Technical Project Lead (TPL) Review: SE0000067 – SE0000068

SE0000067: Tareyton Soft Pack	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	83 mm
Diameter[1]	7.79 mm
Ventilation	16%
Characterizing Flavor	None
SE0000068: Tareyton 100's Soft Pack	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	98 mm
Diameter[1]	7.79 mm
Ventilation	20%
Characterizing Flavor	None
Common Attributes of SE Reports	
Applicant	R.J. Reynolds Tobacco Company
Report Type	Provisional
Product Category	Cigarettes
Product Sub-Category	Combusted, Filtered
Recommendation	
Issue Substantially Equivalent (SE) orders.	

[1] The applicant submitted the circumference which allowed for a calculation of diameter.

Technical Project Lead (TPL):

Digitally signed by Jeannie H. Jeong-im -S
Date: 2019.08.16 13:43:42 -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 Matthew R. Holman -S
Date: 2019.08.16 14:01:20 -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:

SE0000067: Tareyton Soft Pack	
Product Name	Camel Light Hard Pack
Package Type	Box
Package Quantity	20 cigarettes
Length	83 mm
Diameter[1]	7.79 mm
Ventilation	32%
Characterizing Flavor	None
SE0000068: Tareyton 100's Soft Pack	
Product Name	Camel Filters Hard Pack
Package Type	Box
Package Quantity	20 cigarettes
Length	83 mm
Diameter[1]	7.79 mm
Ventilation	23%
Characterizing Flavor	None

The predicate tobacco products are combusted, filtered cigarettes manufactured by the applicant.

1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

On December 28, 2010, FDA received two SE Reports from RAI Services Company on behalf of R.J. Reynolds Tobacco Company. On February 14, 2011, FDA issued Acknowledgement letters to the applicant. On June 5, 2012, FDA issued an Advice/Information (A/I) Request letter. On June 15, 2012, FDA received the applicant's response (SE0004573) to FDA's June 10, 2012 request, seeking confirmation that the list of products and their corresponding tracking numbers accurately reflects the SE Reports submitted by the applicant to FDA. On June 15, 2012, FDA received the applicant's request for an extension to respond to the A/I request letter (SE0004581 and SE0004592). On July 3, 2012, FDA issued an Extension Granted letter with a response due date of September 11, 2012. On September 10, 2012, FDA received the applicant's response to the A/I request letter (SE0004894 and SE0004895).

On September 13, 2012, FDA completed Public Health Impact (PHI) reviews and assigned the SE reports to PHI Tier 1 based on insufficient information to determine whether other PHI tiers were more appropriate. On May 10, 2013, FDA issued a PHI A/I request letter. FDA issued a Correction letter on May 15, 2013, to correct the name of the new tobacco products. On August 8, 2013, FDA received the applicant's response to the PHI A/I request letter (SE0009500 and SE0009520). On August 26, 2013, FDA completed PHI reviews and reassigned both SE Reports to PHI Tier 2 based on

the product composition information provided in the applicant's response. On September 13, 2013, FDA completed PHI reviews and reassigned both SE Report to PHI Tier 1 because the products are non-conventional tobacco products.

On May 9, 2014, FDA issued a Notification letter to inform the applicant substantive scientific review would begin on June 23, 2014. On May 27, 2014, FDA received an amendment (SE0010505) from the applicant, amending the name of the predicate tobacco product for SE0000067. On June 20, 2014, FDA received amendments providing additional information for the SE Reports (SE0010543 and SE0010545). On January 23, 2015, FDA received unsolicited amendments (SE0010844 and SE0010845) containing corrections to the ingredient formulation provided in the June 20, 2014, amendments. On July 19, 2017, FDA issued an A/I request letter. On August 4, 2017, FDA received the applicant's request for an extension to conduct literature reviews and analytical research, and then use this information to conduct risk assessments of identified ingredients and/or their pyrolysis products (SE0014229). On September 8, 2017, FDA issued an Extension Granted letter with a response due date of September 17, 2018. On September 6, 2018, FDA received the applicant's response to the A/I request letter which included the applicant's request for a claim of categorical exclusion for both SE Reports (SE0014867). On November 20, 2018, FDA issued a Preliminary Finding (PFind) letter. On May 13, 2019, FDA received the applicant's response to the PFind letter (SE0015230).

Product Name	SE Report	Amendments
Tareyton Soft Pack	SE0000067	SE0004573 SE0004581 SE0004894 SE0009500 SE0010505 SE0010545 SE0010844 SE0014229 SE0014867 SE0015230
Tareyton 100's Soft Pack	SE0000068	SE0004573 SE0004592 SE0004895 SE0009520 SE0010543 SE0010845 SE0014229 SE0014867 SE0015230

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 Jennifer German on June 5, 2012, and Marcella White on December 20, 2012.

The reviews conclude that the SE Reports are not administratively complete because the following information was not included in the SE Reports:

1. Unique identification of the new tobacco products

This information was provided during the scientific review process. A regulatory review completed by Jennifer Schmitz on November 20, 2018, states 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 in the United States other than exclusively in test markets as of February 15, 2007). The OCE reviews dated May 28, 2014, 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.[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 Tricia L. Johnson on September 4, 2014[3], and by Robert Gahl on November 9, 2018, and July 2, 2019.

The final chemistry review concludes that the new tobacco products have different characteristics related to product chemistry 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:

SE0000067:

- 68% decrease in (b) (4) [redacted]
- 6% decrease in (b) (4) [redacted]

[2] An addendum review was completed on May 21, 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 grandfather determination dated May 28, 2014.

[3] An addendum was completed on July 10, 2017, to update the deficiencies in the review to be conveyed to the applicant in the A/I request letter based on amendments received on January 23, 2015.

- 170% increase in [redacted]
- Addition of [redacted]
- 370% increase in [redacted]
- 8% decrease in the total amount of tobacco ([redacted])
- Addition to cigarette paper
  - [redacted]
  - [redacted]
  - [redacted]
- Increases of the following harmful and potentially harmful constituents (HPHCs):
  - 25% in B[a]P (ISO)
  - 122% in formaldehyde (ISO) and 76% (CI)

SE0000068:

- 65% decrease in [redacted]
- 28% increase in [redacted]
- 129% increase in [redacted]
- 237% increase in [redacted]
- 112% increase in [redacted]
- 8% decrease in the total amount of tobacco [redacted]
- 26% [redacted] increase in [redacted]
- 104% [redacted] increase in [redacted]
- Addition to cigarette paper
  - [redacted]
  - [redacted]
- Increases of the following HPHC:
  - 37% in formaldehyde (ISO) and 49% (CI)

The principle difference between the new and corresponding predicate tobacco products is the incorporation of [redacted] in the filter tow of the new tobacco products while the corresponding predicate tobacco products only utilize [redacted] There is an 8% decrease in the total amount of tobacco in the new tobacco products compared to the corresponding predicate tobacco products. However, changes in the tobacco blend ranged from a 65% – 68% decrease in [redacted] in the new tobacco products compared to the corresponding predicate tobacco products, and a [redacted] addition (SE0000067) or 237% increase (SE0000068) in [redacted] Increases of 170% and 129% in [redacted] in SE0000067 and SE0000068, respectively, as well as 370% and 112% increases in [redacted] in the new tobacco products compared to the corresponding predicate tobacco products in SE0000067 and SE0000068, respectively, were also reported. These changes in tobacco may affect TNCO, benzo[a]pyrene (B[a]P), NNN and NNK yields. For SE0000068, there is a 26% increase in [redacted] in the [redacted] and a 104% increase in [redacted]

(b) (4) There is also the addition of (b) (4) in the cigarette paper as well as addition of (b) (4) in SE0000067, only. The applicant submitted mainstream smoke yields for TNCO and 16 other HPHCs under the ISO and CI smoking regimens: 1,2-butadiene, 1-aminonaphthalene, 2-aminonaphthalene, 4-aminobiphenyl, acetaldehyde, acetone, acrolein, acrylonitrile, ammonia, benzene, B[a]P, crotonaldehyde, ethylbenzene, formaldehyde, furan, isoprene, naphthalene, NNK, NNN, propionaldehyde, propylene oxide, styrene, toluene, vinyl acetate. These smoke yields were provided to demonstrate that the different tobacco blends, changes in the ingredients added to the tobacco, and differences in structural components, as well as the (b) (4) (b) (4) in the filter tow of the new tobacco products do not cause the new products to raise different questions of public health. Under the ISO regimen there were increases in the B[a]P (25% in SE0000067) and formaldehyde (122% in SE0000067 and 37% in SE0000068) in the new tobacco products that were beyond an important analytical difference. Under the CI regimen, there was also an increase in formaldehyde (76% in SE0000067 and 49% in SE0000068) beyond an important analytical difference. These increases have been deferred to toxicology. The levels of TNCO and the other HPHCs in the new and corresponding predicate tobacco products are either analytically equivalent or are not analytically equivalent but are present in the new tobacco products at lower levels. 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 Julie Morabito on September 5, 2014[4], Raymond Williamson on November 5, 2018, and Morgan E. Lee on July 1, 2019.

The final engineering review concludes that the new tobacco products have different 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:

SE0000067:

- Addition of (b) (4) to the filter
- Tobacco filler mass decrease (7.3%)
- Tobacco rod density decrease (16.3%)
- Cigarette paper base paper porosity decrease (4.2%)
- Cigarette paper band width increase (16.7%)
- Cigarette paper band space decrease (10%)
- Filter total denier decrease
- Filter denier per filament increase
- Filter density increase (35.6%)
- Filter pressure drop decrease (38%)
- Filter length decrease (22.2%)

[4] An addendum was completed on July 7, 2017, to confirm deficiencies in the review to be conveyed to the applicant in the A/I request letter remain appropriate despite information provided in amendments received on January 23, 2015.

- Filter ventilation decrease (16%)
- Tipping paper length decrease (19.4%)

SE0000068:

- Addition of (b) (4) to the filter
- Cigarette length increase (18.1%)
- Tobacco filler mass decrease (8.9%)
- Tobacco rod density decrease (15.7%)
- Cigarette paper base paper porosity decrease (60%)
- Cigarette paper band porosity decrease (78.3%)
- Cigarette paper band width increase (16.7%)
- Cigarette paper band space decrease (10%)
- Filter total denier increase
- Filter denier per filament increase
- Filter density increase (33.1%)
- Filter length increase (47.6%)
- Filter ventilation decrease (3%)
- Tipping paper length increase (40%)

There are many design parameter changes in the new tobacco products compared with the corresponding predicate tobacco products. Some of these changes are: cigarette length increase by 18.1% (SE0000068), filler mass decreases by 7.3% – 8.9%, tobacco rod density decreases by 15.7%-16.7%, cigarette paper base paper porosity decreases by 4.2% – 60%, cigarette paper band width increases by 16.7%, filter density increases 33.1% – 35.6%, filter ventilation decreases by 3% – 16%, and tipping paper length decrease by 19.4% (SE0000067) and increase by 40% (SE0000068). These design parameter differences may impact the following smoke constituents: tar, nicotine, carbon monoxide, and B[a]P; therefore, evaluation of these have been deferred to chemistry. The main difference between the new tobacco products and the corresponding predicate tobacco products is the presence of a (b) (4) filter in the new tobacco products. The applicant fully characterized the (b) (4) filter and demonstrated that it is unlikely that (b) (4) breakthrough would occur and be released for inhalation by the consumer. They also submitted additional HPHCs for evaluation, which has been deferred to chemistry. 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 Xin Fu on June 16, 2017, Sheila M. Healy on November 19, 2018, and Mamata De on July 3, 2019.

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:

SE0000067:

- Differences in tobacco blend
- Addition to cigarette paper:
  - (b) (4) /cigarette)
  - (b) (4) /cigarette)
  - (b) (4)
    ((b) (4) cigarette)
- Addition to flavor ingredients:
  - (b) (4) /cigarette)
  - (b) (4) cigarette)
  - (b) (4) /cigarette)
  - (b) (4) /cigarette)
  - (b) (4) cigarette)
  - (b) (4) cigarette)
- Increase in cigarette side seam adhesive ingredients:
  - 13% ((b) (4) /cigarette) (b) (4)
  - 12% (b) (4) cigarette) (b) (4)
- Changes in tipping base paper and brown ink
- Increases of the following HPHCs:
  - 25% in B[a]P (ISO)
  - 122% in formaldehyde (ISO) and 76% (CI)

SE0000068:

- Differences in tobacco blend
- 26% ((b) (4) /cigarette) increase in (b) (4)
- 104% (b) (4) /cigarette) increase in (b) (4)
- Addition to cigarette paper:
  - (b) (4) /cigarette)
  - (b) (4) /cigarette)
- Addition in flavor ingredients:
  - (b) (4) ug/cigarette)
  - (b) (4) cigarette)
  - (b) (4) cigarette)
  - (b) (4) /cigarette)
  - (b) (4) /cigarette)
- Increased in flavor Ingredients:
  - 4247% ((b) (4) cigarette) (b) (4)
  - 117% ((b) (4) /cigarette) (b) (4)
- Changes in tipping base paper and brown ink
- Increases of the following HPHC:
  - 37% in formaldehyde (ISO) and 49% (CI)

There are differences in the tobacco blend, cigarette paper, flavor ingredients, and cigarette side seam adhesive. The quantities of these differences are small (<1.3 mg/cigarette) and are not likely to impact smoke HPHCs upon combustion. Also, the applicant did not provide the complex ingredient data for tipping paper and brown ink. Exposure to these ingredients from inhalation, oral, or dermal routes is expected to be negligible since these are not combusted. Therefore, the tipping paper replacement and addition of brown ink to the tipping paper do not raise

toxicological concerns or different questions of public health from a toxicological perspective. The applicant also provided raw HPHC and replicate data which confirmed the HPHC data used in the quantitative risk assessment (QRA). The following HPHCs were not analytically equivalent: B[a]P and formaldehyde in SE0000067 and formaldehyde in SE0000068. The QRA was adequate to demonstrate substantial equivalence of HPHCs from a toxicological perspective. Therefore, the addition of side seam adhesive ingredients (b) (4) and (b) (4) in SE0000067, differences in the tobacco blend, and differences in flavoring do not raise any toxicological concerns or different questions of public health from a toxicological perspective. Therefore, the HPHC differences reported in SE0000067 and SE0000068 compared to the corresponding predicate tobacco products are not likely to cause the new tobacco products to raise different questions of public health from a toxicological perspective.

4.4. SOCIAL SCIENCE

A Social science review was completed by Amber R. Koblitz on September 23, 2014.

The social science review did not identify any differences in characteristics between the new and corresponding predicate tobacco products that could cause the new tobacco products to raise different questions of public health from a social science perspective. 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 social science perspective.

5. ENVIRONMENTAL DECISION

Under 21 CFR 25.35(a), issuance of SE orders under section 910(a) of the FD&C Act for these provisional SE Reports (SE0000067-SE0000068) are categorically excluded and, therefore, normally do not require the preparation of an environmental assessment (EA) or an 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 key differences in characteristics between the new and predicate tobacco products:

SE0000067:

- 68% decrease in (b) (4) (b) (4) /cigarette)
- 6% decrease in (b) (4) (b) (4) /cigarette)
- 170% increase in (b) (4) (b) (4) /cigarette)

- Addition of (b) (4) /cigarette)
- 370% increase in (b) (4) (b) (4) /cigarette)
- 8% decrease in the total amount of tobacco (b) (4) /cigarette)
- Addition to cigarette paper:
  - (b) (4) /cigarette)
  - (b) (4) cigarette)
  - (b) (4) (b) (4) /cigarette)
- Addition to flavor ingredients:
  - (b) (4) /cigarette)
  - (b) (4) /cigarette)
  - (b) (4) cigarette)
  - (b) (4) /cigarette)
  - (b) (4) cigarette)
  - (b) (4) /cigarette)
- Increase in cigarette side seam adhesive ingredients:
  - 13% ((b) (4) /cigarette) (b) (4)
  - 12% (b) (4) /cigarette) (b) (4)
- Addition of (b) (4) to the filter
- Tobacco filler mass decrease (7.3%)
- Tobacco rod density decrease (16.3%)
- Cigarette paper base paper porosity decrease (4.2%)
- Cigarette paper band width increase (16.7%)
- Cigarette paper band space decrease (10%)
- Filter total denier decrease
- Filter denier per filament increase
- Filter density increase (35.6%)
- Filter pressure drop decrease (38%)
- Filter length decrease (22.2%)
- Filter ventilation decrease (16%)
- Tipping paper length decrease (19.4%)
- Increases of the following HPHCs:
  - 25% in B[a]P (ISO)
  - 122% in formaldehyde (ISO) and 76% (CI)

SE0000068:

- 65% decrease in (b) (4) (b) (4) /cigarette)
- 28% increase in (b) (4) (b) (4) /cigarette)
- 129% increase in (b) (4) (b) (4) cigarette)
- 237% increase in (b) (4) /cigarette)
- 112% increase in (b) (4) (b) (4) /cigarette)
- 8% decrease in the total amount of tobacco (b) (4) /cigarette)

- 26% ([b] (4) /cigarette) increase in [b] (4)
- 104% ([b] (4) /cigarette) increase in [b] (4)
- Addition to cigarette paper:
  - [b] (4) cigarette)
  - [b] (4) /cigarette)
- Addition in flavor ingredients:
  - [b] (4) /cigarette)
  - [b] (4) cigarette)
  - [b] (4) /cigarette)
  - [b] (4) /cigarette)
  - [b] (4) /cigarette)
- Increased in flavor Ingredients:
  - 4247% ([b] (4) cigarette) [b] (4)
  - 117% ([b] (4) cigarette) [b] (4)
- Addition of [b] (4) to the filter
- Cigarette length increase (18.1%)
- Tobacco filler mass decrease (8.9%)
- Tobacco rod density decrease (15.7%)
- Cigarette paper base paper porosity decrease (60%)
- Cigarette paper band porosity decrease (78.3%)
- Cigarette paper band width increase (16.7%)
- Cigarette paper band space decrease (10%)
- Filter total denier increase
- Filter denier per filament increase
- Filter density increase (33.1%)
- Filter length increase (47.6%)
- Filter ventilation decrease (3%)
- Tipping paper length increase (40%)
- Increases of the following HPHC:
  - 37% in formaldehyde (ISO) and 49% (CI)

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 decreases in [b] (4) and [b] (4) but an increase in [b] (4) and addition of [b] (4) This accounts for a net decrease of 8% in the total amount of tobacco. Also, for SE0000068, these is a 26% increase in [b] (4) in the [b] (4) and a 104% increase in [b] (4) n the [b] (4) Changes in tobacco blend and an increase in sugars can impact smoke chemistry.[5] There were many small changes (<1.4 mg/cigarette) in the cigarette paper and flavor ingredients in both SE Reports as well as in the cigarette side seam adhesive ingredients in SE0000067. These small changes are not expected to

[5] a) Ding YS, Zhang L, Jain RB, et al. Levels of tobacco-specific nitrosamines and polycyclic aromatic hydrocarbons in mainstream smoke from different tobacco varieties. *Cancer Epidemiol Biomarkers Prev.* 2008; 17 (12):3366-3371;
b) Hoffmann D, Hoffmann I. The changing cigarette: chemical studies and bioassays. Risks Associated with Smoking Cigarettes with Low Machine-Measured Yields of Tar and Nicotine. *Smoking and Tobacco Control Monograph*. Bethesda, MD: NIH National Cancer Institute, US Dept of Health and Human Services; 2001.159-191. 13.; and c) Roemer E, Schorp MK, Piade JJ; Seeman, JI; et al. Scientific assessment of the use of sugars as cigarette tobacco ingredients: a review of published and other publicly available studies. *Crit Rev Toxicol.* 2012;42(3):244-278.

cause the new tobacco products to raise different questions of public health. There were also numerous design parameter changes in the new tobacco products, such as: decrease in tobacco rod density, increase in cigarette base paper porosity, increase in filter density, and decrease in filter ventilation. The main difference between the new tobacco products and the corresponding predicate tobacco products is the presence of a (b) (4) filter in the new tobacco products. The applicant fully characterized the (b) (4) filter and demonstrated that it is unlikely that (b) (4) breakthrough would occur and be released for inhalation by the consumer. They also submitted tar, nicotine, carbon monoxide and 13 additional HPHCs (acrolein, acrylonitrile, 1-amininaohthalene, 2-aminonaphthalene, 4-aminobiphenyl, ammonia, benzo(a)pyrene, crotonaldehyde, formaldehyde, isoprene, NNK, NNN and 1,3-butadiene). Sufficient information was provided for the HPHC testing methods and all the smoke data was analytically equivalent between the new and corresponding predicate tobacco products except for the following HPHCs: B[a]P (ISO) and formaldehyde (ISO and CI) in SE0000067 and formaldehyde (ISO and CI) in SE0000068. The QRA was adequate to demonstrate substantial equivalence of HPHCs. 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 products (i.e., were commercially marketed in the United States other than exclusively in test markets as of February 15, 2007).

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.

Because the proposed action is issuing SE orders for the provisional SE Reports, it is a class of action that is categorically excluded under 21 CFR 25.35(a). 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 impact statement.

SE order letters should be issued for the new tobacco products in SE0000067 and SE0000068, as identified on the cover page of this review.