

Telephone Conference Memorandum - 6/13/2007 - AFLURIA

- **TELEPHONE CONFERENCE MEMORANDUM**

STN 125254:

CTD BLA for Influenza Virus Vaccine

SPONSOR:

CSL Limited

PRODUCT:

Influenza Virus Vaccine

DATE:

June 13, 2007

Facsimile sent:

June 13, 2007

CBER REPRESENTATIVE:

Katherine Berkhausen

CSL REPRESENTATIVE:

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SUMMARY:

CBER requests additional clarification on the following items:

Regarding the Clinical Information:

Study vaccines were administered by either the intramuscular or deep subcutaneous route for studies CSLCT-NHF-05-15, CSLCT-NHF-05-13, CSLCT-NHF-05-11, and CSLCT-NHF-04-99. Furthermore, Study CSLCT-NHF-05-15 specifies the number of subjects in the Enzira and Influsplit groups who received the vaccines by subcutaneous versus intramuscular route while the other studies do not specify these parameters.

1. Please clarify what is meant by "deep subcutaneous" injection. Was the vaccine purposefully injected into the subcutaneous tissue surrounding the deltoid muscle rather than into the deltoid muscle? Please also clarify whether the route of vaccine administration was randomly assigned to subjects for each study and how the delivery of the vaccine was ascertained to be intramuscular or "deep subcutaneous".
2. If possible, for studies CSLCT-NHF-05-13, CSLCT-NHF-05-11, and CSLCT-NHF-04-99, please provide the exact numbers of subjects in each vaccine group who received the study vaccine by the "deep subcutaneous" versus intramuscular route of administration.
3. In Module 2 Volume 2 you provide an integrated summary of Solicited Adverse Events extracted from studies CSLCT-FLU-05-15, CSLCT-FLU-05-11, CSLCT-FLU-05-13, and CSLCT-FLU-04-99 in the population ≥ 65 years of age. However, we have not been able to locate a similar integrated summary of Unsolicited Adverse Events from these studies. Please provide an integrated summary of Unsolicited AEs from the above studies in the age group ≥ 65 years or indicate

where these data are located in the BLA submission. Please also clarify the duration of follow up for unsolicited AEs in these studies.

4. Regarding Table "Appendix 2.7.4.7.3" located on pg. 179 of Module 2 Volume 2 Section 2.7.4, we note some differences in frequencies in Solicited AEs reported by the applicant from that calculated by the reviewer:

Solicited AE	CSLCL-FLU-05-11	CSLCL-FLU-05-11	CSLCT-FLU-05-13	CSLCT-FLU-05-13
	Fluvax (n=60) Applicant data	Fluvax (n=60) Reviewer result	Fluvax (n=40) Applicant data	Fluvax (n=40) Reviewer result
Ecchymosis	4 (0.7%)	4 (6.7%)		
Pain	1 (0.7%)	1 (1.7%)	7 (2.5%)	7 (17.5%)
Malaise	1 (0.7%)	1 (1.7%)		
Fever>38°C	1 (0.7%)	1 (1.7%)		

5. Please clarify the absolute numbers and the percentages for this table.
6. Regarding the applicant's Table 2.7.4.7.2-4 on p 160 Module 2 Vol 2 Section 2.7.4, we note a difference in the applicant's reported frequency of Malaise from that calculated by the review based on the applicant's data:

Event	Cumulative summary Thimerosal-containing vaccine ≥60to<65years n=73, (%)	Cumulative summary Thimerosal-containing vaccine ≥65years n=245, (%)
Malaise (applicant)	11 (21.6)	36 (18.2)
Malaise (reviewer)	11 (15.1)	36 (14.7)

7. Please clarify the absolute numbers and the percentages for this table.
8. Regarding the Manufacturing

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Regarding Control of Materials

10. Section 3.2.S.2.3.1.2 (Vol 1, page 4) references a USDA Memo 800.65. Please submit this Memo.
11. Section 3.2.S.2.3 (Vol 1, page 16) references a table Specification for the -----
----- Please explain the ----- (it might be -----)
12. Please provide the information on A/Solomon Island working virus seed (Vol 1, page 18, Section 3.2.S.2.3.1.5.).
13. Please include the year of the monographs in your references on USP (Table 3.2.S.2.3-5) and PH.EUR. (Vol 1, pg 28-29, Section 3.2.S.2.3-8).
14. Attachment 3.2.S.2.3.-17 references the TSE Certificate of Suitability dated March 2nd, 2006. Please provide the Certificate of Suitability for 2007.
15. The most recent --- egg Quality Control Sheet from ----- is dated 09/01/06. Please submit an updated control sheet for 2007.
16. Please provide the abbreviation explanation for --- in Table 3.2.S.2.3-4 (Vol 1, pg 28).

Your assistance in addressing these requests is appreciated.

Regards,