3				
Headache	Overall				
	Grade 3				
Fatigue	Overall				
	Grade 3				
Lack of energy	Overall				
	Grade 3				
Muscle pain	Overall				
	Grade 3				
Joint pain	Overall				
	Grade 3				
Nausea	Overall				
	Grade 3				
Chills	Overall				
	Grade 3				
Sweating	Overall				
	Grade 3				

**Table 2: Solicited Adverse Events by Race, Ethnicity, and Treatment Group – Integrated Summary PSC04 and PSC01 [Note to PSC: add columns for “non-Hispanic” and “Other”]**

<b>Race</b>	<b>White</b>		<b>Black</b>		<b>Asian/ Pacif Is</b>		<b>Alaskan/ NativeAm</b>		<b>Hispanic/ Latino</b>	
<b>Treatment group</b>	FB N=	PBO N=	FB N=	PBO N=	FB N=	PBO N=	FB N=	PBO N=	FB N=	PBO N=
<b>Solicited AE, n(%)</b>										
Any local AE										
Pain										
Redness										
Induration/swelling										
Bruising										
<b>Any systemic AE, n(%)</b>										
Fever										
Nausea/vomiting										
Diarrhea										
Loss of Appetite										
Irritability										
<b>Etc.,</b>										
<b>Etc.,</b>										

FB=FluBlok, PBO=placebo

**Table 3: Severity of Solicited AEs according to Race, Ethnicity, and Treatment Group – PSC01 and PSC04 [Note to PSC: please add columns for “non-Hispanic” and “Other”]**

<b>Race</b>	<b>White</b>		<b>Black</b>		<b>Asian/ Pacif Is</b>		<b>Alaskan/ Native Am</b>		<b>Hispanic</b>	
<b>Treatment group</b>	FB N=	PBO N=	FB N=	PBO N=	FB N=	PBO N=	FB N=	PBO N=	FB N=	PBO N=
<b>Solicited AE, n(%)</b>										
Local, n(%)										
Mild										
Moderate										
Severe										
Systemic, n(%)										
Mild										
Moderate										
Severe										

FB=FluBlok, PBO=placebo

**Table 4: Number (and %) of Subjects Reporting Unsolicited AEs Categorized by System Organ Class by Severity, Gender and Treatment Group – Integrated Summary PSC01 and PSC04**

<b>Unsolicited Adverse Event</b>		<b>Gender and Treatment Group</b>			
		<b>Male</b>		<b>Female</b>	
<b>Total Subjects in Safety analysis group</b>		<b>FluBlok N=</b>	<b>Placebo N=</b>	<b>FluBlok N=</b>	<b>Placebo N=</b>
	<b>Intensity</b>				

<b>#subjects with ≥ 1 Unsolicited AE (related and unrelated), n(%)</b>	Overall				
	Grade 3				
	Serious				
<b>System Organ Class *</b>					
Gastrointestinal disorders	Overall				
	Grade 3				
General disorders and administration site conditions	Overall				
	Grade 3				
Infections and Infestations	Overall				
	Grade 3				
Injury, poisoning, and procedural complications	Overall				
	Grade 3				
Musculoskeletal and Connective Tissue Disorders	Overall				
	Grade 3				
Nervous System Disorders	Overall				
	Grade 3				
Etc.	Overall				
	Grade 3				

\*Please include only those SOC categories with overall rate of 5% or more in any overall treatment group (all FluBlok vs all Placebo). Do not need to present data for individual Preferred Terms, just the SOCs.

**Table 5: Unsolicited AEs by Race, Ethnicity, and Treatment Group – Integrated Summary PSC01 and PSC04 [Note to PSC: please add columns for “non-Hispanic” and “Other”]**

<b>Race</b>	<b>White</b>		<b>Black</b>		<b>Asian/ Pacif Is.</b>		<b>Alaskan/ Native Am</b>		<b>Hispanic</b>	
<b>Treatment group</b>	<b>FB N=</b>	<b>PBO N=</b>	<b>FB N=</b>	<b>PBO N=</b>	<b>FB N=</b>	<b>PBO N=</b>	<b>FB N=</b>	<b>PBO N=</b>	<b>FB N=</b>	<b>PBO N=</b>
System Organ Class, n(%)										
Infections and Infestations										
Nervous System Disorders										
Etc.										

\*Please include only those SOC categories with overall rate of 5% or more in any overall treatment group (all FluBlok vs all Placebo). Do not need to present data for individual Preferred Terms, just the SOCs.

**Table 6: Severity of Unsolicited Adverse Events by Race, Ethnicity, and Treatment Group – Integrated Summary PSC01 and PSC04 [Note to PSC: Please add columns for “Serious” and “Non-Serious” under Severity of AE]**

Race	Treatment Group		Severity of AE [Note to PSC: Please add columns for “Serious” and “Non-Serious” under Severity of AE]					
			Severe		Moderate		Mild	
	FB N=	PBO N=	FB N=	PBO N=	FB N=	PBO N=	FB N=	PBO N=
White								
Black								
Asian/Pacific Islander								
Alaskan/ Native Am.								
Hispanic/Latino								
Non-Hispanic/ Latino								
Other								

2. We have the following requests for sub-analyses of efficacy data from PSC01 and PSC04 according to gender, race and ethnicity:
- Immunogenicity – please integrate data from PSC01 and PSC04
  - Vaccine Efficacy – data from PSC04 only

Summary tables might be organized according to the following examples:

**Table 7: Immune Responses by Gender\* - Integrated Summary PSC01 and PSC04**

Immune Response	Male		Female	
	FluBlok	Placebo	FluBlok	Placebo
<b>Total Subjects with Valid Serological Data-H1N1</b>	N=	N=	N=	N=
GMT				
Seroconversion rate				
% HI $\geq$ 1:40**				
<b>Total Subjects with Valid Serological Data-H3N2</b>	N=	N=	N=	N=
GMT				
Seroconversion rate				
% HI $\geq$ 1:40				
<b>Total Subjects with Valid Serological Data- B strain</b>	N=	N=	N=	N=
GMT				
Seroconversion rate				
% HI $\geq$ 1:40				

\*point estimates

\*\*For PSC01, the proportion of subjects with a post-vaccination HI titer of  $\geq$  1:64 was evaluated.

**Table 8: Immune Responses by Race, Ethnicity, and Treatment Group\* - Integrated Summary PSC01 and PSC04 [Note to PSC, please add columns for Asian, Alaskan/Native American, Hispanic/Latino, Non-Hispanic/Latino, and Other]**

Immune Response	White		Black, (add columns for Asian, Alaskan, Native Am, etc.)	
	FluBlok	Placebo	FluBlok	Placebo
<b>Total Subjects with Valid Serological Data-H1N1</b>	N=	N=	N=	N=
GMT				
Seroconversion rate				
% HI $\geq$ 1:40				
<b>Total Subjects with Valid Serological Data-H3N2</b>	N=	N=	N=	N=
GMT				
Seroconversion rate				
% HI $\geq$ 1:40				
<b>Total Subjects with Valid Serological Data- B strain</b>	N=	N=	N=	N=
GMT				
Seroconversion rate				
% HI $\geq$ 1:40				

\*Point estimates

**Table 9: Incidence of Culture-Confirmed Influenza and Vaccine Efficacy in Adults 18 to < 50 years of age by Gender – PSC04**

Variable	Male		Female	
	FluBlok N=	Placebo N=	FluBlok N=	Placebo N=
<b>All isolates, n(%)</b>				
Relative Risk				
Vaccine Efficacy x 100				
95% CI				
<b>Matched strains, n(%)</b>				
Relative Risk				
Vaccine Efficacy x 100				
95% CI				

**Table 10: Incidence of Culture-confirmed Influenza and Vaccine Efficacy - Adults 18 to < 50 years of age by Race, Ethnicity, and Treatment Group – PSC04 [Note to PSC: Please add columns for “Hispanic”, “non-Hispanic”, and “Other”]**

Race	White		Black		Asian/ Pac Is		Alaskan/ Native Am		Please add columns for “Hispanic”, “non- Hispanic”, and “Other”]	
Endpoints	FB N=	PBO N=	FB N=	PBO N=	FB N=	PBO N=	FB N=	PBO N=	FB N=	PBO N=
<b>All isolates, n(%)</b>										
Relative										

<b>Race</b>	<b>White</b>		<b>Black</b>		<b>Asian/ Pac Is</b>		<b>Alaskan/ Native Am</b>		Please add columns for “Hispanic”, “non- Hispanic”, and “Other”]	
<b>Endpoints</b>	<b>FB N=</b>	<b>PBO N=</b>	<b>FB N=</b>	<b>PBO N=</b>	<b>FB N=</b>	<b>PBO N=</b>	<b>FB N=</b>	<b>PBO N=</b>	<b>FB N=</b>	<b>PBO N=</b>
<b>All isolates, n(%)</b>										
Risk										
Vaccine Efficacy x 100										
95% CI										
<b>Matched strains, n(%)</b>										
Relative Risk										
Vaccine Efficacy x 100										
95% CI										

3. For each analysis/table, please include a description with your interpretation of the results.
4. Please provide the statistical programs and datasets used to perform the requested analyses with your response.

Please provide your response as an Amendment to STN 125285. Please respond at your earliest convenience and no later than one month from the receipt of this request. If you have any questions, please contact the Regulatory Project Chair, Dr. Timothy A. Fritz, at 301-796-2640.

Thank you.

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