

Application Type	BLA
STN	125696/0
CBER Received Date	December 21, 2018
PDUFA Goal Date	January 25, 2020
Division / Office	DVRPA /OVRR
Committee Chair	Taruna Khurana
Clinical Reviewer(s)	Kathleen Hise
Project Manager	Diana Oram
Priority Review	No
Reviewer Name(s)	Lei Huang
Review Completion Date / Stamped Date	
Supervisory Concurrence	Tsai-Lien Lin Branch Chief, Vaccine Evaluation Branch, DB, OBE
	John Scott Division Director, Division of Biostatistics, OBE
Applicant	Aimmune Therapeutics, Inc.
Established Name	Peanut (Arachis hypogaea) Allergen Powder
(Proposed) Trade Name	PALFORZIA
Pharmacologic Class	Allergenic
Formulation(s), including Adjuvants, etc	Peanut protein in capsules of 0.5, 1, 10, 20, and 100 mg dosage strengths, and in a sachet of 300 mg dosage strength.
Dosage Form(s) and Route(s) of Administration	Oral powder to be mixed with age-appropriate food prior to administration
Dosing Regimen	Administered in 3 sequential phases: Initial Dose Escalation, Up-Dosing, and Maintenance.
Indication(s) and Intended Population(s)	An oral immunotherapy treatment indicated for the mitigation of allergic reactions, including anaphylaxis, that may occur with accidental exposure to peanut.

Table of Contents

1. Executive Summary	3
2. Regulatory Background	4
3. Sources of data and other information considered in the review	4
3.1 Review Strategy	4
3.2 BLA/IND Document That Serve as the Basis for the Statistical Review	4
4. The July 9, 2019 IR response related to Method TM-0326.....	5
5. Comparability report between tm-0129 and tm-0326	6
5.1 DOC-0318.....	6
5.2 September 23, 2019 IR Response	9
6. Conclusion	10

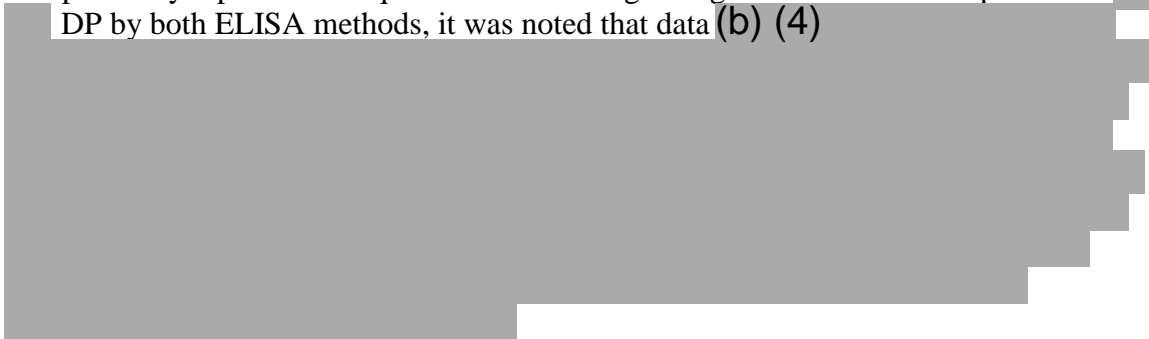
1. EXECUTIVE SUMMARY

Aimmune Therapeutics, Inc. (Aimmune) submitted the original Biologics License Application (BLA 125696) for AR101 (Palforzia). AR101 is a characterized peanut allergen that is used in a regimented oral immunotherapy (OIT) protocol for the mitigation of allergic reactions, including anaphylaxis, that may occur with accidental exposure to peanut. The initiation of AR101 may occur in patients aged 4 through 17 years with a confirmed diagnosis of peanut allergy. AR101 may be continued in patients 18 years of age and older. AR101 is not intended for the immediate relief of peanut allergy symptoms and should be used in conjunction with a peanut-avoidant diet.


This memo covers the statistical review of the non-clinical CMC materials submitted to this BLA. The relative potency of allergenic proteins in AR101 Drug Product (DP) (b) (4) is determined using (b) (4) Enzyme Immunosorbent Assays (ELISAs) for the Ara h1, h2, and h6 protein allergens. Method TM-0129 was developed in February 2015 and was used for testing relative potency mainly for clinical and stability batches. This method was further optimized in 2017 to include changes of moderate and major impacts, and the method was validated and became effective in June 2018 as method TM-0326.

The method development report for TM-0129 was submitted and reviewed under IND 15463. CBER comments were provided to the applicant and were taken into account for method validation. The validation report for TM-0326 was also submitted and reviewed by a statistical reviewer under this IND, and there were a few clarification questions from the reviewer. These IR questions were sent to the applicant after the BLA submission and the applicant provided the responses in STN 125696/0.22. I consider the IR response acceptable and have no additional comments.


During the BLA review, the product reviewer requested that the Method Comparability Report of Relative Potency Methods TM-0129 and TM-0326 (DOC-0318) be reviewed by a statistical reviewer. Therefore, this memo also covers the review of this comparability report. In an equivalence test using data generated from multiple lots of (b) (4) DP by both ELISA methods, it was noted that data (b) (4)



In the September 23, 2019 IR response, the applicant provided the updated equivalence test results. (b) (4)



(b) (4)




I defer to the product reviewer regarding the adequacy of evidence for demonstrating comparability of the two ELISA methods, or whether data from additional samples are needed.

2. REGULATORY BACKGROUND

AR101 contains characterized dosages of total peanut protein from 0.5 mg – 300 mg (0.5, 1, 10, 20, 100, and 300 mg).

The ELISAs are intended to measure the relative potency of the Ara h1, h2, and h6 protein allergens in AR101 DP (b) (4) in comparison to the (b) (4) in house reference standard (IHRS). The IHRS is a characterized lot (b) (4)



The development report of TM-0129 was submitted to IND 15463.110 and the statistical comments were communicated to the applicant on October 20, 2017. The IR response was submitted to IND 15463.119 and the statistical reviewer considered the responses acceptable. The validation report of TM-0326 was submitted to IND 15463.152 and the statistical reviewer considered the results overall acceptable but had a few minor clarification questions. These IR questions were sent to the applicant on June 4, 2019 after the BLA submission and the IR response was submitted to STN 125696/0.22 on July 9, 2019.

3. SOURCES OF DATA AND OTHER INFORMATION CONSIDERED IN THE REVIEW

3.1 Review Strategy

This statistical review focused on the method comparability report for TM-0129 and TM-0326. The July 9, 2019 IR response to the statistical questions regarding validation of TM-0326 was also reviewed.

3.2 BLA/IND Document That Serve as the Basis for the Statistical Review

BLA 125696/0.0 Submitted 12/21/2018

Module 3.2.S.4.3 Validation of Analytical Procedures

REP-0186: Validation Report for TM-0326, Relative Potency of AR101 by ELISA
BLA 125696/0.22 Submitted 07/09/2019

Module 1.11.1 Quality Information Amendment

Response to FDA Information Request #7 (Email Correspondence Dated 31 May 2019)

BLA 125696/0.39 Submitted 09/23/2019

Module 1.11.1 Quality Information Amendment

Response to FDA Information Request #23 (FDA Email Correspondence Dated 06 September 2019)


Of note, the comparability report (DOC-0318) was submitted as an attachment to the July 9, 2019 IR response.

4. THE JULY 9, 2019 IR RESPONSE RELATED TO METHOD TM-0326


FDA comments are repeated here for completeness.

In the validation report, REP-0186:



(b) (4)




(b) (4)



(b) (4)

(b) (4)




Reviewer Comment:

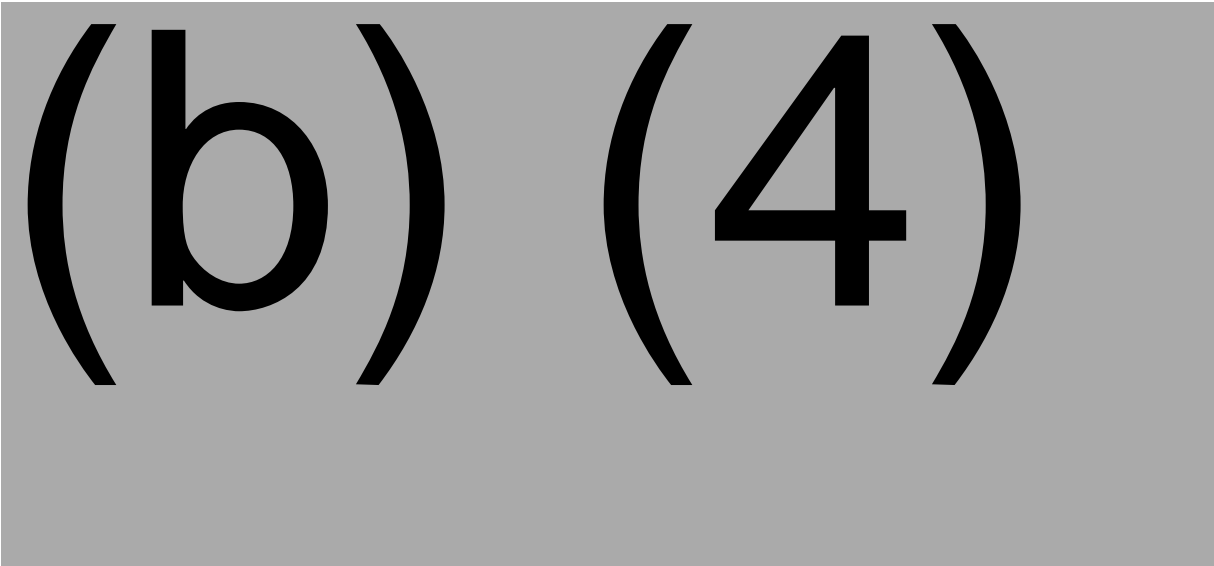
The response is acceptable.

5. COMPARABILITY REPORT BETWEEN TM-0129 AND TM-0326


(b) (4)



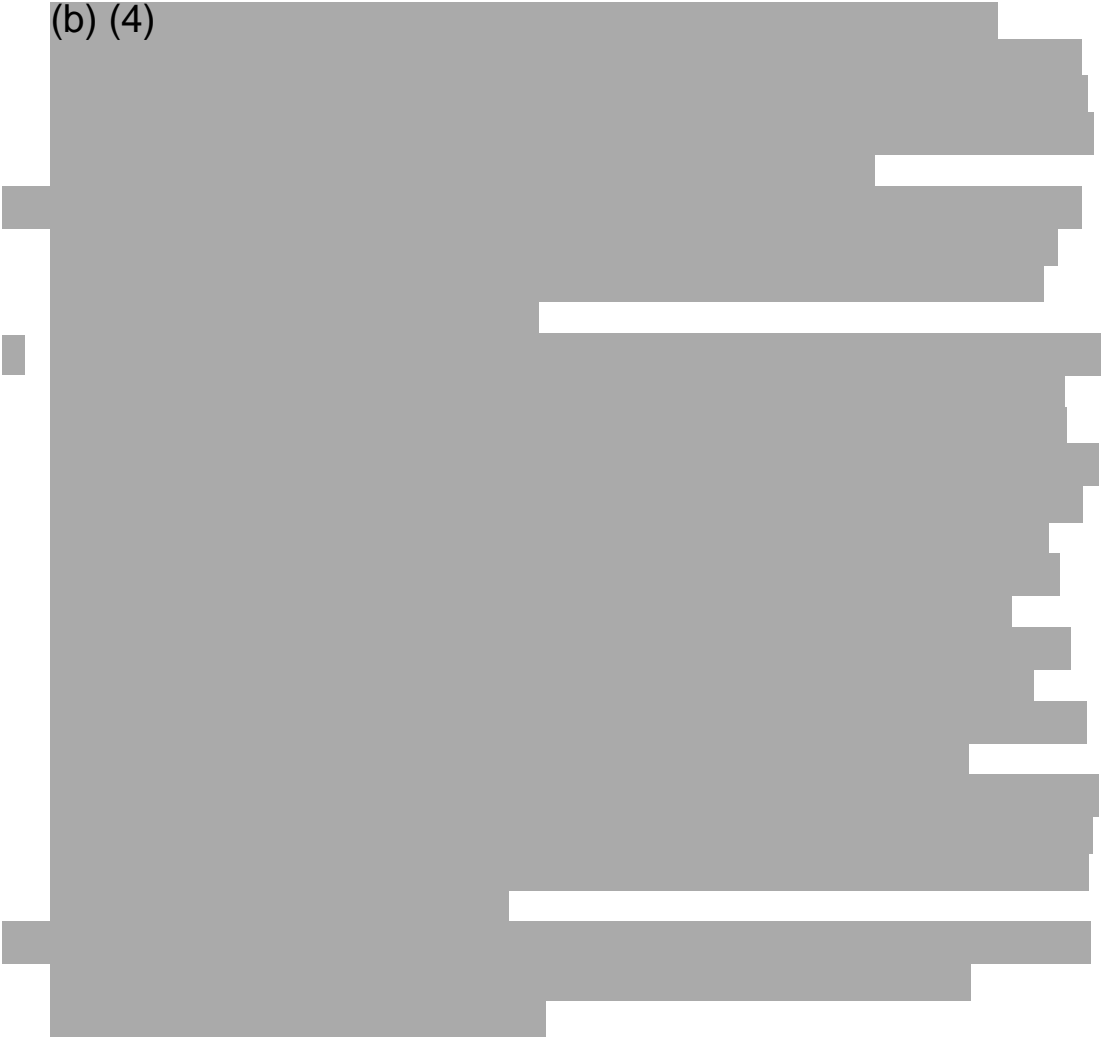
(b) (4)



(b) (4)



(b) (4)




6. CONCLUSION

The validation report for TM-0326 was submitted and reviewed by a statistical reviewer under IND 15463, and there were a few clarification questions from the reviewer. The applicant provided the responses in STN 125696/0.22 and the IR response appeared acceptable. Therefore, I consider the ELISA method TM-0326 validated and suitable for its intended use.

For the Method Comparability Report of Relative Potency Methods TM-0129 and TM-0326 (DOC-0318), it was noted (b) (4)



In the September 23, 2019 IR response, the applicant provided updated equivalence test results. (b) (4)



. I defer to the product reviewer regarding the adequacy of evidence for demonstrating comparability of the two ELISA methods, or whether data from additional samples are needed.