

Record of Telephone Conversation, June 19, 2009 - Flublok

- Submission Type: Original Application Submission ID: 125285/0 Office: OVRR

Product:
Influenza Vaccine

Applicant:
Protein Sciences Corporation

Telecon Date/Time: 19-JUN-2009 04:01 PM Initiated by FDA? Yes
Telephone Number:

Communication Category(ies):
Information Request

Author: TIMOTHY FRITZ

Telecon Summary:
Clinical information request regarding amendment 12 complete response

FDA Participants: Timothy Fritz

Non-FDA Participants: Drs Manon Cox

Trans-BLA Group: No

Related STNs: None

Related PMCs: None

Telecon Body:

Regarding your Complete Response to Clinical questions and comments dated 7 April 2009 we have the following requests for information:

1. Please clarify whether unsolicited AEs were followed to resolution. For example, in PSC04 FluBlok recipient 13-09654-(b)(6)- is a 36 year old African American female who was vaccinated on September 15, 2007 and who subsequently experienced insomnia on September 29, 2007 (14 days after vaccination) and then both headache and pharyngolaryngeal pain on October 12, 2007 (17 days after vaccination). All events were assessed as non-serious. Her headache resolved, but the insomnia and

pharyngolaryngeal pain were categorized as ongoing in both the Interim Study Report and in the final datasets. Were these 2 ongoing events followed beyond Day 28?

2. Please provide a tabular summary of the clinical endpoint data for the 135µg dose only from all four clinical studies, PSC01, PSC03, PSC04, and PSC06. In your table, please include information where possible regarding the number of culture-positive influenza cases in all treatment groups for each strain, all strains, matched and regardless of match. For placebo-controlled trials, please provide point estimates of vaccine efficacy with 95% CIs. For active controlled trials, please provide the relative risk and relative protective efficacy for FluBlok with 95% CIs. If desired, please include culture-confirmed CDC ILI endpoints. Please organize your table(s) as you feel appropriate, but consider the following examples:

Clinical Efficacy of FluBlok against Culture-Confirmed Influenza – Placebo-controlled Trials

	FluBlok	Placebo	
PSC04 2007-2008	N#cases (%)	N#cases (%)	%Efficacy (95% CI)
Matched strains			
-all strains			
-A/H1N1			
-A/H3N2			
-B			
Regardless of match			
-all strains			
-A/H1N1			
-A/H3N2			
-B			
PSC01 2004-2005			
Etc.			

Relative Protective Efficacy of FluBlok against Culture-Confirmed Influenza – Active-controlled Trials

	FluBlok	TIV		
PSC06 2007-2008	N#cases (%)	N#cases (%)	Relative risk	Relative Protective Efficacy (95% CI)
Matched strains				
-all strains				
-A/H1N1				
-A/H3N2				
-B				

	FluBlok	TIV		
Regardless of match				
-all strains				
-A/H1N1				
-A/H3N2				
-B				
PSC03				
2006-2007				
Etc.				

3. Under the Pediatric Research Equity Act (PREA) of 2003 clinical studies must be conducted in children for biological products under development, and there must be adequate data to support safety and effectiveness, dosing and administration in this population. The Pediatric Review Committee (PeRC) of the FDA must review your requests for deferral and partial waiver and your pediatric development plan prior to approval of your BLA. Your pediatric plan must outline the pediatric studies that you plan to conduct in all relevant age groups, and it must also address the development of an age-appropriate formulation. At a minimum the PeRC requests that your plan include the following elements:

- a. Indication(s) to be studied;
- b. Route of administration;
- c. Formulation;
- d. Dosage;
- e. Regimen;
- f. Study design(s);
- g. Age groups and populations in which the study(ies) will be performed;
- h. Number of patients to be studied and expected power of the study(ies)
- i. *Entry criteria;
- j. *Clinical endpoints;
- k. *Timing of assessments;
- l. *Statistical analyses to be performed.
- m. Timeframe for conducting the studies and submitting the complete study reports. Evidence must be provided that the studies will be conducted with due diligence and at the earliest possible time.

*submission of this information is optional at the time of the PeRC review but is useful if available.

In your original BLA, submitted April 18, 2008, Module 1, Volume 1, Section 1.3.10, Request for Deferral of Pediatric Studies, you requested a deferral of pediatric studies in children ages 6 months to 17 years and a partial waiver for children from birth to less than 6 months of age. You also outlined a general approach to your pediatric development plan and indicated that you intended to submit a formal Pediatric Plan to

the IND in 2008. We request that you submit an updated detailed plan that will satisfy the requirements of PREA and the PeRC.

4. Regarding your proposed Package Insert, Original Submission STN 125285/0, Module 1, Volume 1, Section 1.4.1, 14 Clinical Studies, pp13-19:

- a. Please update all prose and tables to include the 57 subjects that were missing from the immunogenicity analyses in your Interim Study Report for PSC04. The immunogenicity population should now be n=448 rather than n=391;
- b. Please update the prose describing clinical efficacy to include the new clinical endpoint data from studies PSC04 and PSC06. Please provide a tabular summary of the clinical efficacy data for the 135µg dose from all four clinical studies, PSC01, PSC03, PSC04, and PSC06. Please see Comment #2 above for an example of the tabular summaries we are requesting.

If you have any questions, please contact the Regulatory Project Managers, Katherine L. Matrakas or Timothy A. Fritz at 301-827-3070.