

Record of Telephone Conversation, October 26, 2012 am - Flucelvax

Submission Type: BLA Submission ID: 125408/0 Office: OVRR
Product:
Influenza Virus Vaccine
Applicant:
Novartis Vaccines and Diagnostics, Inc.
Telecon Date/Time: 26-Oct-2012 10:00 AM Initiated by FDA? Yes
Telephone Number:
Communication Category(ies):
1. Advice

Author: TIMOTHY NELLE
Telecon Summary: **Correcting problems in Module 2 and 3.**
FDA Participants:
TIMOTHY NELLE
DAVID SCHWAB
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BRENDA BALDWIN
Non-FDA Participants:
MATTHEW GOLLWITZER
KAREN MASTROFILIPO
Trans-BLA Group: No

Related STNs: None
Related PMCs: None
Telecon Body:
The purpose of this teleconference was to discuss the issues with recent updates to Modules 2 and 3 of the BLA eCTD file and Novartis's plans for corrective actions.

CBER's General issues with M3 Update:

- *General Issue #1: There are multiple files that share the same file name (e.g., "Quality Information Amendment") under Module 1.11.*

Discussion:

CBER initially requested that the Module 1.11 sharing the same file name be renamed to differentiate the documents. NVD explained that this would require resubmitting the documentation. **CBER agreed to leave the names "as-is" as this was not a critical issue. Plus, the resubmission of files would require CBER to re-review all the affected files again.**

- *General Issue #2: The 'status' of files that have been replaced with new versions are still appearing as "current". For an example, please see item 3 below.*

Discussion:

NVD agreed and will delete the documents marked as "current" that are no longer valid

- *General Issue #3: Files that were originally submitted under Module 1.11 but later moved/copied into other modules, are still indicated as "current" under 1.11. These files should have their 'status' changed to "withdrawn". For example, the "Cleaning Validation Report (doc No: 289146-01) is provided as "289146 – Cleaning Validation Report (b)(4) under Module 3.2.A.1 and "0022 CVR_------(b)(4)-----..." under Module 1.11.*

Discussion:

NVD agreed to delete the M1 documents that were relocated to M3. Therefore only 1 version of the document will be indicated as "current"

Some specific problems identified to date:

1. *Correct specifications for Drug Substance, Drug Product and final container were provided in Module 3 (10/19/12), Amendment 40 (DS: 3.2.S.4.1 page 3, DP: 3.2.P.5.1 page 3, Final container: 3.2.P.5.1 page 4) but out of date specifications were provided in in Module 2 (10/22/12), Amendment 41 (DS: 2.3.S page 43 of 54, DP: 2.3.P page 20 of 33, Final container: 2.3.P page 20 of 33). Please update Module 2 Drug Substance, Drug Product and final container specifications with the same specifications as those provided for Module 3 and submit.*

Discussion:

NVD agreed to update the appropriate M2 documents and will resubmit to replace the versions submitted in Sequence 0042

2. *Document # 294074 (Strategy Paper Determination of Acceptance Limit for Cleaning Validation Based on Process Capabilities) of Amendment 40, Module 3.2.A.1 contains limits based on-(b)(4) standard deviations but information in Amendment 32 proposed using limits -(b)(4) above sample results. Thus, the information in these 2 submissions is contradictory. Please submit correct version.*

Discussion:

NVD agreed to delete previous versions that are no longer valid so that the most current documents will be considered "current".

3. *Both updated (current) and outdated cleaning validation protocols (i.e. 294077, 294078, 294110, 294723) were provided in Amendment 40. Please change the status settings to indicate which versions are 'current' and which have been 'replaced'*

Discussion:

Please see discussion under “General Issue #2”.

4. *Endotoxin test ----(b)(4)---- is one of the release tests for --(b)(4)--- in the LRP, but it is not included in the updated --(b)(4)--- release specifications. Please insure that Endotoxin test and specification are listed in the appropriate sections of Modules 2 and 3.*

Discussion:

NVD will update appropriate sections of M2 and M3 to reflect Endotoxin testing for the --(b)(4)---- release

5. *Mycoplasma in the control cells was added to the LRP protocol; however, the Mycoplasma test in the control cells is not listed in the BLA release specifications (Tables 2.3.S.2.4-4 and 3.2.S.4.1-1). Please correct and submit.*

Discussion:

NVD agreed to update M2 appropriately. NVD clarified that Mycoplasma is an in-process control test so it does not belong in 3.2.S.4.1-1, rather it was updated in Sequence 0040 and appended to Section 3.2.S.2.

6. *Regarding the LRP:*
 - a. *In the LRP on page 26 of 41 (3.2.R.1-2, amendment 41, 10/22/12), please correct the “Mykoplasma” spelling.*
 - b. *The LRP submitted in amendment 41 is acceptable; however, we would like you to add the BPL results for the -----(b)(4)----- . Since this will only be for the lots already submitted the results could be added as an attachment to the lot specific lot release protocols.*

Discussion:

NVD agreed to update the LRP template to correct the misspelling and include BPL results for the --(b)(4)----. NVD proposes to attach protocol 294885 (submitted in Sequence 0028) to the LRPs. This protocol includes all the test results for the ----(b)(4)----- utilized for 2012/2013 trivalent bulks submitted to CBER. Brenda Baldwin to determine how to confirm acceptability of attaching protocol 294885 to the Lot Release Protocols and how to submit the data to the LRP’s already submitted to the Product Release Branch.