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Subject: Philip Morris USA SE Report: SE0000603

### **Background**

A TPL review was signed on July 27, 2018, by Matthew Walters. The review identifies a statistically significant increase in formaldehyde yield (19%) from the new product compared to the surrogate predicate product under the Canadian Intense (CI) smoking regimen. The review recommends that an NSE order be issued for the SE Report with the basis for the recommendation being a single deficiency regarding the formaldehyde yield increase. The applicant provided toxicity assessment relying on threshold of toxic concern (TTC), occupational exposure limit (OEL), and literature review as supporting evidence that the formaldehyde increase does not cause the new product to raise different questions of public health. The formaldehyde deficiency indicates that the toxicity assessments is inadequate to demonstrate that the formaldehyde yield increase does not cause the new product to raise different questions of public health.

### **Discussion**

I agree that the formaldehyde yield increases are significant and may cause the new product to raise different questions of public health. However, I found that all of the information in the administrative record, when evaluated in totality, is sufficient to conclude that the increases in formaldehyde yields do not cause the new product to raise different questions of public health.

The toxicology review by Eric Beier on January 19, 2018, concludes that the TTC, OEL, and literature review have shortcomings that prevent FDA from drawing conclusions about the toxicity of the new product relative to the predicate product. I agree with this conclusion. However, I do not believe TTC, OEL, and literature review are needed to demonstrate that the increase in formaldehyde does not cause the new product to raise different questions of public health from a toxicology perspective. The chemistry review by Caroline Agarabi on January 22, 2018, includes harmful or potentially harmful constituent (HPHC) data results

for the new and surrogate predicate products in Tables 6-8. Data was reported for the following HPHCs under ISO and CI smoking regimens:

1. Nicotine
2. Tar
3. Carbon Monoxide (CO)
4. Acetaldehyde
5. Acetone
6. Acrolein
7. Benzene
8. Benzon(a)pyrene
9. 1,3-Butadiene
10. Formaldehyde
11. NNK
12. NNN Phenol
13. Propylene glycol
14. Propylene oxide
15. Toluene
16. Vinyl acetate

The chemistry reviewer, toxicology reviewer, and TPL conclude that none of the HPHCs *except* formaldehyde had significant increases. They also conclude that formaldehyde yields were significantly increased under one of the smoking regimens but not the other. Based on the extensive list of HPHCs tested under both smoking regimens which did not reveal significant increases in HPHC yields other than formaldehyde, it does not seem likely that the formaldehyde yield increases under a single regimen is going to increase the toxicity of the new product. Furthermore, smoke yields for other volatile organic compounds (VOCs) such as acrolein, acetaldehyde, and benzene did not show statistically significant increase in the new product compared the surrogate predicate product. It seems unlikely that the increase in formaldehyde yield would increase the toxicity of the new product in light of the fifteen other HPHCs that did not increase. Therefore, taking all of the HPHC data together, I conclude that the increase in formaldehyde does not cause the new product to raise different questions of public health.

## Conclusion

Based on the totality of the information within this SE Report, in this case, the formaldehyde yield increase under a single smoking regimen does not cause the new product to raise different questions of public health. Therefore, OS will issue an SE order for the new product.

Under 21 CFR 25.35(a), issuance of SE orders under section 910(a) of the FD&C Act for this provisional SE Report is categorically excluded and, therefore, normally does 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.