



Technical Project Lead (TPL) Review:

SE0007297-SE0007304

SE0007297: Largo Sun Grown Natural 8oz Bag	
Package Type	Bag
Package Quantity	227 grams
Characterizing Flavor	None
SE0007298: Largo Sun Grown Natural 0.35oz Pouch	
Package Type	Pouch & Booklet
Package Quantity	9.9 grams & 32 sheets
Length	70 mm
Width	39 mm
Characterizing Flavor	None
SE0007299: Largo Full Flavor 0.35oz Pouch	
Package Type	Pouch & Booklet
Package Quantity	9.9 grams & 32 sheets
Length	70 mm
Width	39 mm
Characterizing Flavor	None
SE0007300: Largo Gold 0.35oz Pouch	
Package Type	Pouch & Booklet
Package Quantity	9.9 grams & 32 sheets
Length	70 mm
Width	39 mm
Characterizing Flavor	None
SE0007301: Largo Sun Grown Natural 3oz Bag	
Package Type	Bag
Package Quantity	85 grams
Characterizing Flavor	None
SE0007302: Largo Menthol 0.35oz Pouch	
Package Type	Pouch & Booklet
Package Quantity	9.9 grams & 32 sheets
Length	70 mm
Width	39 mm
Characterizing Flavor	Menthol

SE0007303: 4 Aces Turkish 3.5oz Canister	
Package Type	Can & Booklet
Package Quantity	99 grams & 200 sheets
Length	70 mm
Width	39 mm
Characterizing Flavor	None
SE0007304: 4 Aces Turkish 0.35oz Pouch	
Package Type	Pouch & Booklet
Package Quantity	9.9 grams & 32 sheets
Length	70 mm
Width	39 mm
Characterizing Flavor	None
Administrative Attributes of SE Reports	
Applicant	Top Tobacco, L.P.
Report Type	Regular
Product Category	Roll-Your-Own Tobacco Product
Product Sub-Category	Tobacco Filler ¹ Rolling Paper & Tobacco Filler Co-Package ²
Recommendation	
Issue Substantially Equivalent (SE) orders.	

¹ SE0007297 and SE007301

² SE0007298, SE0007299, SE0007300, SE0007302, SE0007303, and SE0007304

Technical Project Lead (TPL):

Digitally signed by Matthew J. Walters -S
Date: 2017.05.17 17:26:45 -04'00'

Matthew J. Walters, Ph.D., M.P.H
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: 2017.05.18 07:39:16 -04'00'

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

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1. BACKGROUND

1.1. PREDICATE TOBACCO PRODUCTS

The applicant submitted the following predicate tobacco products:

SE0007297: Largo Sun Grown Natural 8oz Bag	
Product Name	Top Regular Canister
Package Type	Can & Booklet
Package Quantity	170 grams & 200 sheets
Length	70 mm
Width	39 mm
Characterizing Flavor	None
SE0007298: Largo Sun Grown Natural 0.35oz Pouch	
Product Name	Top Regular Pouch
Package Type	Pouch & Booklet
Package Quantity	21.0 grams & 32 sheets
Length	70 mm
Width	39 mm
Characterizing Flavor	None
SE0007299: Largo Full Flavor 0.35oz Pouch	
Product Name	Top Regular Pouch
Package Type	Pouch & Booklet
Package Quantity	21.0 grams & 32 sheets
Length	70 mm
Width	39 mm
Characterizing Flavor	None
SE0007300: Largo Gold 0.35oz Pouch	
Product Name	Top Lite Pouch
Package Type	Pouch & Booklet
Package Quantity	21.0 grams & 32 sheets
Length	70 mm
Width	39 mm
Characterizing Flavor	None
SE0007301: Largo Sun Grown Natural 3oz Bag	
Product Name	Top Regular Canister
Package Type	Can & Booklet
Package Quantity	170 grams & 200 sheets
Length	70 mm
Width	39 mm
Characterizing Flavor	None

SE0007302: Largo Menthol 0.35oz Pouch	
Product Name	Top Menthol Pouch
Package Type	Pouch & Booklet
Package Quantity	21.0 grams & 32 sheets
Length	70 mm
Width	39 mm
Characterizing Flavor	Menthol
SE0007303: 4 Aces Turkish 3.5oz Canister	
Product Name	Top Regular Canister
Package Type	Can & Booklet
Package Quantity	170 grams & 200 sheets
Length	70 mm
Width	39 mm
Characterizing Flavor	None
SE0007304: 4 Aces Turkish 0.35oz Pouch	
Product Name	Top Regular Pouch
Package Type	Pouch & Booklet
Package Quantity	21.0 grams & 32 sheets
Length	70 mm
Width	39 mm
Characterizing Flavor	None

The predicate tobacco products are roll-your-own (RYO) tobacco filler and rolling paper co-packages manufactured by the applicant.

1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

On February 11, 2013, the applicant submitted these SE Reports. FDA issued Acknowledgement letters on March 14, 2013. FDA issued an Advice/Information Request letter (A/I letter) on March 14, 2013. In response, the applicant submitted amendments SE0008201-SE0008208 on April 05, 2013. On August 9, 2013, the applicant submitted amendment SE0009609 in response to FDA's request for additional information. On August 16, 2013, the applicant submitted amendment SE0009616 to revise and provide additional product information in response to FDA's request for additional information. On December 6, 2013, FDA issued a Notification letter, indicating that scientific review was expected to begin on January 20, 2014. On December 23, 2013, the applicant submitted amendment SE0010085 in response to FDA's request for additional information. After scientific review of the SE Reports, FDA issued an A/I letter on August 11, 2014. In response, the applicant submitted amendment SE0010705 on September 30, 2014. On March 16, 2016, FDA issued a Preliminary Finding letter. In response, the applicant submitted amendment SE0013313 on April 14, 2016. On July 13, 2016, FDA issued a second

Preliminary Finding letter because the first Preliminary Finding letter did not include deficiencies from the environmental review. In response, the applicant submitted amendment SE0013567 on August 9, 2016.

Product Name	SE Report	Amendments
Largo Sun Grown Natural 8 oz Bag	SE0007297	SE0008201- SE0008208 SE0009609 SE0009616 SE0010022 SE0010023 SE0010028 SE0010029 SE0010057 SE0010085 SE0010091- SE0010094 SE0010148 SE0010705 SE0013313 SE0013567
Largo Sun Grown Natural 0.35 oz Pouch	SE0007298	
Largo Full Flavor 0.35 oz Pouch	SE0007299	
Largo Gold 0.35 oz Pouch	SE0007300	
Largo Sun Grown Natural 3 oz Bag	SE0007301	
Largo Menthol 0.35 oz Pouch	SE0007302	
4 Aces Turkish 3.5 oz Canister	SE0007303	
4 Aces Turkish 0.35 oz Pouch	SE0007304	

1.3. SCOPE OF REVIEW

This review captures all regulatory, compliance, and scientific reviews completed for these SE Reports.

2. REGULATORY REVIEW

Regulatory reviews were completed by Marcella White on March 14, 2013, and by Ryan Nguy on June 3, 2013 for SE0007299 and June 4, 2013 for SE0007297, SE0007298, SE0007300-SE0007304. On December 5, 2016, the Office of Science (OS) signed a Regulatory Review that stated all deficiencies identified in the second completeness reviews are resolved at this time. Therefore, the SE Reports are administratively complete.

The final review concludes that the SE Reports are administratively complete.

3. COMPLIANCE REVIEW

The Office of Compliance and Enforcement (OCE) completed reviews to determine whether the applicant established that the predicate tobacco products are grandfathered products (i.e., were commercially marketed as of February 15, 2007). The OCE reviews dated February 3, 2014, for SE0007299 and February 4, 2014, for SE0007297- SE0007298, SE0007300-SE0007304, conclude that the evidence submitted by the applicant is adequate to demonstrate that the

predicate tobacco products are grandfathered and, therefore, are eligible predicate tobacco products.

OCE also completed reviews to determine whether the new tobacco products are in compliance with the Federal Food, Drug, and Cosmetic Act (FD&C Act), as required by section 905(j)(1)(A)(i) of the FD&C Act. The OCE reviews dated October 14, 2016, February 13, 2017, and April 21, 2017 conclude that the new tobacco products are in compliance with the FD&C Act.

4. SCIENTIFIC REVIEW

Scientific reviews were completed by the OS for the following disciplines:

4.1. CHEMISTRY

Chemistry reviews were completed by Jiu Ai on April 16, 2014, and December 12, 2014, and by Selvin Edwards on June 3, 2016.

The final chemistry review concludes that the new tobacco products have different characteristics related to product composition compared to the corresponding predicate tobacco products but the differences do not cause the new tobacco products to raise different questions of public health. The review identifies the following significant issues related to product composition:

- Differences in tobacco blend (b) (4)
- Increased (b) (4) smoke yields in SE0007302 by 2%
- Increased (b) (4) smoke yields in SE0007299 by 5%
- Increased (b) (4) smoke yields in SE0007299, SE0007302, SE0007303, and SE0007304 by 10-15%

The review concludes that all of these increases except a 15% (b) (4) increase are *not* statistically significant. The 15% (b) (4) increase is statistically significant but reflects environmental and agricultural variability expected in tobacco according to the review. Furthermore, measurement of metals such as (b) (4) and other HPHCs, often have increased analytical variability with roll-your-own tobacco products compared to mass produced cigarette tobacco products. The increase in (b) (4) is within the acceptable variability of the analytical method. Therefore, the increases in (b) (4) smoke yields of this magnitude are not a concern in this specific case because they are within expected variability and other HPHC yields were not significantly increased. Given the totality of the evidence including the agricultural variability, sample to sample variability, as well as instrument variability, the slight increase in the yields of (b) (4) in smoke is relatively small and this change does not raise different questions of public health. Other HPHC smoke yields were comparable or lower between the new and

corresponding predicate tobacco products, therefore the tobacco blend differences do not appear to negatively impact the composition of the new tobacco products. Therefore, the review concludes that the differences in characteristics between the new and corresponding predicate tobacco products do not cause the new tobacco products to raise different questions of public health from a chemistry perspective.

4.2. ENGINEERING

Engineering reviews were completed by Julie Morabito on April 16, 2014, December 8, 2014, May 31, 2016, and October 4, 2016.

The final engineering review concludes that the new tobacco products have different characteristics related to product design compared to the corresponding predicate tobacco products and there is insufficient information to demonstrate that the differences do not cause the new tobacco products to raise different questions of public health. The review identifies the following unresolved deficiency:

1. All of your SE Reports provide test data summaries, but do not provide raw test data for tobacco filler cut width for any of the new and corresponding predicate products. You do not provide details of the test protocols that were followed to determine tobacco filler cut width for the new and predicate products. In addition, you do not provide a detailed description of the manufacturing process for the new and predicate products, which, if identical, may be used to demonstrate whether the new and predicate product tobacco filler cut width are also identical. Without raw data sets and detailed test protocols, the test data provided are not adequate to confirm that design parameter specifications for tobacco filler cut width have been met for each new and predicate product. Therefore, provide the test data (i.e., measured values of design parameters), including test protocols, quantitative acceptance (pass/fail) criteria, data sets, and a summary of the results for tobacco filler cut width for the new and corresponding predicate products to demonstrate that the specification for tobacco filler cut width has been met for each new and corresponding predicate product.

Certificates of analysis from the material supplier may satisfy this deficiency. Additionally, if tobacco filler cut width was tested according to national or international standards identify the standards and state what deviations, if any, from the standards occurred.

Therefore, the review concludes that there was inadequate information from an engineering perspective to determine that the differences in characteristics between the new and predicate tobacco products do not cause the new tobacco products to raise different questions of public health.

4.3. TOXICOLOGY

Toxicology reviews were completed by Brian Erkkila on August 6, 2014, and by James Hobson on March 2, 2016, and June 13, 2016.

The final toxicology review concludes that the new tobacco products have different characteristics related to product toxicology compared to the corresponding predicate tobacco products but the differences do not cause the new tobacco products to raise different questions of public health. The review identifies the following issue related to product toxicology:

- Differences in tobacco blend (b) (4)
- Addition of (b) (4) in SE0007298, SE0007299, SE0007300, SE0007302, and SE0007304
- Addition of (b) (4), which contains (b) (4), in SE0007298, SE0007299, SE0007300, SE0007302, and SE0007304
- Increased (b) (4) smoke yields in SE0007302 by 2%
- Increased (b) (4) smoke yields in SE0007299 by 5%
- Increased (b) (4) smoke yields in SE0007299, SE0007302, SE0007303, and SE0007304 by 10-15%

The applicant provided HPHC smoke data demonstrating that differences in tobacco blend and addition of (b) (4) and (b) (4), does not increase the toxicity of the new tobacco products compared to the corresponding predicate tobacco products. The review concludes that all of these increases except a 15% (b) (4) increase are *not* statistically significant. The 15% (b) (4) increase is statistically significant but falls within measurement variability as the measurement of metals such as (b) (4) and other HPHCs, often have increased analytical variability with roll-your-own tobacco products compared to mass produced cigarette tobacco products. The increase in (b) (4) is within the acceptable variability of the analytical method. Therefore, the increases in (b) (4) smoke yields of this magnitude are not a concern in this specific case because they are within expected variability and other HPHC yields were not significantly increased. Given the totality of the evidence including the agricultural variability, sample to sample variability, as well as instrument variability, the slight increase in the yields of (b) (4) in smoke is relatively small and this change does not raise different questions of public health. Therefore, the review concludes that the differences in characteristics between the new and corresponding predicate tobacco products do not cause the new tobacco products to raise different questions of public health from a chemistry perspective.

4.4. SOCIAL SCIENCE

Social science reviews were completed by David Portnoy on March 13, 2014, and by Wendy Slavitt on December 16, 2014. Additionally, an addendum was prepared on April 14, 2017 to address an error in the December 16, 2014 review.

The social science review concludes that the new tobacco product has different characteristics compared to the predicate tobacco product but the differences do not cause the new tobacco product to raise different questions of public health related to consumer perception. The review identifies the following differences related to consumer perception and use:

- Increased (b) (4) in SE0007297 by 33%
- Decreased (b) (4) in SE0007298-SE0007304 by 41-50%
- Removal of rolling papers in SE0007297 and SE0007301

The review concludes that there is no currently available direct scientific evidence indicating that the differences in (b) (4) and removal of rolling papers will influence consumer perception and use. It is unlikely that a different quantity of (b) (4) of this magnitude or the removal of rolling papers will influence consumer perception and use. These differences may, in some cases, reduce barriers to initiation (e.g., decrease in package quantity may lower the price, or make the product easier to conceal), or make it more difficult for current users to quit (e.g., larger quantities may lead people to not worry about running out of product, or increase consumption); however, it is unlikely that changes of this magnitude for these products would raise different questions of public health. Therefore, the review concludes that the differences in characteristics between the new and corresponding predicate tobacco products do not cause the new tobacco products to raise different questions of public health from a social science perspective.

The review also evaluated the health information summary for each new tobacco product. The review concludes that the applicant's health information summary for each new tobacco product does not violate section 911 of the FD&C Act.

5. ENVIRONMENTAL DECISION

A finding of no significant impact (FONSI) was signed by Kimberly Benson, Ph.D. on October 5, 2016. The FONSI was supported by an environmental assessment prepared by FDA on October 3, 2016.

6. CONCLUSION AND RECOMMENDATION

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

- Differences in tobacco blend (b) (4)
- Increased (b) (4) smoke yields in SE0007302 by 2%
- Increased (b) (4) smoke yields in SE0007299 by 5%
- Increased (b) (4) smoke yields in SE0007299, SE0007302, SE0007303, and SE0007304 by 10-15%
- Addition of (b) (4) in SE0007298, SE0007299, SE0007300, SE0007302, and SE0007304
- Addition of (b) (4), which contains (b) (4), in SE0007298, SE0007299, SE0007300, SE0007302, and SE0007304
- Increased (b) (4) in SE0007297 by 33%
- Decreased (b) (4) in SE0007298-SE0007304 by 41-50%
- Increased (b) (4) in SE0007298-SE0007300, SE0007302-SE0007304 by 44%
- Removal of rolling papers in SE0007297 and SE0007301

All of the reviews *except* engineering conclude that these differences in characteristics do not cause the new tobacco products to raise different questions of public health. I concur with all of the reviews except engineering. The engineering review identifies one deficiency, which indicates that the applicant did not submit test data demonstrating that new and predicate tobacco products meet specifications for tobacco filler cut size. I agree with this concern. However, in light of all of the other information provided by the applicant, it seems highly unlikely that this single issue will cause the new tobacco products to raise different questions of public health. For example, the test data for all other design parameters demonstrate that the new and predicate tobacco products meet specifications for all of those design parameters. In addition, the tobacco filler cut size specifications are the same for the new and corresponding predicate tobacco products. Therefore, even if the products fall slightly outside specifications, the difference in cut size would be so small as to not cause the new tobacco products to raise different questions of public health. As a consequence, I conclude that the new tobacco products are substantially equivalent to the corresponding predicate tobacco products.

The predicate tobacco products meet statutory requirements because they are grandfathered products (i.e., were commercially marketed in the United States as of February 15, 2007).

The new tobacco products are currently in compliance with the FD&C Act.

FDA examined the environmental effects of finding these new tobacco products substantially equivalent and made a finding of no significant impact.

SE order letters should be issued for the new tobacco products in SE0007297-SE007304, as identified on the cover page of this review.