



DBSQC/OCBQ ANALYTICAL METHOD REVIEW MEMO

To: The file: STN 125696/0

From:

Reviewer	Role	Date finalized	Stamp	Supervisor	Stamp
Emnet Yitbarek	Lead Reviewer	10/23/2019		Kori Francis	
Claire Wernly	Reviewer	10/23/2019		James Kenney	

Through Maryna Eichelberger, PhD.
Division Director, DBSQC

Applicant: Aimmune Therapeutics

Subject: Review of Analytical Methods used for Peanut [*Arachis hypogaea*] Allergen Powder (Palforzia) Drug Substance and Drug Product Lot Release

Recommendation: Approvable

Summary:

The following analytical methods used for lot release of Palforzia and the associated analytic method validations or qualifications, were reviewed:

1. Microbial (b) (4) (Claire Wernly)
2. (b) (4) (Claire Wernly)
3. Total protein assay in AR101 (b) (4) drug product by combustion (TM-0066); (Emnet Yitbarek)
4. Determination of (b) (4) in AR101 (b) (4) (Emnet Yitbarek)
5. (b) (4) of AR101 (b) (4) (Emnet Yitbarek)
6. (b) (4) Protein Integrity of AR101 in (b) (4) Drug Products by (b) (4)-HPLC (TM-0067); (Emnet Yitbarek)
7. Determination of (b) (4) (Emnet Yitbarek)

Documents Reviewed

Information in sections of the original submission that describe control of DS and DP (3.2.S.4 and 3.2.P.5, respectively), including descriptions of DS and DP specifications, analytical procedures of DS and DP and validation of these analytical procedures were reviewed. Additional information in amendments specified by each reviewer were also reviewed.

Background:

Aimmune submitted a BLA, STN 125696 for Palforza, a peanut (*Arachis hypogaea*) allergen powder, on 12/21/2018. The Drug Substance (DS) is a partially defatted peanut powder, that contains (b) (4) protein. The Drug Product (DP) is available in 0.5, 1, 10, 20, 100, and 300mg dosage strengths and is composed of different amounts of peanut powder and excipients, including microcrystalline cellulose (MCC), partially pregelatinized maize starch, colloidal silicon dioxide, and magnesium stearate. This product is proposed for regimented oral immunotherapy (OIT) to reduce the risk of anaphylaxis in a peanut-allergic individual after accidental exposure to peanuts in patients 4 through 17 years old.

1. Microbial (b) (4) (Claire Wernly)

(b) (4)

(b) (4)

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(b) (4) . CBER finds the information provided acceptable.

Conclusion: The Microbial (b) (4) test is adequately described and qualified for testing (b) (4) DP.

(b) (4)

(b) (4)

(b) (4)



3. Total protein and content uniformity determination in AR101 by Dumas combustion method (TM-0066); (Emnet Yitbarek)


The Analytical Procedure TM-0066, is a quantitative combustion method used for the determination of total protein and content uniformity in (b) (4) drug product (DP) samples. The test will be performed at CoreRx, Inc. laboratory. The specifications for total protein content in (b) (4) drug product release are as follows:

- Total protein content:
 - (b) (4)
 - DP (0.5 and 1 mg): (b) (4) of label claim



- DP (10, 20, 100 and 300 mg): (b) (4) of label claim
- Content Uniformity (CU):
 - DP (0.5 and 1 mg): Individual values within (b) (4) of label claim; RSD (b) (4)
 - DP (10, 20, 100, and 300 mg): Acceptance Value (AV) (b) (4) variability in protein content between (b) (4) vials; if AV (b) (4) then test (b) (4) additional units. In the latter case, AV must be (b) (4) and criteria must be met for individual units.

Method

The combustion assay (TM-0066) is based on the Dumas method which determines total nitrogen content in a sample. (b) (4)



(b) (4)



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Method Validation

Performance of the assay (TM-0066) was validated for specificity, accuracy, linearity, precision, and robustness, using (b) (4) drug product samples. The validation was performed at CoreRx Inc laboratory.

Specificity was evaluated by demonstrating (b) (4)

. Hence, the acceptance criteria were met and specificity of the test for DP has been demonstrated.

Accuracy was determined (b) (4)

Hence, the acceptance criterion for accuracy was met.

Precision was determined (b) (4)

The results for precision (IP, inter- & intra-run precision) all met the %RSD acceptance criteria.

Linearity was determined (b) (4)

(b) (4)

]

(b) (4)

Review of the Response:

The sponsor provided the requested data on 08/30/2019 (STN 125696/0.34) to demonstrate linearity by assessing (b) (4)

The range of the method was demonstrated (b) (4)

The robustness of the method was evaluated (b) (4)

Therefore, robustness criteria were met.

Conclusion: The Dumas combustion method is adequately described and validated for determining total protein and content uniformity of (b) (4) DP.

4. (b) (4) Protein Integrity of AR101 (b) (4)
Drug Products by (b) (4) High Performance Liquid
Chromatography (b) (4)-HPLC), TM-0067; (Emnet Yitbarek)

TM-0067 is used for the (b) (4)
to determine protein integrity from the (b) (4)
DP samples. The method uses (b) (4)


The
information requests are included in italics below, followed by a summary of the
manufacturer's response and my review of the response:

Information request was submitted to the sponsor on 05/31/2019; the sponsor's
response was received on 07/03/2019.

(b) (4)


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Information request was submitted to the sponsor on 08/22/2019; the sponsor's response was received on 08/30/2019.

(b) (4)

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Review of the Response:

The sponsor understands the method (TM-0067) lacks (b) (4)

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Procedure suitability criteria and specifications: (b) (4)

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(b) (4)

Method validation

The following validation parameters were evaluated for TM-0067: specificity, repeatability, intermediate precision, linearity, accuracy and range.

Specificity was demonstrated by (b) (4)

hence the requirement for specificity was met.

Repeatability was determined (b) (4)

hence, the requirement for repeatability was

met.

Intermediate precision (IP) was determined (b) (4)

hence, the requirement for IP was met.

Linearity was determined (b) (4)

hence, the requirement for linearity was met.

Accuracy was determined (b) (4)

(b) (4)

hence, the requirement for accuracy was met.

Range was established based the (b) (4)

the results demonstrate the method was repeatable, linear and accurate over the specified range.

Conclusion: The (b) (4)-HPLC method is adequately described and validated for determining (b) (4) protein integrity of (b) (4) in (b) (4) DP.

(b) (4)

(b) (4)

(b) (4)

