White Paper for Substantial Equivalence

Altria Client Services LLC ("ALCS"), on behalf of Philip Morris USA ("PM USA") has provided comments to the Food and Drug Administration ("FDA" or "the Agency") and the Center for Tobacco Products ("CTP" or "Agency") periodically and through various methods (e.g., comments to particular dockets) disagreeing with, and objecting to, certain of CTP's or FDA's interpretations and implementation of the Tobacco Control Act, including issues specifically related to substantial equivalence. Nor is ALCS alone. Recently, the United States District Court for the District of Columbia has rejected certain of the Agency's positions regarding substantial equivalence.[1] ALCS reiterates and summarizes its position on these issues below. ALCS requests that the Agency reconsider its positions regarding substantial equivalence in evaluating the pending application.

Substantial equivalence is an inherently comparative evaluation between (1) the new and predicate products, or (2) if there are material differences in characteristics, between the new product and the tobacco marketplace as to questions of public health.

The Act defines "substantial equivalence" or "substantially equivalent" to mean that a new tobacco product

> (i) has the same characteristics as the predicate tobacco product; or
>
> (ii) has different characteristics and the information submitted contains information, including clinical data if deemed necessary by the Secretary, that demonstrates that it is not appropriate to regulate the product under [section 910] because the product does not raise different questions of public health.[2]

Under subsection (i), the comparison of a new tobacco product to a predicate tobacco product turns on the *characteristics* of the products—that is, whether the product characteristics are the "same." For these purposes, "characteristics" is clearly defined to mean "the materials, ingredients, design, composition, heating source, or other features of a tobacco product."[3] If the characteristics of the new and predicate products are not the "same" then the inquiry shifts to a comparison under subsection (ii) of the new product to the tobacco marketplace to determine whether the new product raises different questions of public health.

"Same characteristics"

The Agency previously interpreted the phrase "same characteristics" to mean "identical characteristics." This position was rejected by the US District Court for the District of Columbia.[4] The court clarified that Congress "created a less burdensome 'same characteristics' prong that seemingly was intended for physical changes that were more than 'minor,' but yet not so significant so to require a showing, through clinical data if demanded, that 'the product does not raise different questions of public health.'"[5] ALCS agrees with this interpretation. Under

[1] *Philip Morris USA, Inc. v. FDA*, __ F. Supp. 3d __, No. 15-1590, 2016 WL 4378970 (D.D.C. Aug. 16, 2016).
[2] 21 U.S.C. § 387j(a)(3)(A).
[3] *Id.* § 387j(a)(3)(B).
[4] *Philip Morris USA, Inc. v. FDA*, __ F. Supp. 3d __, No. 15-1590, 2016 WL 4378970 (D.D.C. Aug. 16, 2016).
[5] *Id. at *17.*

this interpretation, differences in characteristics of a type or magnitude that do not raise questions of public health do not render the products different within the meaning of Substantial Equivalence (i.e., the two products have the "same characteristics" under the first prong of Substantial Equivalence). ALCS agrees that if the differences in characteristics between the two products are so significant that they do raise a question of public health, the focus shifts to the second prong of the Substantial Equivalence test to determine if the differences raise questions of public health that are different from questions already posed in the marketplace by existing products.

For example, based on previous CTP decisions, we are aware of several categories of changes in products that CTP itself has acknowledged should not raise questions of public health. In the context of smokeless tobacco products, CTP has found that the inclusion of ingredients that are generally recognized as safe for inclusion in food does not raise different questions of public health.[6] CTP has also indicated that it focuses its review on differences of 5% or more between the new and predicate products because differences less than 5% are minimal "and [do] not cause the new products to raise different questions of public health."[7] Similarly, CTP has indicated that it focuses its review "on ingredients present at concentrations of at least 0.1 percent of the total weight of the cigarette."[8] Finally, in the context of both cigarette and smokeless tobacco products, CTP has indicated that where HPHC yields are lower in the new product, this indicates that the changes in the new product do not raise different questions of public health.[9] In all of these examples, substantial equivalence review is appropriate under the "same characteristics" prong because the differences between the new and predicate products do not raise questions of public health.

"Does not raise different questions of public health"

Section 910(a)(3)(A)(ii), which sets forth the second prong evaluation for substantial equivalence, makes no reference to the predicate product with respect to the public health inquiry. If Congress intended manufacturers to demonstrate that a new tobacco product "does

[6] CTP Technical Project Lead (TPL) Memorandum: SE Reports SE0001762, SE0003525, SE0003526, SE0003528, SE0003529, SE0004386, SE0004387, SE0004388 ("Timber Wolf TPL"), dated Nov. 15, 2013 at p. 10.

[7] CTP 2nd Cycle Chemistry Review of SE Reports Submitted by Philip Morris USA Inc. for Combustible Filtered Cigarettes (SE0009408-SE0009434) at pp. 17-18; see also Premarket Tobacco Application (PMTA) Technical Project Lead Review for PM0000010-PM0000017, dated Nov. 3, 2015 at p. 15 ("Due to testing variability, values for the new products that are out of industry range by less than 5% are considered to be within range and acceptable.")

[8] CTP Chemistry Review of SE Reports Submitted by Altria Client Services for Conventional Filtered Cigarettes (SE0003629, SE0003654-SE0003671, SE0003673, SE0003705, SE0003707-SE0003710, SE0004209, SE0004210), dated Oct. 23, 2012, at p. 14.

[9] CTP Technical Project Lead (TPL) Review: SE0009408, SE0009412, SE0009416, SE0009424, SE009427, SE0009431, SE0009433 at p.11 ("The different cigarette paper does not cause significant increases in the yields of tar, nicotine, or carbon monoxide (TNCO) in the new products. For all of the SE Reports, TNCO yields decreased by 2 to 20 percent in the new tobacco products relative to the corresponding predicate tobacco products. Therefore, the differences in characteristics related to product composition … do not cause the new tobacco products to raise different questions of public health."); Timber Wolf TPL at p. 12 ("Although there are differences in tobacco blend and other ingredients in the new tobacco products … [t]he HPHC data indicates that these differences in characteristics do not cause the new tobacco products to be more toxic …. More specifically, the TSNA quantities in the new tobacco products are lower than those in the corresponding predicate tobacco products, which does not cause the new tobacco products to raise different questions of public health.").

not raise different questions of public health" based on a comparison between the new and predicate products, then it would have said so.[10] Rather, this public health inquiry necessarily requires a comparison to the marketplace to determine whether the new product would raise different questions of public health. Such a marketplace comparison is also consistent with conversations between ALCS and CTP's Office of Science in September and October 2016 regarding the use of "surrogates" to provide evidence that a new tobacco product does not raise different questions of public health. If submitted "information, including clinical data if deemed necessary by the Secretary" demonstrates that the new product fits within the ranges of characteristics for the marketplace or has similar risk or addictiveness profile as other products in the marketplace, then the product is substantially equivalent.

[10] The substantial equivalence provisions of the Tobacco Control Act are modeled after those in the Medical Device Act. The second prong of the substantial equivalence inquiry for medical devices evaluates whether the new product "is as safe and effective as a legally marketed device, and …does not raise different questions of safety and effectiveness *than the predicate device*." 21 U.S.C. § 360c(i)(1)(A)(ii)(I)(emphasis added). Congress modified this inquiry in the Tobacco Control Act by omitting the phrase "than the predicate device" to require only a showing that "the product does not raise different questions of public health." That omission was purposeful and reflects Congress's intent that the "different questions of public health" inquiry for a tobacco product pertain to the tobacco marketplace as a whole. *See Keene Corp. v. United States*, 508 U.S. 200, 208 (1993)("[W]here Congress includes particular language in one section of a statute but omits it in another…, it is generally presumed that Congress acts intentionally and purposely in the disparate inclusion or exclusion.")