

# RECORD OF TELEPHONE CONVERSATION

## Submission Information

<b>Application Type</b>	BLA
<b>STN</b>	125510/0.0
<b>Review Office</b>	OVRR
<b>Applicant</b>	Novartis Vaccines and Diagnostics, Inc. / Lic. # 1751
<b>Product</b>	Influenza Vaccine, Adjuvanted
<b>Trans-BLA Group:</b>	No

## Telecon Details

<b>Telecon Date/Time</b>	10-SEP-2015 03:32 PM
<b>Author</b>	BALDWIN, BRENDA
<b>EDR</b>	No
<b>Post to Web</b>	No
<b>Outside Phone Number</b>	
<b>FDA Originated?</b>	Yes
<b>Communication Categories</b>	IR - Information Request
<b>Related STNs</b>	None
<b>Related PMCs</b>	None
<b>Telecon Summary</b>	Discrepancy in death reports and table in extension studies
<b>FDA Participants</b>	Brenda Baldwin, Theodore Garnett
<b>Applicant Participants</b>	Mayuresh Gadre

**From:** Baldwin, Brenda [<mailto:Brenda.Baldwin@fda.hhs.gov>]  
**Sent:** Thursday, September 10, 2015 4:27 PM  
**To:** GADRE, MAYURESH  
**Cc:** Garnett, Theodore  
**Subject:** BLA 125510

Hi Mayuresh,

## RECORD OF TELEPHONE CONVERSATION

We note in the Integrated Summary of Safety, table 14.3.4.3 Summary of Adverse Events, RCT Extension: Safety Analysis Set YEAR 1 (page 3 of 9) that no deaths are reported. However, review of the clinical study reports for V7P3, V7P5, V7P7, V7P8 and V7P25 (first dose of the 5 extension studies submitted to this BLA) reveals that there were a total of 31 deaths reported (13 deaths in the Fluad group and 18 deaths in the unadjuvanted influenza group). Please indicate if the Novartis clinical team would be available for a teleconference on Monday morning to explain this discrepancy.

Regards,

Brenda

---

**From:** GADRE, MAYURESH [<mailto:mayuresh.gadre@novartis.com>]

**Sent:** Friday, September 11, 2015 2:28 PM

**To:** Baldwin, Brenda

**Cc:** Garnett, Theodore

**Subject:** RE: BLA 125510

Hi Brenda,

Please see the company response below. Please let me know if a teleconference is required on Monday. Novartis clinical team will be available for a teleconference as required.

***CBER Comment:***

*We note in the Integrated Summary of Safety, table 14.3.4.3 Summary of Adverse Events, RCT Extension: Safety Analysis Set YEAR 1 (page 3 of 9) that no deaths are reported. However, review of the clinical study reports for V7P3, V7P5, V7P7, V7P8 and V7P25 (first dose of the 5 extension studies submitted to this BLA) reveals that there were a total of 31 deaths reported (13 deaths in the Fluad group and 18 deaths in the unadjuvanted influenza group). Please indicate if the Novartis clinical team would be available for a teleconference on Monday morning to explain this discrepancy."*

**Novartis Response:**

"The analysis for safety in the revaccination studies was performed by including only subjects from the parent studies who participated in the extension studies as described in Section 2.2.4 of the ISS. The total analysis population in the first season of studies V7P3, V7P5, V7P7, V7P8 and V7P25 was n=713 (aTIV) and n=501 (TIV). Therefore, the safety data, including deaths, reported by subjects who did not enroll in the second and third seasons of the revaccination studies were excluded from the original analyses in the ISS. The rationale for this approach was to understand the safety data in those individuals who actually experienced multiple serial vaccinations. This was prespecified as well in the statistical analysis plan (sections 4.3 and 8.1) in advance of analyzing the ISS data. Furthermore, in the statistical analysis plan, imputation of deaths and hospitalizations was described, as the intent was to ensure that hospitalizations and deaths

## RECORD OF TELEPHONE CONVERSATION

were represented in full. The combination of these two approaches explains the differences in the numbers observed. In addition, Table 52 of the Novartis briefing book restores the deaths that were otherwise removed with the original analysis approach. Novartis will be available to discuss this further on Monday and will accommodate CBER's schedule to ensure that our collective understanding on these events is clear.

Best Regards,

Mayuresh

---

**From:** Baldwin, Brenda [<mailto:Brenda.Baldwin@fda.hhs.gov>]  
**Sent:** Friday, September 11, 2015 3:40 PM  
**To:** GADRE, MAYURESH  
**Cc:** Garnett, Theodore  
**Subject:** RE: BLA 125510

Thank you Mayuresh - your response is adequate. We do not need a teleconference on Monday.

Regards,  
Brenda