FDA U.S. FOOD & DRUG ADMINISTRATION

Technical Project Lead (TPL) Review:

SE0000603

SE0000603: Lark White Pack Soft Pack	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	83 mm
Diameter	7.89 mm
Ventilation	45%
Characterizing Flavor	None
Common Attributes of SE Reports	
Applicant	Philip Morris USA, Inc.
Report Type	Provisional
Product Category	Cigarette
Product Sub-Category	Combusted Filtered
Recommendation	
Issue a Not Substantially Equivalent (NSE) order.	

Technical Project Lead (TPL):

Matthew J. Walters -S
2018.07.27 09:49:31 -04'00'

Matthew J. Walters, Ph.D., MPH
CDR, US Public Health Service
Deputy Director
Division of Product Science

Signatory Decision:

☐ Concur with TPL recommendation and basis of recommendation

☐ Concur with TPL recommendation with additional comments (see separate memo)

☒ Do not concur with TPL recommendation (see separate memo)

Digitally signed by Matthew R. Holman -S
Date: 2018.07.27 09:58:10 -04'00'

Matthew R. Holman, Ph.D.
Director
Office of Science

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1. BACKGROUND

1.1. PREDICATE TOBACCO PRODUCT

The applicant submitted the following predicate tobacco product:

SE0000603: Lark White Pack Soft Pack	
Product Name	Lark Lights Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.89 mm
Ventilation	45%
Characterizing Flavor	None

The predicate tobacco product is a combusted filtered cigarette manufactured by the applicant.

1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

FDA received a SE Report (SE0000603) for Lark White Pack Soft Pack on March 18, 2011, which was submitted by Altria Client Services Inc. (ALCS) on behalf of Philip Morris USA Inc. (PM USA). FDA acknowledged the SE Report on September 1, 2011. FDA issued an Advice/Information Request (A/I) letter on October 25, 2012. On November 19, 2012, FDA received the response to the A/I letter (SE0005128)[1] . On December 16, 2012, FDA assigned these products to PHI Tier 3. On January 24, 2013, FDA received an amendment (SE0006706) to correct previously submitted data. On May 30, 2013, FDA received the environmental assessment in response to the October 25, 2012, A/I letter (SE0008797). On March 28, 2014, FDA requested the applicant to provide the number of cigarettes per pack for the new tobacco product. On March 30, 2014, FDA received the response to the applicant's response to the information request (SE0010332). FDA issued Notification letter on April 4, 2014, indicating scientific review was expected to begin on May 20, 2014. On May 16, 2014, FDA received an amendment (SE0010491) to update information previously submitted. On September 18, 2015, FDA received an amendment (SE0012370) to correct the ingredient table in the previous submissions. The scientific review resulted in a finding of new information regarding the use of (b) (4) filters. This prompted a second PHI review on December 19, 2016, in which FDA reassigned SE0000603 to PHI Tier 2. Therefore, as explained in the March 14, 2017 memo, FDA continued with scientific review. FDA issued an Advice/Information Request (A/I) letter on March 16, 2017. On March 23, 2017, FDA received an email from the applicant to request a clarification of Deficiency 9 within the A/I Request letter. FDA provided the response to the applicant's clarification questions on March 27, 2017. On March 30, 2017, FDA received a time extension request (SE0014011). On April 7, 2017, FDA conducted a telecon to request additional information concerning the harmful or potentially harmful constituents (HPHCs) and products that will be tested pertaining to the extension request. On April 12, 2017, FDA received the response to the information

[1] FDA completed an administrative review on March 28, 2013, and incorrectly entered the first commercial market date. The first commercial market date entered did not meet the criteria necessary for provisional SE Report status. After commencement of scientific review, FDA identified that the first commercial market dates noted in our records were incorrect. On December 29, 2015, a review corrected this error.

request (SE0014029). FDA issued the Extension Granted letter on April 13, 2017. On June 27, 2017, FDA received a request (SE0014186) to the Extension Granted letter dated April 13, 2017, which stated that, due to a manufacturing issue with the laboratory, the applicant needed additional time to remanufacture the predicate products. To address the manufacturing issue with the laboratory and obtain the data needed to respond to the March 16, 2017, A/I letter, the applicant requested an additional two-week extension and proposed a new response due date of July 31, 2017. On July 6, 2017, FDA contacted the applicant for the details of the manufacturing issue. The applicant explained that the cigarette making system did not make the cigarettes with the correct weight; specifically, the filler weight did not meet their specifications. On July 12, 2017, FDA issued the second Extension Granted letter. On August 15, 2017, FDA received an amendment (SE0014238) in response to the A/I letter dated March 16, 2017. On October 23, 2017, FDA issued a Preliminary Finding (PFind) letter. On November 21, 2017, FDA received the response to the PFind letter (SE0014406), which included a claim of categorical exclusion.

Product Name	SE Report	Amendments
Lark White Pack Soft Pack	SE0000603	SE0005128 SE0006706 SE0008797 SE0010332 SE0010491 SE0012370 SE0014011 SE0014029 SE0014186 SE0014238 SE0014406

1.3. SCOPE OF REVIEW

This review captures all regulatory, compliance, and scientific reviews completed for this SE Report.

2. REGULATORY REVIEW

Regulatory reviews were completed by Jennifer German on October 25, 2012, Jonathan Kwan on March 28, 2013, and Grace Kaiyuan on December 29, 2015.

The reviews conclude that the SE Report is administratively complete.

3. COMPLIANCE REVIEW

The Office of Compliance and Enforcement (OCE) completed a review to determine whether the applicant established that the predicate tobacco product is a grandfathered product (i.e., was commercially marketed in the United States other than exclusively in test markets as of February 15, 2007). The OCE review dated April 24, 2014, conclude that the evidence submitted by

the applicant is adequate to demonstrate that the predicate tobacco product is grandfathered and, therefore, is an eligible predicate tobacco product[2].

4. SCIENTIFIC REVIEW

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

4.1. CHEMISTRY

Chemistry reviews were completed by Katherine Lovejoy on July 30, 2014, Stephanie Daniels on October 13, 2017, and Caroline Agarabi on January 22, 2018.

The final chemistry review concludes that the new tobacco product has different characteristics related to product chemistry compared to the predicate tobacco product but the differences do not cause the new tobacco product to raise different questions of public health. The review identified the following differences:

- Increase in (b) (4)
- Increase in (b) (4)
- Increase in (b) (4)
- Decrease in (b) (4)
- Addition of (b) (4)
- Decrease in (b) (4)
- Increase in formaldehyde (19%) yield under the Canadian Intense (CI) smoking regimen

The predicate product identified by the applicant was unavailable for HPHC testing. As a result, the applicant remanufactured the predicate product, which is referred to as a surrogate predicate product. The review determined the surrogate predicate product to be suitable as the tobacco blends, ingredients, and product design parameters were identical or nearly identical to these characteristics in the predicate product, allowing extrapolation of HPHC data to the predicate product. The difference in formaldehyde levels between the new and surrogate predicate product was determined to be statistically significant and ,as such, was evaluated further by toxicology to determine if this difference causes the new product to raise different questions of public health following an evaluation of the acceptability of the analytical methods from chemistry, which were determined to be acceptable. Therefore, the differences in characteristics between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health related to product chemistry.

4.2. ENGINEERING

Engineering reviews were completed by Julie Morabito on July 30, 2014, and Michael Morschauser on October 6, 2017, and January 23, 2018.

The final engineering review concludes that the new tobacco product has different characteristics related to product engineering compared to the predicate tobacco product but

[2] An addendum review was completed on February 16, 2018, to clarify that the characterizing flavor of the predicate tobacco product is “none.” The addendum review does not change the conclusion of the initial determination.

the differences do not cause the new tobacco product to raise different questions of public health. The review identified the following issue related to product engineering:

- Decrease in filler mass
- Decrease in the cigarette length

The new and predicate product use (b) (4) in the filters. The distribution of the (b) (4) as well as the lengths of each filter subsection, are identical for the new and predicate product, and therefore do not cause the new products to raise different questions of public health. The new product has a tobacco filler mass that is lower than the predicate product. However, the change is minimal (5%). In addition, the tobacco filler mass reduces smoke yield constituents as provided by the applicant, the HPHCs yields decreased . Therefore, this change does not cause the new product to raise different questions of public health. The new and predicate products initially used multiple materials for filter tow, plug wrap, and tipping paper. However, the multiple materials have since been withdrawn and only a single filter tow, plug wrap, and tipping paper was identified. Therefore, the differences in characteristics between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health related to product engineering.

4.3. TOXICOLOGY

Toxicology reviews were completed by Prabha Kc on November 23, 2016, and on October 13, 2017, and Eric Beier on January 19, 2018.

The final toxicology review concludes that the new tobacco product has different characteristics related to product toxicity compared to the predicate tobacco product and that the SE Report does not contain sufficient detail to determine that the differences with respect to product toxicology does not cause the new tobacco product to raise different questions of public health. The review identifies the following deficiency[3] that has *not* been adequately resolved:

1. SE0000603 indicates that that the yield under the Canadian Intense smoking regimen of formaldehyde is significantly higher (↑19.4%) in the new product relative to the predicate product. As formaldehyde is a known human carcinogen and potentially contributes to cigarette smoke-related chronic obstructive lung disease, you needed to provide adequate scientific evidence and rationale for why this increase in formaldehyde yields does not cause the new product to raise different questions of public health.

Therefore, the review concludes that the applicant did not demonstrate that the differences in characteristics between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health from a toxicology perspective.

[3] The final toxicology review refers to an increase in formaldehyde relative to the predicate product. However, it should state it is relative to the surrogate predicate product.

5. ENVIRONMENTAL DECISION

Under 21 CFR 25.35(b), issuance of an order finding a tobacco product not substantially equivalent (NSE) under section 910(a) of the FD&C Act is categorically excluded and, therefore, normally does not require the preparation of an environmental assessment (EA) or environmental impact statement. FDA has considered whether there are extraordinary circumstances that would require the preparation of an EA and has determined that none exist.

6. CONCLUSION AND RECOMMENDATION

The following are the differences in characteristics between the new and corresponding predicate tobacco products:

- Increase in (b) (4)
- Increase in (b) (4)
- Increase in (b) (4)
- Decrease in (b) (4)
- Addition of (b) (4)
- Decrease in (b) (4)
- Decrease in filler mass
- Decrease in the cigarette length
- Increase in formaldehyde (19%) yield under the Canadian Intense (CI) smoking regimen

The applicant has failed to demonstrate that these differences in characteristics does not cause the new tobacco product to raise different questions of public health. Formaldehyde is a known human carcinogen and potentially contributes to cigarette smoke-related chronic obstructive lung disease. The applicant did not adequately provide scientific evidence and rationale for why this increase in formaldehyde yield does not cause the new product to raise different questions of public health. Therefore, the applicant has failed to provide sufficient information to support a finding of substantial equivalence.

The predicate tobacco product meets statutory requirements because it is a grandfathered product (i.e., was commercially marketed in the United States other than exclusively in test markets as of February 15, 2007).

The toxicology review concludes that the new tobacco product has different characteristics compared to the predicate tobacco product and that the SE Report lacks adequate evidence to demonstrate that the differences do not cause the new tobacco product to raise different questions of public health. I concur with this review and recommend that an NSE order letter be issued.

Because the proposed action is issuing an NSE order, it is a class of action that is categorically excluded under 21 CFR 23.35(b). FDA has considered whether there are extraordinary circumstances that would require the preparation of an environmental assessment and has determined that none exist. Therefore, the proposed action does not require preparation of an environmental assessment or an environmental or an environmental impact statement.

A NSE order letter should be issued for the new tobacco product in SE0000603 as identified on the cover page of this review. The NSE order letter should cite the following deficiency:

1. Your SE Report indicates that that the yield under the Canadian Intense smoking regimen of formaldehyde is significantly higher (19%) in the new product relative to the surrogate predicate product. As formaldehyde is a known human carcinogen and potentially contributes to cigarette smoke-related chronic obstructive lung disease, you needed to provide adequate scientific evidence and rationale for why this increase in formaldehyde yields does not cause the new product to raise different questions of public health.