

Technical Project Lead (TPL) Review: SE0015758 and SE0015764

| SE0015758: Bull Durham Regular 100MM | |
|---|----------------------|
| Package Type | Box |
| Package Quantity | 200 tubes |
| Length | 100 millimeters (mm) |
| Diameter | 8.2 mm |
| Ventilation | None ¹ |
| Characterizing Flavor | None |
| SE0015764: Bull Durham Menthol King Size | |
| Package Type | Box |
| Package Quantity | 200 tubes |
| Length | 84 mm |
| Diameter | 8.2 mm |
| Ventilation | None ¹ |
| Characterizing Flavor | Menthol |
| Attributes of SE Reports | |
| Applicant | Republic Tobacco LP |
| Report Type | Regular |
| Product Category | Roll-Your-Own |
| Product Sub-Category | Filtered Tubes |
| Recommendation | |
| Issue Substantially Equivalent (SE) orders. | |

¹ The applicant states the ventilation is “none” or “not-applicable” since the products are not ventilated. FDA has interpreted this as 0%.

Technical Project Lead (TPL):

Digitally signed by Jeannie H. Jeong-im -S
Date: 2020.10.19 08:43:18 -04'00'

Jeannie Jeong-Im, Ph.D.
Chemistry Branch Chief
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 Todd L. Cecil -S
Date: 2020.10.19 08:51:31 -04'00'

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

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1. BACKGROUND

1.1. PREDICATE TOBACCO PRODUCTS

The applicant submitted the following predicate tobacco products:

| SE0015758: Bull Durham Regular 100MM | |
|---|-----------------------|
| Product Name | TOP Regular 100MM |
| Package Type | Box |
| Portion Count | 200 tubes |
| Length | 100 mm |
| Diameter | 8.2 mm |
| Ventilation | None ¹ |
| Characterizing Flavor | None |
| SE0015764: Bull Durham Menthol King Size | |
| Product Name | Top Menthol King Size |
| Package Type | Box |
| Portion Count | 200 tubes |
| Length | 84 mm |
| Diameter | 8.2 mm |
| Ventilation | None ¹ |
| Characterizing Flavor | Menthol |

The predicate tobacco products are roll-your-own (RYO) filtered tubes manufactured by the applicant.

1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

On March 6, 2020, FDA received two SE Reports from Republic Tobacco LP. FDA issued an Acknowledgement letter to the applicant on March 12, 2020. FDA received amendments in response to OCE request for more information on March 12, 2020, and March 13, 2020, for SE0015758 and SE0015764 respectively (SE0015773 and SE0015775). On March 24, 2020, FDA received an in response to a supplemental OCE request information for SE0015758 (SE0015789) OCE Following the review of the original and amended SE Report, a deficiency letter was issued to the applicant on May 14, 2020. FDA received the applicant’s responses (SE0016778) on July 2, 2020.

| Product Name | SE Report | Amendments |
|-------------------------------|------------------|-------------------------------------|
| Bull Durham Regular 100MM | SE0015758 | SE0015773 SE0015789 SE0016778 |
| Bull Durham Menthol King Size | SE0015764 | SE0015775 SE0016778 |

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 Fredris Wiley on March 10, 2020 and March 16, 2020. The final reviews conclude 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 March 30, 2020 and April 5, 2020, 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 a review 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 review dated October 8, 2020 concludes that the new tobacco products are in compliance with the FD&C Act.

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 Robert Gahl on April 22, 2020² and August 21, 2020.

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

Chemistry evaluation:

SE0015758:

- Cigarette Paper
 - 590% higher amount (b) (4) mg/tube) of (b) (4)
 - 21% higher amount ((b) (4) mg/tube) of (b) (4)
 - Addition of (b) (4) mg/tube (b) (4) and (b) (4)
- Addition of (b) (4) (b) (4) mg/tube) in the plug wrap

² An addendum review was completed on May 1, 2020 to correct a deficiency to be communicated to the applicant.

- 94% higher amount (b) (4) mg/tube) of (b) (4)
- 36% higher amount (b) (4) mg/tube) of (b) (4) in the filter
- Addition of (b) (4) (b) (4) mg/tube) in the filter adhesive
- Addition of (b) (4) (b) (4) mg/tube) in the tipping adhesive
- 20% higher base paper porosity

SE0015764:

- Tipping Paper
 - 12% amount (b) (4) mg/tube) of (b) (4)
 - 61% amount (b) (4) mg/tube) of (b) (4)
 - 1100% higher amount (b) (4) g/tube) of (b) (4)
- Filter
 - 30% higher amount (b) (4) mg/tube) of (b) (4)
 - 30% higher amount (b) (4) mg/tube) of (b) (4)
- 46% higher amount (b) (4) mg/tube) of (b) (4) in the plug wrap
- Addition of (b) (4) (b) (4) mg/tube) in the tipping adhesive
- Lower MSS yields of nicotine
 - 19% lower (b) (4) mg/tube) under the ISO regimen
 - 16% lower (b) (4) mg/tube) under the CI regimen

All SE reports contain single ingredient information about the components of filtered roll-your-own cigarette tubes and mainstream smoke yields for tar, nicotine, and carbon monoxide under the ISO and CI smoking regimens in the new and predicate tobacco products. (b) (4) collected the mainstream smoke data. Sufficient information about the methods and validation reports was provided. The mainstream smoke yields of tar, nicotine, and carbon monoxide in the new tobacco products were either analytically equivalent or lower by TOST³ analyses than the mainstream smoke yields in the corresponding predicate tobacco products in all SE reports. SE0015764 has 16 – 19% lower MSS yields of nicotine compared to the predicate tobacco product. This change may alter the use behavior of these new tobacco products; therefore, SE0015764 has been deferred to Behavioral and Clinical Pharmacology for review. The base paper porosity is 20% higher in the new tobacco product of SE0015758. The mainstream smoke yields of acetaldehyde, acrolein, crotonaldehyde, and formaldehyde under the ISO and CI regimens in the new and predicate tobacco products in SE0015758 were provided. TOST³ analysis of these HPHC yields showed these carbonyls yields were either equivalent or lower in the new tobacco product compared to the predicate tobacco product. Therefore, 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 Michael Morschauer on April 21, 2020.

The engineering review concludes that the new tobacco products have different

³ Two One-Sided T-test (TOST) is a statistical tool that calculates important analytical differences (IADs) using the Horwitz-Thompson equation.

characteristics related to product engineering 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 identified the following differences:

Engineering evaluation:

SE0015758:

- Increase in cigarette paper base paper porosity (20%)
- Decrease in filter total denier (7%)
- Increase in filter pressure drop (12%)

SE0015764:

- Increase in overall tube weight (11%)
- Decrease in filter total denier (6%)
- Decrease in filter denier per filament (14%)
- Decrease in filter density (5%)
- Increase in filter pressure drop (35%)
- Increase in filter length (33%)

The applicant submitted target specifications and range limits for all necessary engineering parameters for each new and corresponding predicate tobacco product. For SE0015758, the new tobacco product has increases in cigarette paper base paper porosity and filter pressure drop, and a decrease in filter total denier as compared to the predicate tobacco product. A difference in cigarette paper base paper porosity may affect smoke constituent yields. For SE0015764, the new tobacco product has increases in overall tube weight, filter pressure drop, and filter length, and decreases in filter total denier, denier per filament, and filter density as compared to the corresponding predicate tobacco product. Differences in overall tube weight may affect smoke constituent yields. Therefore, these differences were deferred to chemistry for evaluation of any potential effects it may have on smoke chemistry including tar, nicotine, and carbon monoxide. Therefore, 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 an engineering perspective.

4.3. TOXICOLOGY

Toxicology reviews were completed by Vyomesh Patel on April 29, 2020 and August 24, 2020.

The final toxicology review concludes that the new tobacco products have different characteristics related to 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 identified the following differences:

Toxicology evaluation complete:

- Cigarette paper:
 - o (b) (4) is added (b) (4) mg) in SE0015758.
 - o (b) (4) is added in SE0015758 (b) (4) mg).
 - o (b) (4) is increased in SE0015758 (↑(b) (4) mg).

- o (b) (4) is increased in SE0015758 (\uparrow (b) (4) mg).
- o (b) (4) is added in SE0015758 (b) (4) mg).
- Tipping paper
 - o (b) (4) is increased in SE0015764 (\uparrow (b) (4) mg).
 - o (b) (4) is added in SE0015758 (b) (4) mg).
 - o (b) (4) and (b) (4) is increased in SE0015764 (\uparrow (b) (4) mg).
 - o (b) (4) is added in SE0015758 (b) (4) mg). (b) (4) is added in SE0015758 (b) (4) mg) and SE0015764 (b) (4) mg). (b) (4) and (b) (4) (b) (4) are added to SE0015764 (b) (4) mg).
 - o (b) (4) is added in SE0016764 (b) (4) mg) and SE0015758 (b) (4) mg).
 - o (b) (4) is added in SE0015764 (b) (4) mg).
 - (b) (4) is increased in SE0015758 (\uparrow (b) (4) mg) and SE0015764 (\uparrow (b) (4) mg).
 - o (b) (4) is increased in SE0015758 (\uparrow (b) (4) mg) and SE0015764 (\uparrow (b) (6) mg).
 - o (b) (4) and (b) (4) added in SE0015764 (b) (4) mg).
- Plug Wrap
 - o (b) (4) (b) (4) mg) is deleted and (b) (4)) is added in SE0015758 and (b) (4) increased in SE0015764 (b) (4) mg).
 - o (b) (4) is added in SE0015758 (b) (4) mg) and SE0015764 (b) (4) mg),
 - o (b) (4) is added in SE0015758 (b) (4) mg) and SE0015764 (b) (4) mg),
 - o (b) (4) is increased in SE0015758 (\uparrow (b) (4) m) and added in SE0015764 (b) (4) mg).
- Acetate Tow
 - o (b) (4) and (b) (4) are added in SE0015758 (b) (4) mg)
 - (b) (4) is increased in SE0015758 (\uparrow (b) (4) and SE0015764 from (\uparrow (b) (4) mg).
 - o (b) (4) is increased in SE0015758 (\uparrow (b) (4) mg) and SE0015764 (\uparrow (b) (4) mg).
 - o (b) (4) is increased in SE0015758 (\uparrow (b) (4) mg) and SE0015764 (\uparrow (b) (4) mg).
 - o (b) (4) s increased in SE0015764 (\uparrow (b) (4) mg).
 - o (b) (4) is increased in SE0015764 (\uparrow (b) (4) mg).
- (b) (4)
 - o (b) (4) is increased in SE0015758 (b) (4) mg) and SE0015764 (b) (4) mg).
- (b) (4)
 - o (b) (4) mg), (b) (4) mg), (b) (4) ,
- (b) (4) mg) are added in SE0015764.
- Glue Filter
 - o (b) (4) is added SE0015758 (b) (4) mg).
- Tipping Glue
 - o (b) (4) is added in SE0015758 (b) (4) mg).
 - o (b) (4) is added in SE0015758 (b) (4) mg).
 - o (b) (4) mg), (b) (4) and (b) (4) mg and (b) (4) mg, respectively) are added in SE0015758 and SE0015764.

There are many modifications to the ingredients in the new tobacco products. Some of these

ingredient changes may influence HPHC smoke yields in the new tobacco products upon pyrolysis. TNCO smoke yields generated by ISO and CI smoking regimens were provided for both the new and predicate tobacco products, and they were found analytically equivalent or lower in the new tobacco products. Therefore, 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 toxicology perspective.

4.4. BEHAVIORAL AND CLINICAL PHARMACOLOGY

Behavioral and clinical pharmacology reviews were completed by Tyler Nighbor on August 20, 2020.

The behavioral and clinical pharmacology review did not identify any differences in characteristics between the new and predicate tobacco products that could cause the new tobacco products to raise different questions of public health from a behavioral and clinical pharmacology perspective for SE0015764. Therefore, the differences in characteristics between the new and predicate tobacco products of SE0015764 do not cause the new tobacco product to raise different questions of public health related to consumer use of the product and impact on exposure and behavior.

5. ENVIRONMENTAL DECISION

An environmental review was completed by Dilip Venugopal on August 12, 2020.

A finding of no significant impact (FONSI) was signed by Luis Valerio Jr., Ph.D., ATS on September 10, 2020. The FONSI was supported by an environmental assessment prepared by FDA on September 10, 2020.

6. CONCLUSION AND RECOMMENDATION

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

SE0015758

- Cigarette Paper
 - Addition of (b) (4) mg)
 - Deletion of (b) (4) mg)
 - 590% increase in (b) (4) mg)
 - 21% increase in (b) (4) mg)
 - Addition of (b) (4) mg/tube (b) (4) and (b) (4)
 - Addition of (b) (4) mg).
 - Addition of (b) (4) mg).
- Tipping paper
 - Addition of (b) (4) mg).
 - Addition of (b) (4) mg) and (b) (4) mg).
 - Addition of paraffin wax (0.01 mg).
 - 52% increase of (b) (4) mg).

- 4% increase of (b) (4) is increased (b) (4) mg).
- Plug Wrap
 - Addition of (b) (4) mg).
 - Deletion of (b) (4) mg).
 - Addition of (b) (4) mg).
 - Addition of (b) (4) mg).
 - 100% increase of (b) (4) mg)
- Filter
 - Addition of (b) (4) and (b) (4) mg).
 - 94% increase in (b) (4) mg).
 - 31% increase in (b) (4) mg).
 - 4% increase in (b) (4) mg).
 - 36% increase in (b) (4) mg).
- Glue Filter
 - Addition of (b) (4) mg).
- Tipping Glue
 - Addition of (b) (4) mg)
 - Addition of (b) (4) mg).
 - Addition of (b) (4) mg), (b) (4) mg), and (b) (4) mg).
- 20% increase in cigarette paper base paper porosity
- 7% decrease in filter total denier
- 12% increase in filter pressure drop

SE0015764:

- Tipping Paper
 - 12% increase in (b) (4) mg) of (b) (4)
 - 61% increase in (b) (4) mg)
 - 1100% increase in (b) (4) mg)
 - Addition of (b) (4) mg) and (b) (4) mg).
 - Addition of (b) (4) mg).
 - Addition of (b) (4) mg).
 - 57% increase in (b) (4) mg).
 - 1100% increase in (b) (4) mg).
 - Addition of (b) (4) mg).
- Plug Wrap
 - 46% increase in (b) (4) mg).
 - 11% decrease in (b) (4) mg)
 - Addition of (b) (4) mg).
 - Addition of (b) (4) mg).
 - Addition of (b) (4) mg).
- Filter
 - 28% increase in (b) (4) mg).
 - 30% increase in (b) (4) mg).
 - 30% increase in (b) (4) mg).
 - 30% increase in (b) (4) mg).
 - 30% increase in (b) (4) mg).

- 18% increase in (b) (4) mg).
- Glue Filter Hot Melt
 - Addition of (b) (4) mg)
 - Addition of (b) (4) mg)
 - Deletion of (b) (4) mg)
 - Addition of (b) (4) ;
(b) (4) ;
(b) (4) mg).
 - Addition of (b) (4) mg), and
(b) (4) mg).
- 11% increase in overall tube weight
- 6% decrease in filter total denier
- 14% decrease in filter denier per filament
- 5% decrease in filter density
- 35% increase in filter pressure drop
- 33% increase in filter length

The applicant has demonstrated that these differences in characteristics do not cause the new tobacco products to raise different questions of public health. There are many changes in ingredients to the cigarette paper, tipping paper, plug wrap, filter, and adhesives. There are also changes in the base paper porosity, filter total denier, denier per filament, filter pressure drop, overall tube weight, and length. The applicant provided TNCO (SE0015758 and SE0015764) and carbonyls (SE0015758, i.e., acetaldehyde, acrolein, crotonaldehyde, formaldehyde) of the new and predicate products of both of these SE Reports under ISO and CI smoking regimens. All the HPHCs were either equivalent under TOST³ or lower in the new products when compared to the corresponding predicate products. Therefore, 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.

The predicate tobacco products meet statutory requirements because it was determined that they are grandfathered tobacco products (i.e., were commercially marketed in the United States other than exclusively in test markets as of February 15, 2007).

The new tobacco products are currently in compliance with the FD&C Act. In addition, all of the scientific reviews conclude that the differences between the new and corresponding predicate tobacco products are such that the new tobacco products do not raise different questions of public health. I concur with these reviews and recommend that SE order letters be issued.

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 SE0015758 and SE0015764, as identified on the cover page of this review