

FILING MEETING SUMMARY

To: The File
Application number: BLA STN 125682/0
Product name: Dengue Tetravalent Vaccine (Live, Attenuated) (DENGIVAXIA)
Proposed Indication: Prevention of dengue disease caused by dengue virus serotypes 1, 2, 3 and 4 in individuals 9 through 45 years of age with laboratory-confirmed previous dengue infection and living in endemic areas. Previous dengue infection can be assessed through a medical record of a previous laboratory confirmed dengue infection or through current serotesting.
Applicant: Sanofi Pasteur, Inc.
Meeting date & time: October 15, 2018, 1:00 – 2:30 PM
Committee Chair: Kirk Prutzman, Ph.D.
Meeting Recorders: Ramachandra Naik, Ph.D.
 Stephanie Polo

1.0 PURPOSE AND BACKGROUND

BLA STN 125682/0 was submitted by Sanofi Pasteur, Inc. (Sanofi) on August 31, 2018, and received by CBER on August 31, 2018. The purpose of this meeting was to discuss the completeness of the BLA submission and ensure it is acceptable to file.

Table 1: Review Committee and Discipline Filing Decision Summary

Review Discipline	Name	Attended meeting	Fileable	RTF	Deficiencies Identified
Chair	Kirk Prutzman, PhD	Yes	X		
RPM	Ramachandra Naik, PhD	Yes	X		
RPM	Stephanie Polo	Yes	X		
Clinical	Ralph LeBlanc, MD	Yes	X		
Toxicology	Nabil Al-Humadi, PhD	Yes	X		
Toxicology	Claudia Wrzesinski, PhD	No			
Statistics-Clinical Safety and Assays	Lei Huang, PhD	Yes	X		
Statistics-Clinical Efficacy	Mridul Chowdhury, PhD	Yes	X		
CMC and CMC Inspector	Dino Feigelstock, PhD	Yes	X		
DS and DP release assays	Tao Pan, PhD	Yes	X		
DS and DP release assays	Simleen Kaur, PhD	Yes	X		
DS and DP release assays	Noel Baichoo, PhD	Yes	X		
LRP and Testing Plan Development	Marie Anderson, PhD	Yes	X		
Lot Release Protocol	Cheryl Hulme	No	X		

Review Discipline	Name	Attended meeting	Fileable	RTF	Deficiencies Identified
CMC, CCIT, Facilities reviewer and inspector	Jie He	Yes	X		
BIMO	Christine Drabick	Yes	X		
	Malcolm Nasirah	Yes			
Advertising/Promotional Labeling	Oluchi Elekwachi	No	X		
Pharmacovigilance	Wambui Chege, PhD	Yes	X		
Benefit-risk assessment	Hong Yang, PhD	Yes	X		
DMPQ RPM	Marian Ortiz-Rodriguez	No	X		
OBE Regulatory Coordinator	Lori Austin-Hansberry, MSA, BSN	No	X		
Labeling	Daphne Stewart	Yes	X		
Electronic Integrity	David Schwab, MSIS	No	X		
Consult – Data Integrity	Brenda Baldwin, PhD	Yes	X		

OTHER PARTICIPANTS

Belete Teferedegne	Muhammad Shahabuddin	Lucia Lee
Maryna Eichelberger	Douglas Pratt	Deepa Arya
Sara Gagnetten	Martin (Dave) Green	Loris McVittie
Suzanne Carter	Doran Fink	Tsai-Lien Lin
Marion Gruber	Philip Krause	Nikunj Sharma
Denis Cato	Carmen Collazo	Jeff Roberts
Sarah Browne	Adamma Mba-Jonas	

REGULATORY CONCLUSIONS / DEFICIENCIES

- 1. Does the application, on its face, appear to be suitable for filing or is the application unsuitable for filing and will require a RTF letter?**
Fileable.
- 2. If fileable, list any substantive deficiencies or issues that have significant impact on the ability to complete the review or approve the application:**
The reviewers indicated that the submission is complete for their reviews. Some deficiencies were identified, and it was agreed to resolve them through Information Requests (IRs).
- 3. If RTF, list any substantive deficiencies or issues that would make this application unsuitable for filing:**
NA

FILING MEETING DISCUSSION, IF FILED:

4. Indicate any comments on the status of the proprietary name review (PNR).

PNR completed (September 27, 2018) – DENG VAXIA acceptable.

5. Indicate whether the product sh/would be subject to lot release, surveillance, or exempt from lot release. Verify sample availability.

Product should be subject to lot release.

6. Confirm review schedule of this application.

Priority Review

7. Indicate the decision regarding the need for an Advisory Committee.

Advisory Committee meeting needed, and VRBPAC scheduled for March 6-7, 2019.

8. Indicate whether the submission triggers PREA; if yes, a PeRC meeting is needed.

The submission triggers PREA, and PeRC meeting is needed.

9. Is a comprehensive and readily located list of all clinical sites included or referenced in the application?

Yes.

10. Is a comprehensive and readily located list of all manufacturing facilities included or referenced in the application?

Out of the five sites listed on form FDA 356h, one site ((b) (4)) is not registered with FDA and does not have a FEI#. CBER asked Sanofi to register this site. Sanofi complied.

11. Indicate any updates since the First Committee Meeting on pre-license inspection, pre-approval inspection, or BIMO sites requiring inspections (Is the establishment(s) ready for inspection?)

DMPQ is planning to schedule the pre-license inspection to occur in December 2018. BIMO inspections were assigned.

12. If the application is affected by the Application Integrity Policy (AIP), has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?

Not affected by AIP.

13. Is the product an Original Biological Product or a New Molecular Entity (NME) for an NDA?

Original Biological Product.

FOR APPLICATIONS IN THE PDUFA PROGRAM (NME NDAs/Original BLAs), IF FILED

14. Confirm that any late submission components were submitted within 30 days. List any late submission components that arrived after 30 days.

There are no late submission components.

15. Was the application otherwise complete upon submission, including those applications where there were no agreements regarding late submission components?

Submission complete.

ADMINISTRATIVE DETAILS, IF FILED:

16. Review the Milestone Schedule and indicate if there are any issues with the schedule. Note: This is a confirmation to capture any changes made since the First Committee Meeting.

There are no issues with the Milestone Schedule.

2.0 DISCUSSION

- Reviewers had no objections to the Priority Review designation or to the Proprietary Name “Dengvaxia”.
- Reviewers indicated that the submission is complete for their reviews, and the deficiencies will be resolved through IRs.
- BIMO reviewers stated that all the planned clinical site inspections are issued.
- Statistical reviewer indicated that the submission is lacking the validation of NS1 assay, and he will formulate an IR after discussion with the CMC reviewer.
- CMC reviewer indicated that he will formulate an IR for the missing potency SOP, and he will work with the DBSQC reviewers for similar issues.
- DMPQ reviewer indicated that he has listed the IR items in his filing checklist.

3.0 CONCLUSION

- During the Filing Meeting, the committee agreed that the application could be filed.

4.0 SUMMARY OF ACTION ITEMS

- Finalize Filing Checklists and upload to EDR via eMRP.
- Finalize the comments to be sent to Sanofi via IRs.
- Issue the Filing/No Deficiencies Identified letter on or before October 30, 2018.
