FDA U.S. FOOD & DRUG ADMINISTRATION

Technical Project Lead (TPL) Review of SE Report

New Product Subject of this Review	
Submission tracking number (STN)	SE0015386
Common Attributes	
Submission date	August 6, 2019
Receipt date	August 6, 2019
Applicant	BBK Tobacco & Foods LLP dba HBI International
Product manufacturer	BBK Tobacco & Foods LLP dba HBI International and Blaugrana Corporation
Application type	Regular
Product category	Cigars
Product subcategory	Cigar Component
Cross-Referenced Submission	
SE0015386	(b)(4)
Supporting FDA Memoranda Relied Upon in this Review	
SE0015386	• Behavioral and Clinical Pharmacology (BCP) Reviews of Characteristic Changes in SE Reports (March 05, 2018) • Product quantity changes in Substantial Equivalence Reports (SE Reports) for statutorily regulated tobacco products (December 7, 2018) • Addendum to February 24, 2017, Equivalence Testing for SE Evaluations Memo (February 24, 2017 and April 16, 2019) • Harmful and potentially harmful constituent (HPHC) comparison and evaluation procedure for comparing two tobacco products in the substantial equivalence reports, February 21, 2019 • Engineering review of substantial equivalence (SE) Reports for originally regulated Products (March 2019) • BCP Consult Request Memo for SE0015386 (April 29, 2021)
Recommendation	
Issue a Substantially Equivalent (SE) order for the new tobacco product subject of this review.	

Technical Project Lead (TPL):

Digitally signed by Karen M. Coyne -S
Date: 2021.06.21 08:10:24 -04'00'

Karen Coyne, Ph.D.
Associate Director, Division of Product Science
Office of Science

Signatory Decision: Concur with TPL recommendation and basis of recommendation

Todd L. Cecil, Ph.D.
Deputy Director
Office of Science

TABLE OF CONTENTS

1. BACKGROUND

1.1. NEW AND PREDICATE PRODUCTS

The applicant submitted information for the new and predicate products listed in detail in Appendix A.

1.2. REGULATORY ACTIVITY

On August 27, 2019, FDA issued an Acceptance letter. On October 28, 2019 and June 3, 2020, FDA issued Deficiency letters to the applicant. See Appendix B for amendments.

1.3. SCOPE OF REVIEW

This review captures all compliance, regulatory, and scientific reviews completed for the new product that is the subject of this review. Tobacco product master file (TPMF) (b)(4) , was reviewed by chemistry on March 31, 2021.

Table 1. Disciplines reviewed

Discipline	Cycle 1		Cycle 2	
	Reviewer	Review Date	Reviewer	Review Date
Regulatory	Kaylene Charles	8/27/2019	Not Assigned	N/A
Chemistry	Melis Coraggio	10/15/2019	Melis Coraggio	5/27/2020
Engineering	Nashaat Rasheed	10/11/2019	Rashele Moore	5/20/2020
Toxicology	Eric Beier	9/27/2019	Not Assigned	N/A
Social Science	Catherine Kemp	10/2/2019	Not Assigned	N/A
Environmental Science	Rudaina Alrefai-Kirkpatrick	9/27/2019	Rudaina Alrefai-Kirkpatrick	5/15/2020

Discipline	Cycle 3	
	Reviewer	Review Date
Regulatory	Not Assigned	N/A
Chemistry	Delauren McCauley	5/3/2021
Engineering	Mary Searing	4/26/2021
Toxicology	Atinuke Ajiboye	4/27/2021
Social Science	Not Assigned	N/A
Environmental Science	Vyomesh Patel	4/26/2021

Table 2. Consults

Discipline	Reviewer	Review Date
Behavioral and clinical pharmacology	Allison Kurti	4/29/2021

2. COMPLIANCE REVIEW

The Office of Compliance and Enforcement (OCE) completed a review to determine whether the applicant established that the predicate product is a grandfathered product (i.e., was commercially marketed in the United States as of February 15, 2007). The OCE review dated September 27, 2019, concludes that the evidence submitted by the applicant is adequate to demonstrate that the predicate product is grandfathered and, therefore, is an eligible predicate product.

OCE also completed a review to determine whether the new product is in compliance with the Federal Food, Drug, and Cosmetic Act (FD&C Act) (see section 910(a)(2)(A)(i)(II) of the FD&C Act). The OCE review dated April 26, 2021, concludes that the new product is in compliance with the FD&C Act.

3. SCIENTIFIC REVIEW

Scientific reviews were completed by the Office of Science (OS) for the following disciplines:

3.1. CHEMISTRY

The final chemistry review concludes that the new product has different characteristics compared to the predicate product, but the differences do not cause the new product to raise different questions of public health from a chemistry perspective.

The new and predicate product are cigar cones made of (b)(4) and a paper tip secured with both paper tip adhesive and side seam adhesive. The new product is 2.54 cm shorter and composed of 24.8% (b)(4) mg/cone) less (b)(4). The applicant provided the composition of the (b)(4) and demonstrated that the decrease in product length in the new product is proportional to the decrease in ingredients in the (b)(4). The package quantity increased from one cigar tube per plastic container in the predicate product, to two cigar tubes per plastic container in the new product. Social science evaluated the increase in package quantity.

The paper tip in the new product is unbleached and the paper tip in the predicate product is bleached. The tip is not intended to be combusted and is entirely covered by the (b)(4), so it is not expected to come into direct contact with the user. As a result, the difference in the bleaching of the tips and the resulting color difference between the tips are not expected to cause the new product to raise different questions of public health from a chemistry perspective.

Sweetener, flavor, and adhesives are applied manually to the manufactured cones. The applicant provided quantities of the sweetener, flavor, and adhesive relative to the total stuffed cone weights in the new and predicate product. All ingredient differences are minor and not expected to significantly affect the mainstream smoke yields between the new and predicate product. Therefore, the ingredients in the new product do not raise different questions of public health, from a chemistry perspective.

For mainstream smoke analysis, the applicant used a third-party lab, who authorized the applicant to reference their TPMF (b)(4)). The TPMF contained sufficient information to support this review.

The applicant provided method summaries, raw data for harmful and potentially harmful constituents (HPHC), and reference data. American Spirit RYO tobacco was used to generate mainstream smoke yields for the new and predicate product. Tar, nicotine, and carbon monoxide (TNCO) smoke yields were generated using CORESTA Recommended Method No. 64 (CRM 64, Routine Analytical Cigar-Smoking Machine – Specification, Definitions and Standard Conditions). The applicant adequately justified using CRM 64 rather than the Canadian Intense (CI) smoking regimen. The applicant stated that the new and predicate products are cigar components. Furthermore, the total particulate matter (TPM) values were above 150 mg when using the CI regimen. The applicant stated that TPM greater than 150 mg on a 44 mm Cambridge pad can lead to breakthrough, and thus they used CRM 64 for TNCO testing instead. All other HPHC mainstream smoke yields for the new and predicate products were generated using the CI regimen. Acrolein, N-nitrosonornicotine (NNN), and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) smoke yields in the new and predicate product, were determined to be analytically equivalent. There was a 20% analytically nonequivalent increase in formaldehyde in the new product. All other mainstream smoke yields were analytically nonequivalent, but decreased in the new product: acetaldehyde (↓36%), acrylonitrile (↓29%), benzene (↓26%), benzo[a]pyrene (↓17%), butadiene (↓22%), crotonaldehyde (↓38%), isoprene (↓35%), toluene (↓33%), tar (↓32%), carbon monoxide (↓42%), and nicotine (↓32%). The decreased yields do not cause the new product to raise different questions of public health from a chemistry perspective. The decrease in nicotine was evaluated by behavioral and clinical pharmacology. Additionally, the analytically nonequivalent increase in formaldehyde and analytically nonequivalent decreases in tar, nicotine, and carbon monoxide in mainstream smoke yields were deferred to toxicology.

Therefore, the differences in characteristics between the new and predicate product do not cause the new product to raise different questions of public health from a chemistry perspective.

3.2. ENGINEERING

The final engineering review concludes that the new product has different characteristics compared to the predicate product, but the differences do not cause the new product to raise different questions of public health from an engineering perspective.

The applicant provided target specifications, range limits, and test data to characterize the new and predicate products. There was a 25% decrease in overall length, 10% increase in minimum width, 44% decrease in wrapper mass, and 43% decrease in cone volume. Changes in these design parameters can affect TNCO mainstream smoke yields, and these changes were deferred to chemistry. Social science evaluated the decreases in length and volume as they may affect consumer perceptions.

Therefore, the differences in characteristics between the new and predicate product do not cause the new product to raise different questions of public health from an engineering perspective.

3.3. TOXICOLOGY

The final toxicology review concludes that the new product has different characteristics compared to the predicate product, but the differences do not cause the new product to raise different questions of public health from a toxicology perspective.

Toxicology determined that there are no differences between the ingredients in the new and predicate product that cause toxicological concern. Chemistry deferred the analytically nonequivalent increase in formaldehyde (20%) and analytically nonequivalent decreases in tar (32%), nicotine (32%), and carbon monoxide (42%) in mainstream smoke yields to toxicology. The analytically nonequivalent lower yields of TNCO in the new product do not cause toxicological concern. Furthermore, toxicology determined that the higher formaldehyde yield in the new product is offset by lower yields of acetaldehyde (36%), acrylonitrile (29%), benzene (26%), benzo[a]pyrene (17%), butadiene (22%), carbon monoxide (31%), crotonaldehyde (38%), isoprene (35%), and toluene (33%) in the new product.

Therefore, the differences in characteristics between the new and predicate product do not cause the new product to raise different questions of public health from a toxicology perspective.

3.4. BEHAVIORAL AND CLINICAL PHARMACOLOGY

The behavioral and clinical pharmacology consult concludes that the new product has different characteristics compared to the predicate product, but the differences do not cause the new product to raise different questions of public health from a behavioral and clinical pharmacology perspective.

Nicotine yield was substantially lower in the new product (2.73 mg) compared to the predicate product (4.04 mg; 32% lower, or 1.31 mg less nicotine/cone). Systematic evaluations of the relationship between nicotine yield and cigarette use behaviors and smoking topography have demonstrated compensatory smoking of lower nicotine yield cigarettes (i.e., smoking more intensely or frequently to recover some of the nicotine lost in lower-yield cigarettes). However, comparable studies have not been published for cigar products.

Although there is some variability in nicotine yield across commercial cigarettes, most commercial cigarettes typically produce nicotine yields around 1 mg, and compensatory puffing is typically observed in cigarettes with nicotine yields at or below this level. However, the new product produced a nicotine yield more than double the average nicotine yield of commercially available cigarettes and nicotine yields at which compensatory puffing has been observed. Compensatory use has not been studied in cigar products or combusted tobacco products with nicotine yields above those typically associated with commercial cigarettes (i.e., above 1 mg). Thus, it remains unknown whether decreases to nicotine yield in products with substantially higher nicotine yields, such as those observed in the new product, will influence use behavior. There is no evidence indicating that compensatory smoking occurs when using lower nicotine yield cigar products.

Therefore, the differences in characteristics between the new and predicate product do not cause the new product to raise different questions of public health from a behavioral and clinical pharmacology perspective.

3.5. SOCIAL SCIENCE

The social science review concludes that the new product has different characteristics compared to the predicate product, but the differences do not cause the new product to raise different questions of public health from a social science perspective.

The new product has two cones per package compared to one cone per package in the predicate, a 100% increase. For statutorily regulated tobacco products such as roll-your-own (RYO) filters, tubes, and paper, changes in quantity of these RYO products do not raise different questions of public health from the social science perspective. Although the new and predicate products are a cigar component, the rationale and conclusions outlined for RYO products is the same for cigar products. There is no cigar component specific scientific information to conclude otherwise. Therefore, based on the evidence available at this time, the change in product quantity does not cause the new product to raise different questions of public health from the social science perspective.

In the new product, the total cone length is 26 mm (25%) shorter, the cone portion that would contain tobacco is 36 mm (38%) shorter in length, and the calculated effective volume is 5497 mm^3 (43%) less. As the new product is shorter in length and smaller in volume, the size of the cone could affect consumer perceptions. However, there is no currently available scientific evidence on the influence of the size of cones on consumer perceptions or use intentions to indicate that such reductions in product size would cause the new product to raise different questions of public health from a social science perspective.

Therefore, the differences in characteristics between the new and predicate product do not cause the new product to raise different questions of public health from a social science perspective.

4. ENVIRONMENTAL DECISION

A finding of no significant impact (FONSI) was signed by Luis Valerio, Ph.D. on May 3, 2021. The FONSI was supported by an environmental assessment prepared by FDA on May 3, 2021.

5. CONCLUSION AND RECOMMENDATION

The new and the predicate product have the following characteristics:

Chemistry evaluation complete:

- Package quantity: The new product is packaged two cones per plastic tube while the predicate product is packaged one cone per plastic tube.
- Cigar Cone:
  - Decrease in (b)(4) (↓24.8%)
  - Blend information and tobacco quantity for the (b)(4)
  - The paper tip in the new product is unbleached and the paper tip in the predicate product is bleached.
- HPHCs:
  - Analytically nonequivalent increase in formaldehyde (↑20%)

  - Analytically nonequivalent decreases in tar (↓32%), nicotine (↓32%), and carbon monoxide (↓42%) (TNCO) and acetaldehyde (↓36%), acrylonitrile (↓29%), benzene (↓26%), benzo[a]pyrene (↓17%), butadiene (↓22%), crotonaldehyde (↓38%), isoprene (↓35%), and toluene (↓33%)
  - Analytically equivalent decreased yields in acrolein (↓11%), N-nitrosonornicotine (NNN) (↓11%), and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) (↓9%)
- Ingredients:
  - Side seam adhesive: ↑0.07% (b)(4) [redacted]
  - Sweetener: ↑0.22% (b)(4) [redacted]
  - Flavor: ↑0.7% (b)(4) [redacted]

Engineering evaluation complete:

- Decrease in overall length (25%)
- Increase in minimum width (10%)
- Decrease in wrapper mass (44%)
- Decrease in cone volume (43%)

Toxicology evaluation complete:

- Tar (↓32%), CO (↓42%), and nicotine (↓32%) are analytically nonequivalent and decreased in the mainstream smoke of the new product compared to the predicate product
- Analytically nonequivalent increase in formaldehyde (↑20%)

Behavioral and clinical pharmacology evaluation complete:

- Decrease in nicotine (↓32%, 1.31 mg/cone)

Social science evaluation complete:

- New product has 100% more product units per package
- Decrease in total length (↓25%) and effective volume (↓43%)

I concur with the conclusions of all the scientific reviews that the applicant has demonstrated that these differences in characteristics do not cause the new product to raise different questions of public health as described in Section 3.1-3.5 above. The new and predicate product are cigar cones with a tip packaged in a plastic tube. The new product has two cones per package compared to one cone per package in the predicate. The new product tip is unbleached while the predicate product tip is bleached. Because the tip is covered completely by the cone, does not contact the lips, and is not combusted, the unbleached new product tip does not raise different questions of public health. The identical container closure system, decrease in (b)(4) [redacted], and minimal differences in sweetener, flavor, and adhesive do not cause the new product to raise different questions of public health. The new product has decreases in overall length, wrapper mass, and cone volume and an increase in minimum width, which were deferred to chemistry to evaluate the impact on TNCO. Mainstream TNCO smoke yields were analytically nonequivalent and decreased in the new product: tar (↓32%) nicotine (↓32%), and carbon monoxide (↓42%). However, formaldehyde smoke yields were , analytically non-equivalently increased 20% in the new product. Because TNCO smoke yields decrease in the new product, the design parameter changes do not cause the new product to raise different questions of public health. Social science determined that the deceases in product size and product quantity do not cause the new product to raise different questions of public health. Additionally, behavioral and clinical pharmacology determined that the significant decrease in

nicotine does not cause the new product to raise different questions of public health based on the available evidence at this time regarding cigar components. Furthermore, toxicology determined that the higher yield of formaldehyde in the new product is offset by lower yields of acetaldehyde (36%), acrylonitrile (29%), benzene (26%), benzo[a]pyrene (17%), butadiene (22%), carbon monoxide (31%), crotonaldehyde (38%), isoprene (35%), and toluene (33%). Therefore, the differences in characteristics between the new and predicate product do not cause the new product to raise different questions of public health.

The predicate product meets statutory requirements because it was determined that it is a grandfathered product (i.e., were commercially marketed in the United States as of February 15, 2007).

The new product is currently in compliance with the FD&C Act. I concur with these reviews and recommend that an SE order letter be issued. FDA examined the environmental effects of finding this new product substantially equivalent and made a finding of no significant impact.

6. APPENDICES

Appendix A. New and predicate products

Common Attributes		
Submission date	August 6, 2019	
Receipt date	August 6, 2019	
Applicant	BBK Tobacco & Foods LLP dba HBI International	
Product manufacturer	BBK Tobacco & Foods LLP dba HBI International and Blaugrana Corporation	
Product category	Cigars	
Product subcategory	Cigar Component	
Attributes	**New Product**	**Predicate Product**
STN	**SE0015386**	**N/A**
Product name	CYCLONES HONEY 2FER[a]	CYCLONES HONEY[a]
Eligibility status	Not applicable	Grandfathered
Package type	Plastic Tube	Plastic Tube
Package quantity	2 Cones	1 Cone
Characterizing flavor	Honey	Honey
Length	79 mm	105 mm
Diameter-1[b,c]	10 mm	10 mm
Diameter-2[b,c]	15 mm	16 mm
Additional property	Plastic Taper Wooden Stick	Plastic Taper Wooden Stick

[a] Brand/sub-brand or other commercial name used in commercial distribution.
[b] Applicant provided radius which allowed for a calculation of diameter
[c] Applicant provided two measurements, one for the widest end of the cone, and the second for the tapered end where the paper tip is set.

Appendix B. Amendments

Submission Date	Receipt Date	Amendment	Applications being amended	Reviewed	Brief Description
September 11, 2019	September 11, 2019	SE0015437	SE0015386	Yes	Response to September 6, 2019, FDA Information Request
September 12, 2019	September 12, 2019	SE0015473	SE0015386	Yes	Response to September 12, 2019, FDA Information Request
April 10, 2020	April 10, 2020	SE0016004	SE0015386	Yes	Response to October 28, 2019, Deficiency Letter
October 14, 2020	October 15, 2020	SE0021982	SE0015386	Yes	Response to June 3, 2020, Deficiency Letter