Altria
Altria Client Services

James E. Dillard III
Senior Vice President
Regulatory Affairs

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Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. FDA-2010-D-0635 (76 Fed. Reg. 789 (Jan. 6, 2011)) – Comments on the "Guidance for Industry and FDA Staff, Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products"

Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC") submit these comments on the above-captioned guidance document ("Guidance").[1] We may supplement these comments at a future date as the FDA's thinking on tobacco product substantial equivalence evolves. We also plan to submit separate comments on the FDA's proposed rule on exemptions from substantial equivalence requirements.[2]

We appreciate the complexity of the issues associated with substantial equivalence reporting. We offer these comments and ask the Agency to take them into account and issue a revised Guidance.[3]

Our comments are organized into the following sections:

- The FDA's Guidance Should Address the Timing of 905(j) Decisions
- The Agency Needs to Clarify its Definition of "New Tobacco Product"
- "As of February 15, 2007" Means On or Before that Date

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[1] Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC") are wholly-owned subsidiaries of Altria Group, Inc. Altria Client Services ("ALCS") is making this submission on behalf of PM USA and USSTC. ALCS provides certain services, including regulatory affairs, to the Altria family of companies. "We" is used throughout to refer to PM USA and USSTC.

[2] *See* 76 Fed. Reg. 737 (Jan 6, 2011).

[3] FDA issued a Final Guidance in contravention to its general rule requiring "public participation" in the development of guidance documents. *See* 21 U.S.C. § 371(h)(1)(A), (C). We urge FDA to consider the public comments it receives and issue a Revised Final Guidance in a timely manner.

Altria Client Services Inc.
2325 Bells Road
Richmond, Virginia 23234
(804) 335-2679
James.E.Dillard@altria.com

- Comparison to Multiple Predicates is Consistent with the Statute and the Scientific Basis of Other FDA Regulatory Processes
- FDA Needs to Address Several Issues About What Constitutes "Same Characteristics"
- Certain of the "Additional Data" FDA Recommends Considering When Analyzing "Different Questions of Public Health" are Not Required by the Statute or Needed for Substantial Equivalence Determinations
- The Agency Needs to Provide Details About How a Manufacturer Can Demonstrate Compliance with the Requirements of the Act
- A Post-March 22, 2011 905(j) Report Should be Deemed to Satisfy the Ingredient Disclosure Requirements of 904(c)

I. The FDA's Guidance Should Address the Timing of 905(j) Decisions.

Revised Guidance should address the timing of the FDA's 905(j) decisions. For products proposed to be first commercially marketed after March 22, 2011, prompt FDA decisions on 905(j) reports are crucial because manufacturers cannot lawfully market such products until the FDA issues a substantial equivalence order. The Agency should establish a reasonable timeframe for its review of such submissions.

For other product submissions to the FDA, the Agency operates under either a statutory or regulatory deadline or an established "performance goal." For example, the FDA committed to issuing a decision on modified risk tobacco product applications within 360 days of receiving the application.[4] For new tobacco products under FDCA § 910, the FDA must respond "as soon as possible, but in no event later than 180 days after receipt of [the] application."[5] A 905(j) submission should require fewer Agency resources and less review time because the statutory requirements for substantial equivalence are fewer and less complex.

In the other FDA-regulated product context most analogous to 905(j) "substantial equivalence" reports—medical device 510(k) "substantial equivalence" submissions[6]—the FDA has committed to issuing a decision for 90% of medical device 510(k)s within 90

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[4] *See* FDA Draft Guidance, "Preliminary Timetable for the Review of Applications for Modified Risk Tobacco Products under the Federal Food, Drug, and Cosmetic Act" (Nov. 2009), *available at* http://www.fda.gov/downloads/TobaccoProducts/GuidanceComplianceRegulatoryInformation/UCM191915.pdf.

[5] 21 U.S.C. § 387j(c)(1).

[6] *Compare* 21 U.S.C. § 360c(i) (medical device "substantial equivalence") *to* 21 U.S.C. § 387j(a)(3) (tobacco product "substantial equivalence"). Neither provision mandates a timeframe in which the FDA must respond to a "substantial equivalence" submission.

days of receipt, and for 98% of them within 150 days.[7] FDA regulations allow 180 days for Agency review of the more complex medical device premarket approval application.[8]

The FDA should establish a "performance goal" of issuing a decision on most, if not all, 905(j) reports required for introduction of a new tobacco product within 90 days of receipt. A 90-day review deadline for 905(j) submissions is reasonable given the user fees paid by manufacturers[9] and the relatively simpler designs (compared to medical devices) that are commonly used in the vast majority of tobacco products in a particular category.

We also suggest that the FDA provide for expedited review of 905(j) reports for situations beyond a manufacturer's control in which a product change is required in a short time frame. For example, an ingredient or material may become unavailable due to uncontrollable supply chain interruptions. It would be unreasonable to require a manufacturer to discontinue production of its affected tobacco products under such circumstances while awaiting the FDA review of a 905(j) report.

II. The Agency Needs to Clarify its Definition of "New Tobacco Product."

The Agency needs to clarify the definition of "new tobacco product" by identifying the specific factors, product attributes, and other considerations that will result in a product being deemed a "new tobacco product."

There are numerous sources of variability inherent in tobacco products that should not constitute a 910(a)(1)(B) "modification." These include variations in manufacturing and differences in materials from lot-to-lot. Adjustments made in response to such variations that are necessary to maintain consistent product characteristics (*e.g.*, adjustments in ventilation parameters to maintain a consistent "tar" per puff, and therefore consistent strength of taste) also should not be considered "modifications." In fact, such adjustments are the opposite of a "modification" since they are intended to maintain a consistent product. In addition, testing variability among different analytical laboratories and (to a lesser extent) within the same laboratory can create the appearance of product variations when, in fact, none actually exists.[10] None of these inherent variations, or adjustments made in response to them, should be considered "modifications."

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[7] *See* FDA Letter to Senator Edward M. Kennedy, Chairman, Committee on Health, Education, Labor, and Pensions, U.S. Senate, Medical Device User Fee Amendments Act of 2007 (MDUFA) Performance Goals and Procedures (Sept. 27, 2007), *available at* http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/UCM109102.pdf.

[8] *See* 21 C.F.R. § 814.40; FDA, Premarket Approval (PMA), available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketApprovalPMA/default.htm.

[9] *See* 21 U.S.C. § 387s(b)(1) (Fiscal year 2009 user fees totaled $85 million; user fees increase in subsequent years until 2019 when the ongoing user fee is $712 million per fiscal year).

[10] "Determination of 'Hoffman Anayltes' in Cigarette Mainstream Smoke. The Coresta 2006 Joint Experiment" Vol. 23 #4 May 2009, p. 161 (available at www.beitraege-bti.de).

Moreover, a product should not be considered "modified" if it is produced within specifications that existed prior to February 15, 2007. For example, there may be a range in paper permeability to permit adjustments to maintain consistent product characteristics. This approach is analogous to the "design space" concept recognized in the regulation of pharmaceutical production.[11]

III. "As of February 15, 2007" Means On or Before that Date.

The phrase "as of February 15, 2007" means on or before the date February 15, 2007. There is no statutory requirement in § 910 or in § 905(j) that a manufacturer provide evidence that a predicate product was marketed nearly four years ago *on* Thursday, February 15, 2007. Such a requirement would not be reasonable or practical, especially given that the Act did not become law until more than 28 months later.

The words "as of" are used to indicate a time or date at which something begins or ends."[12] Thus, February 15, 2007 is the "end" of the period of eligible predicates and grandfathering as "non-new" tobacco products. The following day is the "beginning" of when tobacco products are no longer eligible to serve as predicates (except in the case of products previously found to be substantially equivalent) and may be "new" tobacco products.

Finally, the contrast to the language "after February 15, 2007" (*see* §§910(a)(1)(B) and (a)(2)(B)(i)) clearly indicates that "as of" was intended to mean "on or before."

IV. Comparison to Multiple Predicates is Consistent with the Statute and the Scientific Basis of Other FDA Regulatory Processes.

A multiple predicate approach is consistent with the statute and the scientific basis for FDA's historical treatment of substantial equivalence in other regulated areas. We urge the FDA to consider a "market range" approach to predicate products in which the various attributes of a "new tobacco product" are compared to the various attributes of similar tobacco products, as they existed on or before February 15, 2007.

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[11] An FDA/international regulatory document on drug development, "Guidance for Industry: Q8 Pharmaceutical Development" (May 2006), utilizes the concept of "design space." It defines this concept as: "The multidimensional combination and interaction of input variables (*e.g.*, material attributes) and process parameters that have been demonstrated to provide assurance of quality. Working within the design space is not considered as a change. Movement out of the design space is considered to be a change and would normally initiate a regulatory postapproval change process. Design space is proposed by the applicant and is subject to regulatory assessment and approval." Application of the "design space" concept to tobacco products would of course be somewhat different than it would with respect to drugs, given the differences in the nature of the products and industry design specifications, controls, etc.

[12] *See* Merriam-Webster Online Dictionary at http://www.merriam-webster.com/dictionary/as%20of.

The substantial equivalence provisions of § 910(a) are modeled on the medical device provisions of FDCA, which also refer to "a predicate" product in the singular.[13] FDA interprets this language, however, to permit a new device to be compared to more than one predicate[14] and very recently stated, in its comprehensive plan for improving the 510(k) program, that it "strongly supports the use of multiple predicates."[15] Given this analogous statutory framework, Congress's use of the term "predicate" should be read to allow for the use of multiple predicate products in a substantial equivalence evaluation.[16]

The Institute of Medicine ("IOM") also applied the logic of multiple predicates when it developed the framework for the "No increased risk" threshold in Regulatory Principle 7 "as compared to similar conventional tobacco products."[17] The IOM further noted that tobacco products without health claims should be "at least no more hazardous than in similar contemporaneously marketed products,"[18] an approach that draws from the diversity of products available in the U.S. market and does not limit review to one-to-one product comparisons.

V. FDA Needs to Address Several Issues About What Constitutes "Same Characteristics."

A. "Same Characteristics" Cannot be Interpreted to Mean Identical Characteristics.

The term "same characteristics" cannot be interpreted to mean "identical characteristics." To do so would render the "same characteristics" test meaningless because any product that is new or modified would be automatically evaluated under "different questions of public health." Also, a product that is identical to a predicate is, by definition, neither new nor modified. A basic principle of statutory interpretation is that one must "give effect, if possible, to every clause and word of a statute, avoiding, if it may be, any construction which implies that the legislature was ignorant of the meaning

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[13] *See* 21 U.S.C. § 360c(i)(1)(A) ("'substantially equivalent' ... means, with respect to a device being compared to a predicate device . . .").

[14] *See* FDA Center for Devices and Radiological Health, "Premarket Notification 510(k): Regulatory Requirements for Medical Devices," 1995 WL 17210952 (noting that a device may be compared to one or more predicate devices in claiming substantial equivalence); FDA, "Regulations Restricting the Sale and Distribution of Cigarettes and Smokeless Tobacco to Protect Children and Adolescents," 61 Fed. Reg. 44396, 44410, 1996 WL 482785 (1995) (noting that devices "may not be commercially distributed unless the Agency issues an order finding the device substantially equivalent to one or more predicate devices already legally marketed in the United States").

[15] *See* CDRH, "510(k) and Science Report Recommendations: Summary and Overview of Comments and Next Steps" at § 5.1.2.3, published Jan. 19, 2011 at http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDRH/CDRHReports/UCM239449.pdf.

[16] *Ratzlaf v. United States*, 510 U.S. 135, 143 (1994) ("A term appearing in several places in a statutory text is generally read the same way each time it appears."); *Merrill Lynch, Pierce, Fenner & Smith v. Curran*, 456 U.S. 343, 382 n.66 (1982), quoting *Lorillard v. Pons*, 434 U.S. 575, 580 (1978) ("Congress is presumed to be aware of an administrative . . . interpretation of a statute.").

[17] IOM, Clearing the Smoke: Assessing the Science Base for Tobacco Harm Reduction (2001), 222.

[18] *Id.* at 223.

of the language it employed."[19] A modern variant of this canon is that statutes must be construed "so as to avoid rendering superfluous" any statutory language.[20]

The Guidance does not clearly explain the circumstances under which a tobacco product may be "new" and yet have the "same characteristics" as a predicate(s). Nor does the Guidance explicitly define "same characteristics." The overall implication, however, is that FDA intends to take a narrow view of "same characteristics."[21] For example, it appears that ingredient substitutions that go beyond those described in section V.C of the Guidance would result in a determination that the characteristics are different and trigger an analysis under "different questions of public health." Such a narrow interpretation reads the "same characteristics" test out of the statute.

FDA recently acknowledged the importance of clarifying the criteria that trigger the different pathways of the substantial equivalence framework for medical devices.[22] It should do the same here.

New tobacco products with conventional designs comprising new combinations of ingredients, ingredient levels and materials used in marketed tobacco products would have the same characteristics as those already marketed products in terms of smoke toxicity.[23] It is important to give closer scrutiny to truly novel compositional or design features of a new tobacco product which might have the potential to alter toxicity. This approach is consistent with a reasonable interpretation of both "same characteristics" and "different questions of public health."

The Agency should adopt an interpretation of "same characteristics" that recognizes the range of characteristics on the market on or before February 15, 2007. Such an approach would align with statutory intent and relieve the FDA of the burden of conducting unnecessary reviews.

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[19] *Montclair v. Ramsdell*, 107 U.S. 147, 152 (1883).

[20] *Astoria Federal Savings & Loan Ass'n v. Solimino*, 501 U.S. 104, 112 (1991); *Sprietsma v. Mercury Marine*, 537 U.S. 51, 63 (2003) (interpreting word "law" broadly could render word "regulation" superfluous in preemption clause applicable to a state "law or regulation"). *See also Bailey v. United States*, 516 U.S. 137, 146 (1995) ("we assume that Congress used two terms because it intended each term to have a particular, nonsuperfluous meaning") (rejecting interpretation that would have made "uses" and "carries" redundant in statute penalizing using or carrying a firearm in commission of offense).

[21] *See e.g.*, Guidance section V.A (request for voluminous data to be presented as "side-by-side quantitative and qualitative comparisons of the new tobacco product with the predicate tobacco product with respect to all product characteristics"); section V.C ("same characteristics" will only be found when "a minimal number of ingredients, or materials have been substituted (substitution may include the same ingredient or material but from a different source)," and there is "documentation demonstrating that the substituted ingredient(s) or material(s) meets the required specifications for the replaced ingredient(s) or material(s).").

[22] See, *e.g.*, CDRH, "510(k) and Science Report Recommendations: Summary and Overview of Comments and Next Steps," published Jan. 19, 2011, available at http://www.fda.gov/downloads/AboutFDA/CentersOfffices/CDRH/CDRHReports/UCM239449.pdf.

[23] We alert the Agency to an upcoming special edition of *Inhalation Toxicology* in which we will discuss results from our multi-year testing program of cigarette ingredients. The program investigated dose response relationships of various chemical classes using standard toxicology endpoints that have been used to assess cigarette smoke. The results of this testing lead to the conclusion that the ingredients typically used in modern cigarettes do not substantially alter smoke toxicity.

B. The "Same Characteristics" Analysis Should Not Include a Comparison of Harmful and Potentially Harmful Constituents Between the Predicate(s) and the "New" Product.

Among the "other features" that FDA recommends including in a characteristics comparison between new and predicate tobacco products are "harmful and potentially harmful constituents" (HPHCs). FDA is directed, under §§ 904(d) & (e) of the Act, to establish and publish a list of HPHCs; no such list, however, has been published. As a result, it is unknown what constituents should be measured and reported as part of the substantial equivalence process. Until such time as a list of HPHCs is developed and published, manufacturers can provide information only about those constituents for which validated analytical methods, historical data, and ongoing testing and reporting requirements exist for marketed products, *e.g.*, information submitted to the Federal Trade Commission and the Centers for Disease Control.

For purposes of defining substantial equivalence, "the term 'characteristics' means the materials, ingredients, design, composition, heating source, or other features of a tobacco product."[24] It does not include "constituents." When Congress wanted to address constituents in the Act, it did so explicitly (*e.g.*, the establishment and publishing of a HPHC list under §§ 904(d) & (e); manufacturer testing and reporting of tobacco product constituents under regulations to be promulgated by FDA under § 915; testing and reporting of constituents for new tobacco products 90 days prior to introduction under § 904(c)(1); and FDA's authority under § 907 to establish tobacco product standards, including "for the reduction or elimination of other constituents, including smoke constituents, or harmful components of the product.").

Given this comprehensive framework, and the exclusion of constituents in the substantial equivalence context, it is clear that Congress did not intend for the FDA to require a comparison of constituents as part of a substantial equivalence report.[25] Congressional intent is further evidenced by the timing of the various provisions on constituents. Specifically, substantial equivalence reports are due by March 22, 2011, which is well before the April 1, 2012 deadline by which FDA is required to publish a list of HPHCs and promulgate regulations for testing and reporting.

Regardless of when a HPHC list becomes available, it is highly unlikely that cigarettes and smokeless tobacco products on the market on or before February 15, 2007 still exist, let alone in quantities sufficient to satisfy FDA's future testing

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[24] 21 U.S.C. § 387j(a)(3).

[25] A well-accepted canon of statutory interpretation is that "where 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." *Keene Corp. v. United States*, 508 U.S. 200, 208 (1993) (*quoting Russello v. United States*, 464 U.S. 16, 23 (1983)). *See also Bailey v. United States*, 516 U.S. 137, 146 (1995) (distinction in one provision between "used" and "intended to be used" creates implication that related provision's reliance on "use" alone refers to actual and not intended use); *Bates v. United States*, 522 U.S. 23, 29 (1997) (inclusion of "intent to defraud" language in one provision and exclusion in a parallel provision indicated intent to defraud was not an element of the offense of knowingly and willingly misappropriating student loan funds).

requirements. Therefore, it is impossible to generate constituent data for most, if not all, predicate products.[26]

In the HPHC context and others related to substantial equivalence, the Agency should make clear that roll-your-own tobacco products (RYO) and cigarette tobacco are subject to the same requirements as other cigarettes and smokeless tobacco products, and further explain how it will apply these requirements to these tobacco products. Consumers have multiple options from which to choose when combining commercially marketed RYO and cigarette tobaccos, papers, filters and other materials in different configurations. For example, when the HPHC list is published, it is unclear how such a "consumer assembled product" would be tested to determine HPHC levels. As the Agency considers these types of issues, it should follow the Act's requirement that, unless otherwise stated, the requirements applicable to cigarettes also apply to cigarette tobacco.[27]

VI. Certain of the "Additional Data" FDA Recommends Considering When Analyzing "Different Questions of Public Health" are Not Required by the Statute or Needed for Substantial Equivalence Determinations.

The "Additional Data" listed in the Guidance are not required by the statute or needed for substantial equivalence determinations.

The Guidance does not explicitly state the FDA's views about when a new tobacco product would be deemed to raise "different questions of public health." It appears, however, that the Agency believes that making such a determination could involve an assessment of the "additional data," including consumer perception studies, clinical studies, abuse liability data, and toxicological data.

This additional data is not required by the Tobacco Control Act. The various provisions of the Act have different requirements for the types of data that industry must submit, or that FDA must consider. For example, the criteria for evaluating non-substantially equivalent new tobacco products under § 910(c) of the Act require an evaluation of the risks and benefits to the population as a whole, including users and non users of the tobacco product, and taking into account the increased or decreased likelihood of cessation or initiation of product use.[28] This evaluation may include one or more clinical investigations.

Similar language regarding cessation or initiation effects is also included, *e.g.*, in criteria for authorization of modified risk tobacco products,[29] and for the development of

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[26] For a fuller discussion related to HPHCs and the development of the HPHC list, we refer the FDA to a previous submission in which we discuss our experience with tobacco constituent testing and evaluation of such data as part of our ingredient testing program. *See* Altria Client Services, Inc., Comments dated Aug. 23, 2010, Docket ID No. FDA-2010-D-0281-0003.1, available at http://www.regulations.gov/#!documentDetail;D=FDA-2010-D-0281-0003.1.

[27] *See* 21 U.S.C. § 387(4).

[28] *See* 21 U.S.C. § 387j(c)(4).

[29] *See* 21 U.S.C. § 387k(g)(4)(B) & (C).

tobacco product standards.[30] Moreover, an application for authorization of certain types of modified risk tobacco products (*i.e.,* "reduced exposure" products) requires "testing of actual consumer perception" with respect to risks.[31]

In contrast, Congress excluded from the criteria for substantial equivalence under § 910(a), and for reporting under § 905(j), any consideration of behavioral effects such as initiation or cessation, or of consumer perception studies. This absence shows Congressional intent that the criteria should *not* be considered in the substantial equivalence evaluation.[32]

This approach to addressing "different questions of public health" would be consistent with a tobacco regulatory principle proposed by the IOM, in response to a request from the FDA; *i.e.*, a "'No Increased Risk' Threshold for All Tobacco Products."

> In the absence of any claim of reduced exposure or reduced risk, manufacturers of tobacco products should be permitted to market new products or modify existing products without prior approval of the regulatory Agency after informing the Agency of the composition of the product and upon certifying that the product could not reasonably be expected to increase the risk of cancer, heart disease, pulmonary disease, adverse reproductive effects, or other adverse health effects, compared to similar conventional tobacco products, as judged on the basis of the most current toxicological and epidemiological information.[33]

We have long operated under similar principles. The ALCS Product Integrity Evaluation Guidelines establish the criteria to determine the acceptability of an ingredient or design change in cigarettes. The review process involves comparisons to currently marketed cigarettes and a tiered approach modeled after FDA guidelines for food ingredient exposure as described in FDA's "Office of Food Additive Safety Redbook 2000: Toxicological Principles for the Safety Assessment of Food Ingredients."[34] Guidelines for smokeless tobacco products apply similar principles.

Substantial equivalence evaluations under "different questions of public health" should be limited to standard safety studies; *i.e.*, toxicology and (where deemed necessary by the Secretary) clinical studies. An assessment of health effects based on a hazard evaluation grounded in sound scientific principles can be used to identify "different questions of public health" and will meet both Congressional intent and the "reasonable expectation of no increased risk" criteria proposed by the IOM.

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[30] *See* 21 U.S.C. § 387g(a)(3)(B)(i)(II) & (III).
[31] *See* 21 U.S.C. § 387k(g)(2)(B)(iii).
[32] *See* f.n. 25, *supra.*
[33] *See* IOM, Clearing the Smoke: Assessing the Science Base for Tobacco Harm Reduction (2001), 222.
[34] Although the procedure addressed in the FDA's "Redbook" is related to dietary exposure, PM USA considers its concepts of segregating subject materials by structure and anticipated exposure level into "concern levels" to be useful for the toxicologic evaluation of smoking products and their components.

If the FDA still believes it can request this information, it is not clear whether manufacturers would be expected to submit such data in the initial report or only upon request by the Agency.[35]

VII. The Agency Needs to Provide Details About How a Manufacturer Can Demonstrate Compliance with the Requirements of the Act.

FDA should provide a clear recommendation about the type and format of the information it wants manufacturers to provide to demonstrate compliance with other requirements of the Act.[36] The FDA already has access to information such as a manufacturer's registration and product listings, ingredient list filings, submission of tobacco health information, and any other required regulatory filings. Moreover, the § 905(j)(1)(B) requirement to report "action taken by such person to comply with the requirements under § 907 that are applicable to the tobacco product" seems to have little relevance to products currently on the market since the only tobacco product standard currently in effect is a ban on characterizing flavors in cigarettes other than menthol or tobacco.

If the FDA expects a manufacturer to summarize this information or provide additional information, it should provide that direction in Revised Guidance.

VIII. A Post-March 22, 2011 905(j) Report Should be Deemed to Satisfy the Ingredient Disclosure Requirements of 904(c).

FDA should allow a 905(j) report to fulfill more than one regulatory obligation. If a manufacturer includes the information recommended in the Guidance, the information submitted in its 905(j) report will include a complete disclosure of the ingredients (including additives) that are to be added to a tobacco product, or to any part thereof. As a result, the 905(j) report should simultaneously fulfill the ingredient disclosure requirements of FDCA § 904(c).[37] Moreover, a 905(j) report submitted on or after March 22, 2011 must be submitted at least 90 days before delivering the product

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[35] The Guidance states both that the "FDA may request" such data and that a 905(j) report "should include the[se] data."

[36] *See* section IV.D of the Guidance ("[i]n addition to determining that the product is substantially equivalent, FDA must also determine that the new tobacco product is in compliance with the requirements of the Act before issuing an order under section 910(a)(2)(A)(i).").

[37] 21 U.S.C. § 387d(c)(1) cross-references "the information required under subsection (a)" (which includes "a listing of all ingredients, including tobacco, substances, compounds and additives" added to each part of a tobacco product) and applies to products "not on the market on the date of enactment." A 904(c)(2) disclosure applies to modifications involving new additives or increased usage levels of existing additives, and a 904(c)(3) disclosure applies to modifications involving elimination or decreased usage of an additive, or to additive changes involving additives "designated" by FDA as not carcinogenic or otherwise harmful "under intended conditions of use."

for introduction into interstate commerce. Thus, assuming a manufacturer includes the information recommended in the Guidance, it would also satisfy the ingredient (including additive) disclosures under 904(c), which has a similar 90 days pre- (and in some cases 60 days post-) timing requirement.[38]

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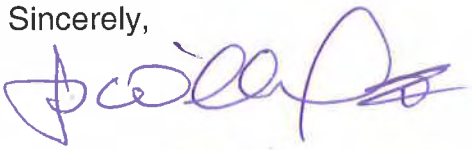
We appreciate the opportunity to submit these comments and urge the Agency to incorporate them in a Revised Guidance. We look forward to further opportunities to provide comments to the Agency as its thinking on substantial equivalence evolves.

Sincerely,



James E. Dillard III

[38] A 904(c)(1) disclosure must be made "[a]t least 90 days prior to the delivery for introduction into interstate commerce of a tobacco product not on the market on the date of enactment;" a 904(c)(2) disclosure must be made "at least 90 days prior to" the "time a tobacco product manufacturer adds to its tobacco products a new tobacco additive or increases the quantity of an existing additive;" and a 904(c)(3) disclosure must be made "within 60 days of" the "time a tobacco product manufacturer eliminates or decreases an existing additive, or adds or increases an additive that has by regulation been designated . . . ."

Altria
Altria Client Services

James E. Dillard III
Senior Vice President
Regulatory Affairs
James.E.Dillard@altria.com

2325 Bells Road
Richmond, VA 23234
(804) 335-2679

March 22, 2011

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. FDA-2010-N-0646 (76 Fed. Reg. 737 (January 6, 2011))
"Tobacco Products, Exemptions from Substantial Equivalence Requirements"

Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC")[1] submit these comments on the above captioned proposed rule "Tobacco Products, Exemptions from Substantial Equivalence Requirements."

As the Agency finalizes the proposed rule, we reference and incorporate our previously filed comments to the "Guidance for Industry and FDA Staff, Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products."[2] We asked the Agency to clarify its definition of a "new tobacco product" and provide additional guidance about what constitutes a "modification." We reiterate that there are numerous sources of variability inherent in tobacco products that should not constitute a "modification." These include variations in manufacturing and differences in materials from lot-to-lot. Adjustments made in response to such variations that are necessary to maintain consistent product characteristics are also not properly considered product "modifications" under the Family Smoking Prevention and Tobacco Control Act ("the Act"). As such, these adjustments do not render a product a "new tobacco product" or require premarket review under Sections 905(j) or 910. We urge the Agency to comply with the statute as it finalizes the rule for the exemption process. If, however, the Agency does not exclude such adjustments, we believe it should consider such adjustments minor modifications exempt from substantial equivalence requirements.[3]

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[1] Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC") are wholly-owned subsidiaries of Altria Group, Inc. Altria Client Services ("ALCS") is making this submission on behalf of PM USA and USSTC. ALCS provides certain services, including regulatory affairs, to the Altria family of companies. "We" is used throughout to refer to PM USA and USSTC.

[2] *See* Attachment A.

[3] This suggestion assumes, for purposes of this submission and participation in the rulemaking process and without prejudice to the statutory interpretation noted above and in our prior comments, that such adjustments could be construed as modifications for purposes of implementing and enforcing the Act.

Congress established an exemption process in section 905(j) of the Act to provide an alternative, less burdensome process to filing a substantial equivalence report. FDA's proposed rule, however, is contrary to Congressional intent because the proposed rule imposes on both the Agency and manufacturers unnecessary and duplicative burdens. For example, the proposed rule requires a manufacturer to file an exemption request and, if the exemption is granted, to file a subsequent 90 day notification that the modification made to the product is covered by the granted exemption and is otherwise in compliance with the Act. These requirements can be met in the exemption request, thus eliminating an additional unnecessary filing. In addition, and as discussed below, the proposed rule conflicts with several provisions of the Act in conditioning exemptions on the submission of data that Congress intended to exclude from substantial equivalence determinations.

A. Analysis of Toxicity Data Should Be the Basis for Agency Decision-Making on Exemptions.

The development of tobacco regulations should be guided by science- and evidence-based decisions. As such, we support the proposed rule where it will ensure that exemption decisions are based on an analysis of changes in toxicity that could result from ingredient (used interchangeably here with "additive") changes or other minor modifications to tobacco products.

We previously described the Product Integrity evaluation process for cigarettes and smokeless tobacco products used by PM USA and USSTC to determine the suitability of materials, ingredients and product designs.[4] This process evaluates proposed materials, ingredients and product designs to assess whether ingredients and design changes could potentially increase the inherent toxicity of cigarette smoke or smokeless tobacco products. These Product Integrity processes are derived from FDA's own well-established approach for the evaluation and approval of food ingredients.[5]

In an upcoming special issue of Inhalation Toxicology (expected April 2011), ALCS will report results from a large, multi-year study designed to investigate the effects of individual ingredients on mainstream cigarette smoke toxicity. Constituents of mainstream smoke and biological studies such as genotoxicity and smoke inhalation were analyzed.

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[4] *See* Altria Client Services, Inc., Comments dated August 23, 2010, Docket ID No. FDA-2010-D-0281-0003.1, available at http://www.regulations.gov/#!documentDetail;D=FDA-2010-D-0281-0003.1. This evaluation process is also described in the ALCS Product Integrity Toxicological Framework Guideline, the ALCS Product Integrity Toxicological Guideline -- Cigarette Products and the ALCS Product Integrity Review and Toxicological Evaluation Guideline: Smokeless Tobacco Products: Test Articles, Prototypes and Products, which were submitted to FDA on April 29, 2010 as part of PM USA's Tobacco Health Documents Submission.

[5] *See* FDA, *Guidance for Indus. and Other Stakeholders: Toxicological Principles for the Safety Assessment of Food Ingredients* (2000), *available at* http://www.fda.gov/downloads/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodIngredientsandPackaging/Redbook/UCM222779.pdf.

Results indicate that tobacco itself drives the biological activity of cigarette smoke and this biological activity is not impacted by the addition of ingredients as commonly used. While occasional single point-in-time analysis of cigarette smoke may demonstrate a numerical difference between the control (without the test ingredient) and experimental cigarette (with test ingredient), such differences are the result of analytical variability and the intrinsic variability of tobacco.

To determine the acceptability of ingredients for use in smokeless tobacco products we rely on recognized processes for evaluating the safety of ingredients for use in foods.[6] A food ingredient is determined safe for use based on a reasonable certainty that a substance is not harmful under the intended conditions of use.[7] Consideration of knowledge of chemical structures and the outcomes of toxicity studies inform this determination. It is scientifically valid to apply these determinations to ingredients used in smokeless tobacco products because the route of exposure is the same as for foods; hence, an extensive testing program such as described above for cigarettes is not necessary. Overall, ingredients added to smokeless tobacco products will not alter the toxicity of the product provided ingredients are used within limitations supported by available toxicological data.

We urge the FDA to promulgate a final rule that establishes a process focused on whether the addition of, or an increase in, the amount of an additive would increase the inherent toxicity of the tobacco product. Manufacturers can provide comparative internal toxicity testing information as part of their exemption request. Toxicity information is also available in the robust body of published scientific literature that shows additives have little influence on the inherent toxicity of cigarettes[8] or, in the case of smokeless tobacco products, have been demonstrated to be safe for use in foods. Once the Agency decides to grant an exemption request for a particular additive, the Agency should establish a categorical exemption for a range of levels of that additive applicable to all similar products (*e.g.*, all cigarettes or all smokeless tobacco products).

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[6] Additives used in smokeless tobacco products are generally recognized as safe (GRAS) as food ingredients by either FDA, the Flavor and Extract Manufacturers Association, or have undergone a self-GRAS process based on available toxicity information.

[7] *See* Title 21 of the Code of Federal Regulations.

[8] *See* Baker et al., (2004) Anal App Pyrol 71:223-311; Baker et al., (2004) Food Chem Toxicol 42 Suppl:S53-S83; Carmines, (2002) Food Chem Toxicol 40:77-91; Carmines et al., (2005) Food Chem Toxicol 43:1303-1322; Carmines and Gaworski, (2005) Food Chem Toxicol 43:1521-1539; Gaworski et al., (1998) Inhal Toxicol 10:357-38; Gaworski et al., (1999) Toxicology 139:1-17; Gaworski et al., (2008) Food Chem Toxicol 46:339-351; Gaworski et al., (2010) Toxicology 269:54-66; Heck et al., (2002) Inhal Toxicol 14:1135-1152; Heck, (2010) Food Chem Toxicol 48(S2):1-38; Paschke et al., (2002) Beitr Tabakforsch Int 20:107-247; Potts et al., (2010) Exp Toxicol Pathol 62:117-126; Renne et al., (2006) Inhal Toxicol 18:685-706; Roemer et al., (2002) Food Chem Toxicol 40:105-111; Rustemeier et al., (2002) Food Chem Toxicol 40:93-104; Stavanja et al., (2003) J Toxicol Environ Health Part A 66:1453-1473; Stavanja et al., (2008) Exp Toxicol Pathol 59:339-353; Vanscheeuwijck et al., (2002) Food Chem Toxicol 40:113-131.

B. Proposed Requirements About Addictiveness and Appeal to or Use by Minors are Not Required by Statute Nor is Such Information Available.

The proposed rule would require a "certification" "providing the rationale for the official's determination that the modification will not increase the product's toxicity, addictiveness, or appeal to or use by minors . . . " As previously noted in Section VI of our comments on the substantial equivalence guidance, behavioral types of effects are not part of the statutory framework for a substantial equivalence determination. They are also not included in the statutory requirements for a minor modification exemption under 905(j)(3), and, therefore, should be eliminated from the categories of data required by the proposed rule.

The Act has different requirements for the types of data that industry must submit, or that FDA must consider, for 905(j) exemptions as compared to non-substantially equivalent new products, modified risk products or the development of product standards. For example, an evaluation of the risks and benefits to the population as a whole, including users and non users of the tobacco product, and taking into account the increased or decreased likelihood of cessation or initiation of product use, is a criteria for FDA evaluation of non-substantially equivalent new tobacco products.[9] Similar language regarding cessation or initiation effects is also included in describing the criteria for authorization of modified risk tobacco products,[10] and for the development of tobacco product standards.[11] Moreover, an application for authorization of certain types of modified risk tobacco products (*i.e.*, "reduced exposure" products) requires "testing of actual consumer perception" with respect to risks.[12]

In contrast, Congress excluded any consideration of behavioral effects from the substantial equivalence criteria. Thus, the statute precludes consideration of behavioral effects as part of the substantial equivalence evaluation or in the evaluation of minor modification exemption requests.[13]

In addition, the proposed rule's data and certification requirements pose insurmountable practical problems. Specifically, the proposed requirement that manufacturers not only produce information about addictiveness and appeal to, or use by, minors, but also make certifications based on that information, is not viable. We do not believe sufficiently

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[9] *See* 21 U.S.C. § 387j(c)(4).
[10] *See* 21 U.S.C. § 387k(g)(4)(B) & (C).
[11] *See* 21 U.S.C. § 387g(a)(3)(B)(i)(II) & (III).
[12] *See* 21 U.S.C. § 387k(g)(2)(B)(iii).
[13] A well-accepted canon of statutory interpretation is that "where 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." *Keene Corp. v. United States*, 508 U.S. 200, 208 (1993) (*quoting Russello v. United States*, 464 U.S. 16, 23 (1983)). *See also Bailey v. United States*, 516 U.S. 137, 146 (1995) (distinction in one provision between "used" and "intended to be used" creates implication that related provision's reliance on "use" alone refers to actual and not intended use); *Bates v. United States*, 522 U.S. 23, 29 (1997) (inclusion of "intent to defraud" language in one provision and exclusion in a parallel provision indicated intent to defraud was not an element of the offense of knowingly and willingly misappropriating student loan funds).

sensitive tools (with the level of accuracy, reliability, and reproducibility required to make regulatory decisions) exist to measure addictiveness or appeal to, or use by, minors. SCENIHR[14] recently evaluated the potential role of tobacco additives in the addictiveness and attractiveness of tobacco products and noted that there are no universal standards for human studies or agreement about various possible endpoints which define whether an additive or a combination of additives increases the addictive potency or attractiveness of the final tobacco product.[15] Uncertainties of testing aside, there are other issues to consider, particularly as it relates to minors. For example, as a matter of policy, PM USA and USSTC do not conduct consumer or clinical research involving tobacco products with anyone under 21 years of age. As a result, we could not provide the information requested about appeal to, or use by, minors.

Toxicity data will likely be needed to evaluate some minor modification exemption requests and that data must be presented in a truthful and balanced manner. To the extent that the Agency believes it is necessary to require a certification, however, we believe the same certification requirement that applies to a medical device substantial equivalence submission under 21 C.F.R. § 807.87(k)[16] should apply in the exemption request process. Such a certification requirement would be sufficient to alert the petitioner that it must present a truthful and balanced summary of the data on the proposed minor modification, including all material facts.

C. Decisions on 905(j)(3) Exemption Requests Should be Rendered Within 90 Days and Minor Modifications Should be "Deemed Notified" Under 905(j)(1)(A)(ii) Upon Establishment of a Categorical Exemption.

The proposed rule establishes no time period in which the FDA must respond to a 905(j)(3) request. For reasons similar to those articulated in Section I of our comments on the substantial equivalence guidance, we believe the final rule should establish a 90 day review period for 905(j)(3) exemption requests. Such a requirement is logical given the 90 day period Congress established for the FDA to conduct a premarket review of additive

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[14] SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks) is one of three independent non-food Scientific Committees providing the European Commission with the scientific advice needed when preparing policy and proposals relating to consumer safety, public health and the environment.

[15] SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks), 2010. Addictiveness and Attractiveness of Tobacco Additives. European Union, Brussels. Available at http://ec.europa.eu/health/scientific_committees/consultations/public_consultations/scenihr_cons_12_en.htm (accessed March 18, 2001). Additionally, SCENIHR found that the clinical criteria for dependence, laboratory measures of self-administration, and preference measurements in humans which indicate that tobacco has a high addictive potential "have limitations when assessing the addictiveness of individual additives in the final tobacco product." With regard to attractiveness, SCENIHR found that adult tobacco user panel studies and surveys conceivably give only limited information regarding the stimulation to use a product, and there are many other direct and indirect factors such as taste, marketing, price etc., which must also be considered. *See also* Henningfield, J.E., et. al. Conference on abuse liability and appeal of tobacco products: Conclusions and recommendations. Drug Alcohol Depend. (2011), doi:10.1016/j.drugalcdep.2010.12.009 (acknowledging the methodological issues and gaps that need to be addressed in the evaluation of tobacco products for abuse liability and product appeal).

[16] A statement that the submitter believes, to the best of his or her knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted.

additions to tobacco products.[17] Failure to establish an efficient and clear timeframe defeats the Congressional intent in the 905(j)(3) exemptions framework.

The final rule should also allow a manufacturer to provide information in the exemption request that its product is in compliance with the Act and serve as the 905(j)(1)(A)(ii) 90 day notification. Thus, the notification requirement would run concurrently with FDA's review of the exemption request and eliminate the inefficiency of requiring an Agency decision on an exemption request before a manufacturer can submit a 90 day notification to FDA under 905(j)(1)(A)(ii).

Additionally, when the FDA establishes a categorical minor modification exemption for a class of products or modifications (*e.g.*, designated additives), it should be "deemed notified" to the Agency for purposes of compliance with 905(j)(1)(A)(ii).[18] The categorical exemption itself will establish that "the modifications are covered by exemptions granted by the Secretary," and the FDA may limit the terms of the exemption to any "product that is commercially marketed and in compliance with the requirements of this Act." Thus, all of the elements of the required notification will already be known to FDA and, in the case of an additive change, the Agency would receive details regarding the modification under separate requirements, *i.e.*, section 904(c).

D. The Reduction or Elimination of an Additive Should be Categorically Exempt From Substantial Equivalence Requirements.

Sections 904(c)(3) and 905(j)(3) both address the addition or removal of tobacco additives. When a manufacturer reduces or eliminates an additive, section 904(c)(3) requires manufacturers to notify the FDA 60 days *after* entering such a modified product into interstate commerce. This requirement for notification after the fact reflects Congress' determination that premarket review by FDA is not necessary to assess the reduction or elimination of an additive prior to the manufacturer entering the modified product into interstate commerce. FDA's final rule for 905(j)(3) exemptions should be consistent with this Congressional determination and categorically exempt from the substantial equivalence requirements all modifications that reduce or eliminate an additive.

Section 904(c)(3) also requires manufacturers to notify the FDA 60 days *after* entering a product into the market when it "adds or increases an additive that has by regulation been designated by the Secretary as an additive that is not a human or animal carcinogen, or otherwise harmful to health under intended conditions of use."[19] Again, the final rule for 905(j)(3) exemptions should categorically exempt such modifications in recognition of the Congressional determination that additions or increases of "designated" additives do not require a regulatory assessment before a manufacturer enters a product into the market. In

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[17] 21 U.S.C. § 387d(c).

[18] 905(j)(1)(A)(ii) requires a notification of "the basis for such person's determination that . . . the modifications are to a product that is commercially marketed and in compliance with the requirements of this Act, and all of the modifications are covered by exemptions granted by the Secretary."

[19] 21 USC § 387d(c)(3).

addition, the final rule should merge the "designation" regulation process, when established, with the 905(j)(3) substantial equivalence exemption process.

E. Additive Modifications that are Part of Blend Maintenance or the Result of Blend Maintenance Should be Exempt from Substantial Equivalence Requirements.

FDA's Final Guidance for Industry and FDA Staff, Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products, states that "FDA does not intend to enforce the requirements of sections 910 and 905(j) for tobacco blending changes required to address the natural variation of tobacco (e.g., blending changes due to variation in growing conditions) in order to maintain a consistent product." As noted above, these types of adjustments do not constitute "modifications" within the definition of a "new tobacco product." If, however, the Agency does not exclude such adjustments, the final rule should categorically exempt blend changes and associated additive changes required to address the natural variation of tobacco.

Such changes are a practical necessity in the tobacco products industry due to crop variability and availability (beyond a manufacturer's control) to maintain a consistent tobacco product. Congress clearly did not intend that blending adjustments and accompanying changes attributable to the natural variation of an agricultural product would result in a 905(j) report or exemption request with no corresponding public health benefit.

F. The Final Rule Should Allow an Exemption Request to Cover Multiple Products or Even an Entire Category of Products and Allow for Modifications Within a Requested Range.

The Final Rule should clarify that an exemption request, once granted, may cover multiple products, or a category of products produced by a manufacturer, *e.g.*, cigarettes or smokeless tobacco products. In addition, a granted exemption should cover modifications within a requested range. For example, if supported by appropriate toxicological data, a granted exemption should allow a manufacturer to add a particular ingredient to any of its cigarette products up to a specified level, without requiring the manufacturer to file a substantial equivalence report or a duplicative exemption request for each product. Otherwise, the Agency and manufacturers will divert resources on exemption requests or substantial equivalence reports for the same additive with no corresponding public health benefit.

FDA recognizes that it may establish such exemptions in the future as it acquires more information, presumably including from the scientific literature and exemption filings, substantial equivalence reports and other information submitted by manufacturers. The Agency should establish such a pathway for these categorical exemptions in the final rule rather than in the future.

G. The Final Rule Should Provide Exemptions for Non-Additive Modifications.

As described above, the Act does not include adjustments made to maintain consistent product characteristics within the definition of a "new tobacco product." If, however, the Agency disagrees, it should also include exemptions for non-additive minor modifications in the final rule. Such exemptions could cover, for example, blend maintenance adjustments or adjustments in cigarette ventilation to maintain consistent strength of taste in response to agronomic variations. As with the blending adjustments discussed in Section E above, these types of modifications involve only a deliberate and minor "change" to maintain a consistent product.

FDA has the authority to promulgate regulations implementing exemptions for substantial equivalence for non-additive modifications under its 701(a) "authority to promulgate regulations for the efficient enforcement of this Act." As with appropriately focused regulations regarding minor modifications to additives, such regulations would promote regulatory efficiency by reducing the number of unnecessary substantial equivalence reports. FDA should, therefore, broaden the scope of minor modification exemptions in the final rule by allowing for exemptions for non-additive modifications.

Conclusion

We appreciate the opportunity to submit these comments and urge the Agency to incorporate them in the final rule. We look forward to further opportunities to work with the FDA as it develops a process to establish exemptions from the substantial equivalence process.

Sincerely,

James E. Dillard III

ATTACHMENT A

Altria

Altria Client Services

James E. Dillard III
Senior Vice President
Regulatory Affairs

February 8, 2011

Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. FDA-2010-D-0635 (76 Fed. Reg. 789 (Jan. 6, 2011)) – Comments on the "Guidance for Industry and FDA Staff, Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products"

Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC") submit these comments on the above-captioned guidance document ("Guidance").[1] We may supplement these comments at a future date as the FDA's thinking on tobacco product substantial equivalence evolves. We also plan to submit separate comments on the FDA's proposed rule on exemptions from substantial equivalence requirements.[2]

We appreciate the complexity of the issues associated with substantial equivalence reporting. We offer these comments and ask the Agency to take them into account and issue a revised Guidance.[3]

Our comments are organized into the following sections:

- The FDA's Guidance Should Address the Timing of 905(j) Decisions
- The Agency Needs to Clarify its Definition of "New Tobacco Product"
- "As of February 15, 2007" Means On or Before that Date

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[1] Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC") are wholly-owned subsidiaries of Altria Group, Inc. Altria Client Services ("ALCS") is making this submission on behalf of PM USA and USSTC. ALCS provides certain services, including regulatory affairs, to the Altria family of companies. "We" is used throughout to refer to PM USA and USSTC.

[2] *See* 76 Fed. Reg. 737 (Jan 6, 2011).

[3] FDA issued a Final Guidance in contravention to its general rule requiring "public participation" in the development of guidance documents. *See* 21 U.S.C. § 371(h)(1)(A), (C). We urge FDA to consider the public comments it receives and issue a Revised Final Guidance in a timely manner.

Altria Client Services Inc.
2325 Bells Road
Richmond, Virginia 23234
(804) 335-2679
James.E.Dillard@altria.com

- Comparison to Multiple Predicates is Consistent with the Statute and the Scientific Basis of Other FDA Regulatory Processes
- FDA Needs to Address Several Issues About What Constitutes "Same Characteristics"
- Certain of the "Additional Data" FDA Recommends Considering When Analyzing "Different Questions of Public Health" are Not Required by the Statute or Needed for Substantial Equivalence Determinations
- The Agency Needs to Provide Details About How a Manufacturer Can Demonstrate Compliance with the Requirements of the Act
- A Post-March 22, 2011 905(j) Report Should be Deemed to Satisfy the Ingredient Disclosure Requirements of 904(c)

I. The FDA's Guidance Should Address the Timing of 905(j) Decisions.

Revised Guidance should address the timing of the FDA's 905(j) decisions. For products proposed to be first commercially marketed after March 22, 2011, prompt FDA decisions on 905(j) reports are crucial because manufacturers cannot lawfully market such products until the FDA issues a substantial equivalence order. The Agency should establish a reasonable timeframe for its review of such submissions.

For other product submissions to the FDA, the Agency operates under either a statutory or regulatory deadline or an established "performance goal." For example, the FDA committed to issuing a decision on modified risk tobacco product applications within 360 days of receiving the application.[4] For new tobacco products under FDCA § 910, the FDA must respond "as soon as possible, but in no event later than 180 days after receipt of [the] application."[5] A 905(j) submission should require fewer Agency resources and less review time because the statutory requirements for substantial equivalence are fewer and less complex.

In the other FDA-regulated product context most analogous to 905(j) "substantial equivalence" reports—medical device 510(k) "substantial equivalence" submissions[6]—the FDA has committed to issuing a decision for 90% of medical device 510(k)s within 90

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[4] *See* FDA Draft Guidance, "Preliminary Timetable for the Review of Applications for Modified Risk Tobacco Products under the Federal Food, Drug, and Cosmetic Act" (Nov. 2009), *available at* http://www.fda.gov/downloads/TobaccoProducts/GuidanceComplianceRegulatoryInformation/UCM191915.pdf.

[5] 21 U.S.C. § 387j(c)(1).

[6] *Compare* 21 U.S.C. § 360c(i) (medical device "substantial equivalence") *to* 21 U.S.C. § 387j(a)(3) (tobacco product "substantial equivalence"). Neither provision mandates a timeframe in which the FDA must respond to a "substantial equivalence" submission.

days of receipt, and for 98% of them within 150 days.[7] FDA regulations allow 180 days for Agency review of the more complex medical device premarket approval application.[8]

The FDA should establish a "performance goal" of issuing a decision on most, if not all, 905(j) reports required for introduction of a new tobacco product within 90 days of receipt. A 90-day review deadline for 905(j) submissions is reasonable given the user fees paid by manufacturers[9] and the relatively simpler designs (compared to medical devices) that are commonly used in the vast majority of tobacco products in a particular category.

We also suggest that the FDA provide for expedited review of 905(j) reports for situations beyond a manufacturer's control in which a product change is required in a short time frame. For example, an ingredient or material may become unavailable due to uncontrollable supply chain interruptions. It would be unreasonable to require a manufacturer to discontinue production of its affected tobacco products under such circumstances while awaiting the FDA review of a 905(j) report.

II. The Agency Needs to Clarify its Definition of "New Tobacco Product."

The Agency needs to clarify the definition of "new tobacco product" by identifying the specific factors, product attributes, and other considerations that will result in a product being deemed a "new tobacco product."

There are numerous sources of variability inherent in tobacco products that should not constitute a 910(a)(1)(B) "modification." These include variations in manufacturing and differences in materials from lot-to-lot. Adjustments made in response to such variations that are necessary to maintain consistent product characteristics (*e.g.*, adjustments in ventilation parameters to maintain a consistent "tar" per puff, and therefore consistent strength of taste) also should not be considered "modifications." In fact, such adjustments are the opposite of a "modification" since they are intended to maintain a consistent product. In addition, testing variability among different analytical laboratories and (to a lesser extent) within the same laboratory can create the appearance of product variations when, in fact, none actually exists.[10] None of these inherent variations, or adjustments made in response to them, should be considered "modifications."

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[7] *See* FDA Letter to Senator Edward M. Kennedy, Chairman, Committee on Health, Education, Labor, and Pensions, U.S. Senate, Medical Device User Fee Amendments Act of 2007 (MDUFA) Performance Goals and Procedures (Sept. 27, 2007), *available at* http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/UCM109102.pdf.

[8] *See* 21 C.F.R. § 814.40; FDA, Premarket Approval (PMA), available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketApprovalPMA/default.htm.

[9] *See* 21 U.S.C. § 387s(b)(1) (Fiscal year 2009 user fees totaled $85 million; user fees increase in subsequent years until 2019 when the ongoing user fee is $712 million per fiscal year).

[10] "Determination of 'Hoffman Anayltes' in Cigarette Mainstream Smoke. The Coresta 2006 Joint Experiment" Vol. 23 #4 May 2009, p. 161 (available at www.beitraege-bti.de).

Moreover, a product should not be considered "modified" if it is produced within specifications that existed prior to February 15, 2007. For example, there may be a range in paper permeability to permit adjustments to maintain consistent product characteristics. This approach is analogous to the "design space" concept recognized in the regulation of pharmaceutical production.[11]

III. "As of February 15, 2007" Means On or Before that Date.

The phrase "as of February 15, 2007" means on or before the date February 15, 2007. There is no statutory requirement in § 910 or in § 905(j) that a manufacturer provide evidence that a predicate product was marketed nearly four years ago *on* Thursday, February 15, 2007. Such a requirement would not be reasonable or practical, especially given that the Act did not become law until more than 28 months later.

The words "as of" are used to indicate a time or date at which something begins or ends."[12] Thus, February 15, 2007 is the "end" of the period of eligible predicates and grandfathering as "non-new" tobacco products. The following day is the "beginning" of when tobacco products are no longer eligible to serve as predicates (except in the case of products previously found to be substantially equivalent) and may be "new" tobacco products.

Finally, the contrast to the language "after February 15, 2007" (*see* §§910(a)(1)(B) and (a)(2)(B)(i)) clearly indicates that "as of" was intended to mean "on or before."

IV. Comparison to Multiple Predicates is Consistent with the Statute and the Scientific Basis of Other FDA Regulatory Processes.

A multiple predicate approach is consistent with the statute and the scientific basis for FDA's historical treatment of substantial equivalence in other regulated areas. We urge the FDA to consider a "market range" approach to predicate products in which the various attributes of a "new tobacco product" are compared to the various attributes of similar tobacco products, as they existed on or before February 15, 2007.

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[11] An FDA/international regulatory document on drug development, "Guidance for Industry: Q8 Pharmaceutical Development" (May 2006), utilizes the concept of "design space." It defines this concept as: "The multidimensional combination and interaction of input variables (*e.g.*, material attributes) and process parameters that have been demonstrated to provide assurance of quality. Working within the design space is not considered as a change. Movement out of the design space is considered to be a change and would normally initiate a regulatory postapproval change process. Design space is proposed by the applicant and is subject to regulatory assessment and approval." Application of the "design space" concept to tobacco products would of course be somewhat different than it would with respect to drugs, given the differences in the nature of the products and industry design specifications, controls, etc.

[12] *See* Merriam-Webster Online Dictionary at http://www.merriam-webster.com/dictionary/as%20of.

The substantial equivalence provisions of § 910(a) are modeled on the medical device provisions of FDCA, which also refer to "a predicate" product in the singular.[13] FDA interprets this language, however, to permit a new device to be compared to more than one predicate[14] and very recently stated, in its comprehensive plan for improving the 510(k) program, that it "strongly supports the use of multiple predicates."[15] Given this analogous statutory framework, Congress's use of the term "predicate" should be read to allow for the use of multiple predicate products in a substantial equivalence evaluation.[16]

The Institute of Medicine ("IOM") also applied the logic of multiple predicates when it developed the framework for the "No increased risk" threshold in Regulatory Principle 7 "as compared to similar conventional tobacco products."[17] The IOM further noted that tobacco products without health claims should be "at least no more hazardous than in similar contemporaneously marketed products,"[18] an approach that draws from the diversity of products available in the U.S. market and does not limit review to one-to-one product comparisons.

V. FDA Needs to Address Several Issues About What Constitutes "Same Characteristics."

A. "Same Characteristics" Cannot be Interpreted to Mean Identical Characteristics.

The term "same characteristics" cannot be interpreted to mean "identical characteristics." To do so would render the "same characteristics" test meaningless because any product that is new or modified would be automatically evaluated under "different questions of public health." Also, a product that is identical to a predicate is, by definition, neither new nor modified. A basic principle of statutory interpretation is that one must "give effect, if possible, to every clause and word of a statute, avoiding, if it may be, any construction which implies that the legislature was ignorant of the meaning

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[13] *See* 21 U.S.C. § 360c(i)(1)(A) ("'substantially equivalent' ... means, with respect to a device being compared to a predicate device . . .").

[14] *See* FDA Center for Devices and Radiological Health, "Premarket Notification 510(k): Regulatory Requirements for Medical Devices," 1995 WL 17210952 (noting that a device may be compared to one or more predicate devices in claiming substantial equivalence); FDA, "Regulations Restricting the Sale and Distribution of Cigarettes and Smokeless Tobacco to Protect Children and Adolescents," 61 Fed. Reg. 44396, 44410, 1996 WL 482785 (1995) (noting that devices "may not be commercially distributed unless the Agency issues an order finding the device substantially equivalent to one or more predicate devices already legally marketed in the United States").

[15] *See* CDRH, "510(k) and Science Report Recommendations: Summary and Overview of Comments and Next Steps" at § 5.1.2.3, published Jan. 19, 2011 at http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDRH/CDRHReports/UCM239449.pdf.

[16] *Ratzlaf v. United States*, 510 U.S. 135, 143 (1994) ("A term appearing in several places in a statutory text is generally read the same way each time it appears."); *Merrill Lynch, Pierce, Fenner & Smith v. Curran*, 456 U.S. 343, 382 n.66 (1982), quoting *Lorillard v. Pons*, 434 U.S. 575, 580 (1978) ("Congress is presumed to be aware of an administrative . . . interpretation of a statute.").

[17] IOM, Clearing the Smoke: Assessing the Science Base for Tobacco Harm Reduction (2001), 222.

[18] *Id.* at 223.

of the language it employed."[19] A modern variant of this canon is that statutes must be construed "so as to avoid rendering superfluous" any statutory language.[20]

The Guidance does not clearly explain the circumstances under which a tobacco product may be "new" and yet have the "same characteristics" as a predicate(s). Nor does the Guidance explicitly define "same characteristics." The overall implication, however, is that FDA intends to take a narrow view of "same characteristics."[21] For example, it appears that ingredient substitutions that go beyond those described in section V.C of the Guidance would result in a determination that the characteristics are different and trigger an analysis under "different questions of public health." Such a narrow interpretation reads the "same characteristics" test out of the statute.

FDA recently acknowledged the importance of clarifying the criteria that trigger the different pathways of the substantial equivalence framework for medical devices.[22] It should do the same here.

New tobacco products with conventional designs comprising new combinations of ingredients, ingredient levels and materials used in marketed tobacco products would have the same characteristics as those already marketed products in terms of smoke toxicity.[23] It is important to give closer scrutiny to truly novel compositional or design features of a new tobacco product which might have the potential to alter toxicity. This approach is consistent with a reasonable interpretation of both "same characteristics" and "different questions of public health."

The Agency should adopt an interpretation of "same characteristics" that recognizes the range of characteristics on the market on or before February 15, 2007. Such an approach would align with statutory intent and relieve the FDA of the burden of conducting unnecessary reviews.

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[19] *Montclair v. Ramsdell*, 107 U.S. 147, 152 (1883).

[20] *Astoria Federal Savings & Loan Ass'n v. Solimino*, 501 U.S. 104, 112 (1991); *Sprietsma v. Mercury Marine*, 537 U.S. 51, 63 (2003) (interpreting word "law" broadly could render word "regulation" superfluous in preemption clause applicable to a state "law or regulation"). *See also Bailey v. United States*, 516 U.S. 137, 146 (1995) ("we assume that Congress used two terms because it intended each term to have a particular, nonsuperfluous meaning") (rejecting interpretation that would have made "uses" and "carries" redundant in statute penalizing using or carrying a firearm in commission of offense).

[21] *See e.g.*, Guidance section V.A (request for voluminous data to be presented as "side-by-side quantitative and qualitative comparisons of the new tobacco product with the predicate tobacco product with respect to all product characteristics"); section V.C ("same characteristics" will only be found when "a minimal number of ingredients, or materials have been substituted (substitution may include the same ingredient or material but from a different source)," and there is "documentation demonstrating that the substituted ingredient(s) or material(s) meets the required specifications for the replaced ingredient(s) or material(s).").

[22] See, *e.g.*, CDRH, "510(k) and Science Report Recommendations: Summary and Overview of Comments and Next Steps," published Jan. 19, 2011, available at http://www.fda.gov/downloads/AboutFDA/CentersOfffices/CDRH/CDRHReports/UCM239449.pdf.

[23] We alert the Agency to an upcoming special edition of *Inhalation Toxicology* in which we will discuss results from our multi-year testing program of cigarette ingredients. The program investigated dose response relationships of various chemical classes using standard toxicology endpoints that have been used to assess cigarette smoke. The results of this testing lead to the conclusion that the ingredients typically used in modern cigarettes do not substantially alter smoke toxicity.

B. The "Same Characteristics" Analysis Should Not Include a Comparison of Harmful and Potentially Harmful Constituents Between the Predicate(s) and the "New" Product.

Among the "other features" that FDA recommends including in a characteristics comparison between new and predicate tobacco products are "harmful and potentially harmful constituents" (HPHCs). FDA is directed, under §§ 904(d) & (e) of the Act, to establish and publish a list of HPHCs; no such list, however, has been published. As a result, it is unknown what constituents should be measured and reported as part of the substantial equivalence process. Until such time as a list of HPHCs is developed and published, manufacturers can provide information only about those constituents for which validated analytical methods, historical data, and ongoing testing and reporting requirements exist for marketed products, *e.g.*, information submitted to the Federal Trade Commission and the Centers for Disease Control.

For purposes of defining substantial equivalence, "the term 'characteristics' means the materials, ingredients, design, composition, heating source, or other features of a tobacco product."[24] It does not include "constituents." When Congress wanted to address constituents in the Act, it did so explicitly (*e.g.*, the establishment and publishing of a HPHC list under §§ 904(d) & (e); manufacturer testing and reporting of tobacco product constituents under regulations to be promulgated by FDA under § 915; testing and reporting of constituents for new tobacco products 90 days prior to introduction under § 904(c)(1); and FDA's authority under § 907 to establish tobacco product standards, including "for the reduction or elimination of other constituents, including smoke constituents, or harmful components of the product.").

Given this comprehensive framework, and the exclusion of constituents in the substantial equivalence context, it is clear that Congress did not intend for the FDA to require a comparison of constituents as part of a substantial equivalence report.[25] Congressional intent is further evidenced by the timing of the various provisions on constituents. Specifically, substantial equivalence reports are due by March 22, 2011, which is well before the April 1, 2012 deadline by which FDA is required to publish a list of HPHCs and promulgate regulations for testing and reporting.

Regardless of when a HPHC list becomes available, it is highly unlikely that cigarettes and smokeless tobacco products on the market on or before February 15, 2007 still exist, let alone in quantities sufficient to satisfy FDA's future testing

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[24] 21 U.S.C. § 387j(a)(3).

[25] A well-accepted canon of statutory interpretation is that "where 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." *Keene Corp. v. United States*, 508 U.S. 200, 208 (1993) (*quoting Russello v. United States*, 464 U.S. 16, 23 (1983)). *See also Bailey v. United States*, 516 U.S. 137, 146 (1995) (distinction in one provision between "used" and "intended to be used" creates implication that related provision's reliance on "use" alone refers to actual and not intended use); *Bates v. United States*, 522 U.S. 23, 29 (1997) (inclusion of "intent to defraud" language in one provision and exclusion in a parallel provision indicated intent to defraud was not an element of the offense of knowingly and willingly misappropriating student loan funds).

requirements. Therefore, it is impossible to generate constituent data for most, if not all, predicate products.[26]

In the HPHC context and others related to substantial equivalence, the Agency should make clear that roll-your-own tobacco products (RYO) and cigarette tobacco are subject to the same requirements as other cigarettes and smokeless tobacco products, and further explain how it will apply these requirements to these tobacco products. Consumers have multiple options from which to choose when combining commercially marketed RYO and cigarette tobaccos, papers, filters and other materials in different configurations. For example, when the HPHC list is published, it is unclear how such a "consumer assembled product" would be tested to determine HPHC levels. As the Agency considers these types of issues, it should follow the Act's requirement that, unless otherwise stated, the requirements applicable to cigarettes also apply to cigarette tobacco.[27]

VI. Certain of the "Additional Data" FDA Recommends Considering When Analyzing "Different Questions of Public Health" are Not Required by the Statute or Needed for Substantial Equivalence Determinations.

The "Additional Data" listed in the Guidance are not required by the statute or needed for substantial equivalence determinations.

The Guidance does not explicitly state the FDA's views about when a new tobacco product would be deemed to raise "different questions of public health." It appears, however, that the Agency believes that making such a determination could involve an assessment of the "additional data," including consumer perception studies, clinical studies, abuse liability data, and toxicological data.

This additional data is not required by the Tobacco Control Act. The various provisions of the Act have different requirements for the types of data that industry must submit, or that FDA must consider. For example, the criteria for evaluating non-substantially equivalent new tobacco products under § 910(c) of the Act require an evaluation of the risks and benefits to the population as a whole, including users and non users of the tobacco product, and taking into account the increased or decreased likelihood of cessation or initiation of product use.[28] This evaluation may include one or more clinical investigations.

Similar language regarding cessation or initiation effects is also included, *e.g.*, in criteria for authorization of modified risk tobacco products,[29] and for the development of

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[26] For a fuller discussion related to HPHCs and the development of the HPHC list, we refer the FDA to a previous submission in which we discuss our experience with tobacco constituent testing and evaluation of such data as part of our ingredient testing program. *See* Altria Client Services, Inc., Comments dated Aug. 23, 2010, Docket ID No. FDA-2010-D-0281-0003.1, available at http://www.regulations.gov/#!documentDetail;D=FDA-2010-D-0281-0003.1.

[27] *See* 21 U.S.C. § 387(4).

[28] *See* 21 U.S.C. § 387j(c)(4).

[29] *See* 21 U.S.C. § 387k(g)(4)(B) & (C).

tobacco product standards.[30] Moreover, an application for authorization of certain types of modified risk tobacco products (*i.e.*, "reduced exposure" products) requires "testing of actual consumer perception" with respect to risks.[31]

In contrast, Congress excluded from the criteria for substantial equivalence under § 910(a), and for reporting under § 905(j), any consideration of behavioral effects such as initiation or cessation, or of consumer perception studies. This absence shows Congressional intent that the criteria should *not* be considered in the substantial equivalence evaluation.[32]

This approach to addressing "different questions of public health" would be consistent with a tobacco regulatory principle proposed by the IOM, in response to a request from the FDA; *i.e.*, a "'No Increased Risk' Threshold for All Tobacco Products."

> In the absence of any claim of reduced exposure or reduced risk, manufacturers of tobacco products should be permitted to market new products or modify existing products without prior approval of the regulatory Agency after informing the Agency of the composition of the product and upon certifying that the product could not reasonably be expected to increase the risk of cancer, heart disease, pulmonary disease, adverse reproductive effects, or other adverse health effects, compared to similar conventional tobacco products, as judged on the basis of the most current toxicological and epidemiological information.[33]

We have long operated under similar principles. The ALCS Product Integrity Evaluation Guidelines establish the criteria to determine the acceptability of an ingredient or design change in cigarettes. The review process involves comparisons to currently marketed cigarettes and a tiered approach modeled after FDA guidelines for food ingredient exposure as described in FDA's "Office of Food Additive Safety Redbook 2000: Toxicological Principles for the Safety Assessment of Food Ingredients."[34] Guidelines for smokeless tobacco products apply similar principles.

Substantial equivalence evaluations under "different questions of public health" should be limited to standard safety studies; *i.e.*, toxicology and (where deemed necessary by the Secretary) clinical studies. An assessment of health effects based on a hazard evaluation grounded in sound scientific principles can be used to identify "different questions of public health" and will meet both Congressional intent and the "reasonable expectation of no increased risk" criteria proposed by the IOM.

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[30] *See* 21 U.S.C. § 387g(a)(3)(B)(i)(II) & (III).
[31] *See* 21 U.S.C. § 387k(g)(2)(B)(iii).
[32] *See* f.n. 25, *supra.*
[33] *See* IOM, Clearing the Smoke: Assessing the Science Base for Tobacco Harm Reduction (2001), 222.
[34] Although the procedure addressed in the FDA's "Redbook" is related to dietary exposure, PM USA considers its concepts of segregating subject materials by structure and anticipated exposure level into "concern levels" to be useful for the toxicologic evaluation of smoking products and their components.

If the FDA still believes it can request this information, it is not clear whether manufacturers would be expected to submit such data in the initial report or only upon request by the Agency.[35]

VII. The Agency Needs to Provide Details About How a Manufacturer Can Demonstrate Compliance with the Requirements of the Act.

FDA should provide a clear recommendation about the type and format of the information it wants manufacturers to provide to demonstrate compliance with other requirements of the Act.[36] The FDA already has access to information such as a manufacturer's registration and product listings, ingredient list filings, submission of tobacco health information, and any other required regulatory filings. Moreover, the § 905(j)(1)(B) requirement to report "action taken by such person to comply with the requirements under § 907 that are applicable to the tobacco product" seems to have little relevance to products currently on the market since the only tobacco product standard currently in effect is a ban on characterizing flavors in cigarettes other than menthol or tobacco.

If the FDA expects a manufacturer to summarize this information or provide additional information, it should provide that direction in Revised Guidance.

VIII. A Post-March 22, 2011 905(j) Report Should be Deemed to Satisfy the Ingredient Disclosure Requirements of 904(c).

FDA should allow a 905(j) report to fulfill more than one regulatory obligation. If a manufacturer includes the information recommended in the Guidance, the information submitted in its 905(j) report will include a complete disclosure of the ingredients (including additives) that are to be added to a tobacco product, or to any part thereof. As a result, the 905(j) report should simultaneously fulfill the ingredient disclosure requirements of FDCA § 904(c).[37] Moreover, a 905(j) report submitted on or after March 22, 2011 must be submitted at least 90 days before delivering the product

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[35] The Guidance states both that the "FDA may request" such data and that a 905(j) report "should include the[se] data."

[36] *See* section IV.D of the Guidance ("[i]n addition to determining that the product is substantially equivalent, FDA must also determine that the new tobacco product is in compliance with the requirements of the Act before issuing an order under section 910(a)(2)(A)(i).").

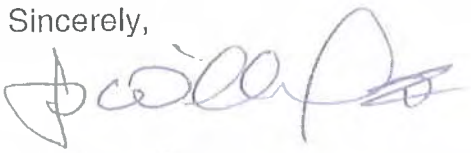
[37] 21 U.S.C. § 387d(c)(1) cross-references "the information required under subsection (a)" (which includes "a listing of all ingredients, including tobacco, substances, compounds and additives" added to each part of a tobacco product) and applies to products "not on the market on the date of enactment." A 904(c)(2) disclosure applies to modifications involving new additives or increased usage levels of existing additives, and a 904(c)(3) disclosure applies to modifications involving elimination or decreased usage of an additive, or to additive changes involving additives "designated" by FDA as not carcinogenic or otherwise harmful "under intended conditions of use."

for introduction into interstate commerce. Thus, assuming a manufacturer includes the information recommended in the Guidance, it would also satisfy the ingredient (including additive) disclosures under 904(c), which has a similar 90 days pre- (and in some cases 60 days post-) timing requirement.[38]

* * * * *

We appreciate the opportunity to submit these comments and urge the Agency to incorporate them in a Revised Guidance. We look forward to further opportunities to provide comments to the Agency as its thinking on substantial equivalence evolves.

Sincerely,



James E. Dillard III

[38] A 904(c)(1) disclosure must be made "[a]t least 90 days prior to the delivery for introduction into interstate commerce of a tobacco product not on the market on the date of enactment;" a 904(c)(2) disclosure must be made "at least 90 days prior to" the "time a tobacco product manufacturer adds to its tobacco products a new tobacco additive or increases the quantity of an existing additive;" and a 904(c)(3) disclosure must be made "within 60 days of" the "time a tobacco product manufacturer eliminates or decreases an existing additive, or adds or increases an additive that has by regulation been designated . . . ."

Altria
Altria Client Services

James E. Dillard III
Senior Vice President
Regulatory Affairs

June 24, 2011

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. FDA-2011-D-0125 (76 Fed. Reg. 22,903 (Apr. 25, 2011)) – Comments on the "Draft Guidance for Industry and FDA Staff: Establishing that a Tobacco Product was Commercially Marketed in the United States as of February 15, 2007"

Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC") submit these comments on the above-captioned draft guidance document ("Draft Guidance").[1]

I. The Draft Guidance Incorrectly States that Products Only in Test Markets as of February 15, 2007 are not "Grandfathered" and are Subject to Premarket Review.

Without explanation, the Draft Guidance states that products that were only in test markets as of February 15, 2007 are not "grandfathered," but instead are "new tobacco products" subject to premarket review.[2] To the contrary, a product in test market as of February 15, 2007 (if not subsequently modified within the meaning of § 910(a)(1)(B)) is "grandfathered" and not subject to premarket review.

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[1] Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC") are wholly-owned subsidiaries of Altria Group, Inc. Altria Client Services ("ALCS") is making this submission on behalf of PM USA and USSTC. ALCS provides certain services, including regulatory affairs, to the Altria family of companies. "We" is used throughout to refer to PM USA and USSTC.

[2] *See, e.g.*, Draft Guidance at § II ("For the purposes of this guidance document, FDA refers to a tobacco product that was commercially marketed (not in test markets) in the United States as of February 15, 2007, as a 'grandfathered' tobacco product."); Draft Guidance at § III ("In addition, under section 910 of the FD&C Act, a tobacco product that was in only test markets in the United States on February 15, 2007, is a new tobacco product (section 910(a) of the FD&C Act; 21 U.S.C. 387j(a))"); Draft Guidance at § III ("FDA recommends that you provide evidence that the tobacco product was commercially marketed in the United States (not in test markets) on February 15, 2007. This information should demonstrate that the tobacco product was not distributed for test marketing only.")

Altria Client Services Inc.
2325 Bells Road
Richmond, Virginia 23234
(804) 335-2679
James.E.Dillard@altria.com

As noted in the Draft Guidance, the term "new tobacco product" is defined in section 910(a)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) as follows:

> (A) any tobacco product (including those products in test markets) that was not commercially marketed in the United States as of February 15, 2007; or
>
> (B) any modification (including a change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient) of a tobacco product where the modified product was commercially marketed in the United States after February 15, 2007.

The Draft Guidance, however, misinterprets the plain meaning of the parenthetical "(including those products in test markets)" in § 910(a)(1)(A). The parenthetical clearly modifies the words before it and explains that "any tobacco product" includes tobacco products only offered in test markets. The parenthetical cannot reasonably be construed to limit the meaning of "commercially marketed." As a general rule of construction, a parenthetical is assumed to explain or modify the word or words that immediately precede it unless the overall context of the statutory provision indicates otherwise.[3] Here, the parenthetical clearly relates to and explains the words that precede it, i.e., "any tobacco product (including those products in test markets)" (emphasis added). This indicates that, as is conventional, the parenthetical is used to modify the words immediately preceding it.[4]

Further confirming Congress's clear intent is a comparison to the language it used to identify an eligible predicate product. An eligible predicate product is

> substantially equivalent to a tobacco product commercially marketed (other than for test marketing) in the United States as of February 15, 2007 . . . .[5]

It is clear that test marketing is considered "commercial marketing," but that test marketing is excluded from the type of commercial marketing that defines an eligible predicate product for substantial equivalence. If Congress intended to exclude test marketed products from "grandfathered" products not subject to premarket review, it would have taken a similar approach in § 910(a)(1)(A).[6] As the statute is actually drafted, however, it is clear that there are different standards for (1) a "grandfathered" product that is exempt from premarket review; and (2) a product that is an eligible

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[3] *See, e.g.,* United States v. Monjaras-Castaneda, 190 F.3d 326, 329 (5th Cir. 1999) ("If the parenthetical referred to 'offense,' it would have been placed directly after that word.").

[4] *Id.* ("Legislators can be presumed to rely on conventional language usage.") (citing Norman J. Singer, 2A Sutherland Statutory Construction § 45.13 at 78 (5th ed. 1992)).

[5] 21 U.S.C. § 387j(a)(2)(A)(i)(I).

[6] Congress could have defined "new tobacco product," for example, to include "any tobacco product that was not commercially marketed (other than for test marketing) in the United States as of February 15, 2007."

predicate product for substantial equivalence. Whereas the former includes products that were only in test markets as of February 15, 2007, the latter does not. Thus, a product in test market as of February 15, 2007 (if not subsequently modified within the meaning of § 910(a)(1)(B)) is indeed "grandfathered" and not subject to premarket review. The Final Guidance should be corrected to reflect Congressional intent.

II. "As of February 15, 2007" Means On or Before that Date.

As noted in previous comments,[7] a plain reading of the phrase "as of February 15, 2007" means on or before the date February 15, 2007. This applies to each of the separate but related questions of (1) whether a tobacco product is a "new tobacco product," and (2) whether a tobacco product is eligible to serve as a predicate for a substantial equivalence evaluation. There is no statutory requirement that a manufacturer provide evidence that a product was marketed (over four years ago) *on* Thursday, February 15, 2007. Such a requirement would not be reasonable or practical, especially given that the Act did not become law until more than 28 months later. If Congress had intended the "new tobacco product" and predicate eligibility provisions to depend on whether a product was marketed *on* February 15, 2007, it would have said so in plain language by using the word "on."[8]

The words "as of" are "used to indicate a time or date at which something begins or ends."[9] Thus, February 15, 2007 is the "end" of the period of eligible predicates and grandfathering as "non-new" tobacco products. The following day is the "beginning" of when tobacco products may be "new" tobacco products and when they are no longer eligible to serve as predicates.[10] Finally, the contrast to the language "after February 15, 2007" (*see* §§ 910(a)(1)(B) and (a)(2)(B)(i)) clearly indicates that "as of" was intended to mean "on or before." The Final Guidance should recognize that a tobacco product marketed on or before February 15, 2007 is "grandfathered," whether or not the manufacturer possesses evidence of marketing efforts on that specific date.

III. The Guidance Should be Limited to Addressing the Question of what is a "New Tobacco Product" under § 910(a)(1)(A), and Should not Address Predicate Eligibility.

The intended scope of the Draft Guidance is not clear. The Federal Register Notice announcing availability of the Draft Guidance states that it "provides recommendations on the information that a manufacturer may use to establish that a tobacco product was commercially marketed in the United States on February 15, 2007, and is, therefore, a grandfathered product not subject to premarket review requirements." The Notice does not mention substantial equivalence or predicate

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[7] *See* Altria Client Services, Inc., Comments dated February 8, 2011, Docket ID No. FDA-2010-D-0635-0008.1.

[8] *See, e.g.,* FDCA § 904(c)(1) (21 U.S.C. § 387d(c)(1)), referencing "a tobacco product not on the market on the date of enactment" as a type of tobacco product requiring pre-market notification of ingredients.

[9] *See* Merriam-Webster Online Dictionary at http://www.merriam-webster.com/dictionary/as%20of.

[10] Except in the case of products previously found to be substantially equivalent; *see* 21 U.S.C. § 387e(j)(1)(A)(i).

eligibility. Nevertheless, the first paragraph of the Draft Guidance mentions predicate eligibility in conjunction with substantial equivalence. Moreover, the title of the Draft Guidance is worded broadly enough to suggest that the Draft Guidance may also apply to determination of predicate eligibility. As discussed above, however, the questions of (1) whether a tobacco product is "grandfathered," i.e. not a "new tobacco product" requiring premarket review; and (2) whether a tobacco product is eligible to serve as a predicate are distinct legal questions with separate analyses.

The Final Guidance should not reference predicate eligibility because (1) the Federal Register Notice did not place the regulated industry on notice that the Draft Guidance, once finalized, may represent FDA's views on predicate eligibility; (2) FDA already has a separate docket and guidance document on substantial equivalence; and (3) non-newness ("grandfathering") and predicate eligibility are distinct legal questions.

IV. The Agency Should Take a Reasonable Approach with Respect to the Evidence Requested to Support a Grandfather Determination.

The Draft Guidance lists nine examples of the types of information that may demonstrate that a tobacco product was marketed as of February 15, 2007. The Draft Guidance also states that "FDA recommends that you submit as much evidence as possible to demonstrate that your tobacco product was commercially marketed in the United States as of February 15, 2007." Taken literally, this could potentially result in a large volume of documents establishing the marketing pedigree of a tobacco product with unnecessary redundancy. The Final Guidance should clarify that only a reasonable amount of evidence is needed to support a grandfather determination.

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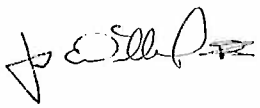
We appreciate the opportunity to submit these comments and urge the Agency to incorporate them in its Final Guidance. We look forward to further opportunities to provide comments to the Agency as its thinking on grandfathered tobacco products evolves.

Sincerely,



James E. Dillard III

Altria

Altria Client Services

James E. Dillard III
Senior Vice President
Regulatory Affairs

November 8, 2011

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. FDA-2011-D-0147 (76 Fed. Reg. 55,927 (Sept. 9, 2011)) – Comments on the "Draft Guidance for Industry and FDA Staff: Demonstrating the Substantial Equivalence of a New Tobacco Product: Responses to Frequently Asked Questions"

Altria Client Services ("ALCS") Inc., on behalf of Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC"),[1] submits these comments on the above-captioned draft frequently asked questions document ("Draft FAQ").

First, the Draft FAQ inappropriately announces for the first time FDA's interpretations of key statutory terms. While FAQ documents can be useful in responding to common questions, they should not be used to advance interpretations of key statutory terms or attempt to establish new legal norms.[2]

Second, the Draft FAQ contains serious substantive flaws. It sets forth, without adequate explanation or support, incorrect interpretations of the Family Smoking Prevention and Tobacco Control Act ("FSPTCA"); raises serious constitutional issues; and reflects policy judgments that merit reconsideration. As discussed in greater detail below, in its Final Guidance FDA should:

- delete any suggestion that the definition of "tobacco product" includes the product's label or packaging and acknowledge that a substantial equivalence report or a 910(b) submission is not required based on a label or packaging change that does not modify the product itself;

[1] PM USA and USSTC are wholly-owned subsidiaries of Altria Group, Inc. ALCS provides certain services, including regulatory affairs, to the Altria family of companies. "We" and "our" are used throughout these comments to refer collectively to PM USA and USSTC.

[2] *See* 21 C.F.R. § 10.115(d). An FAQ document by its very nature is not reasonably expected to include new regulatory requirements or novel statutory interpretations, and it is therefore less likely to be among the key resources stakeholders consult in assessing their compliance responsibilities.

Altria Client Services Inc.
2325 Bells Road
Richmond, Virginia 23234
(804) 335-2679
James.E.Dillard@altria.com

- confirm that a change in the name of a tobacco product is not a modification of the tobacco product and does not require a substantial equivalence report or a 910(b) submission;

- confirm that actions that do not change the finished tobacco product, including (1) tightening the range for a tobacco product additive, (2) changing processing aids, or (3) ensuring product consistency, are not modifications of the tobacco product and do not require a substantial equivalence report or a 910(b) submission;

- provide guidance regarding the level of specificity needed in substantial equivalence reports regarding tobacco product additives; and

- delete newly stated requirements that substantial equivalence reports include reports on harmful or potentially harmful constituents and environmental assessments.

I. The Agency Should Delete From The Draft FAQ Any Suggestion That The Statutory Definition Of "Tobacco Product" Includes The Product's Label Or Packaging And Acknowledge That A Substantial Equivalence Report Or Section 910(b) Submission Is Not Required Based On A Label Or Packaging Change That Does Not Modify The Product Itself.

The Draft FAQ asserts, without explanation or support, that "[t]he label and packaging is part of a tobacco product."[3] The Draft FAQ thus concludes that any change to the label or packaging of a tobacco product that occurs after February 15, 2007 makes that product a "new tobacco product" subject to the requirements of Sections 905(j) and 910(b).[4] However, that interpretation is foreclosed by the text, context and purpose of the statute. Furthermore, the Draft FAQ violates administrative law principles,[5] represents a clear break from FDA's previous statements

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[3] Draft FAQ § II; *see id.* § II(A) ("The label and packaging of a tobacco product is considered a 'part' of that product.").

[4] *Id.* § II(A), FAQ1 ("[W]e do not intend to enforce the premarket requirements of sections 905(j) and 910 ... for modifications to product packaging or labels to remove the descriptors 'light', 'mild', or 'low' or similar descriptors to comply with section 911 ...."); *id.* at FAQ2 ("We do not intend to enforce the premarket requirements of sections 905(j) and 910 ... for a tobacco product that was commercially marketed in the United States on February 15, 2007, and that had no modifications ... other than to comply with the graphic warning requirements of section 201 ...."); *id.* at FAQ3 ("[If] the package was changed from a soft pack to a hard pack (or from a hard pack to a soft pack) after February 15, 2007, and this change did not modify the tobacco product in any other way (e.g., a change in moisture content, shelf life, ingredient composition, nicotine delivery, harmful/potentially harmful constituents), and no other modifications were made ... then we do not intend to enforce the premarket requirements of sections 905(j) and 910 ...."); *id.* at FAQ4 ("[If] a modification to font size, ink color, or background color was made to the packaging or labels after February 15, 2007 and no other modifications were made to the tobacco product after February 15, 2007, then we do not intend to enforce the premarket requirements of sections 905(j) and 910 ... for this type of modification, provided the modification does not raise different questions of public health ... and you are in compliance with all other statutory labeling and packaging requirements ....").

[5] The lack of explanation provides a separate ground on which to conclude that the interpretation in the document is invalid. *See, e.g., Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983) (An agency must "articulate a satisfactory explanation for its action including a 'rational connection between the facts found and the choice made.'") (quoting *Burlington Truck Lines, Inc. v. United States*, 371 U.S. 156, 168 (1962)). There is yet another reason to reject the interpretation in the Draft Guidance: it imposes binding legal requirements without

regarding Sections 905(j) and 910,[6] and does not help achieve the legitimate policy goals underlying the statute, which are amply served by other provisions.

A. A Requirement That Manufacturers Make Premarket Submissions For Label and Packaging Changes Would Be Contrary To The Statute.

A label or packaging change does not transform a tobacco product into a "new tobacco product" that requires premarket submissions by a manufacturer. Under the FSPTCA, a manufacturer must obtain FDA authorization to market a "tobacco product" only if the product is a "new tobacco product," meaning either that it was not commercially marketed as of February 15, 2007 or is a "modification" of a "tobacco product" and commercially marketed after that date.[7] After March 22, 2011, the manufacturer of a "new tobacco product" must submit either (1) a report under Section 905(j) seeking an order that the product is "substantially equivalent," or (2) an application for premarket authorization under Section 910.[8]

Due to the major consequences that flow from "new tobacco product" status, we have urged the Agency to confirm our interpretation of the statute.[9] FDA, however, has stated that further elaboration is unnecessary because the meaning of the statute is clear.[10] That certainly is correct in the statute's treatment of the label and packaging issues addressed in the Draft FAQ. However, the Draft FAQ position that altering a product's label or packaging transforms it into a "new tobacco product" by modifying "part" of the tobacco product has no basis in the statute and is utterly inconsistent with it.

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notice-and-comment rulemaking. *See Appalachian Power Co. v. EPA*, 208 F.3d 1015, 1024 (D.C. Cir. 2000); *Paralyzed Veterans of Am. v. D.C. Arena L.P.*, 117 F.3rd 579, 588 (D.C. Cir. 1997).

[6] The definitions FDA set out in its guidance on demonstrating substantial equivalence tracked the statutory language and gave no indication that FDA would view a product's name, label, or packaging to be part of the tobacco product itself. *See* FDA Guidance, *Guidance for Industry and Food and Drug Administration Staff; Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products* (Jan. 5, 2011) at 4, *available at* http://1.usa.gov/pCVt43 (hereinafter, "905(j) Guidance"). The Agency adopted the same definitions in its newly released guidance on premarket review applications under Section 910. *See* FDA Draft Guidance, *Guidance for Industry; Applications for Premarket Review of New Tobacco Products*, at 3 (Sept. 2011), *available at* http://1.usa.gov/pCVt43.

[7] 21 U.S.C. § 387(a)(1).

[8] *See Id.* §§ 387e(j)(1), 387j(a)(2). *See also* 905(j) Guidance at 5 (explaining that the manufacturer of a tobacco product introduced after February 15, 2007, and prior to March 22, 2011, and who submits a report under Section 905(j) prior to March 23, 2011, may continue to market the product unless or until FDA issues an order that the product is not substantially equivalent). In addition, FDA promulgated regulations describing the process for exempting minor changes in tobacco additives from the premarket review requirements. *See* 21 C.F.R. Pt. 1107.

[9] ALCS, Comments dated February 8, 2011, Docket ID No. FDA-2010-D-0635-0005, at 3, *available at* http://1.usa.gov/pwbTbr (hereinafter, "905(j) Comments"); *see also* ALCS, Comments dated March 22, 2011, Docket ID No. FDA-2010-N-0646-0011, at 1 ("We reiterate that there are numerous sources of variability inherent in tobacco products that should not constitute a 'modification.'"), *available at* http://1.usa.gov/nwfDPk.

[10] *See* 76 Fed. Reg. 38,961, 38,962 (July 5, 2011) ("FDA disagrees with the suggestion in the comments that the term 'new tobacco product' has not been sufficiently defined" in the statute.).

1. The label and packaging of a tobacco product are not "part" of the tobacco product.

The Agency's assertion that the label and packaging of a tobacco product are "part" of the tobacco product is inconsistent with the statutory scheme under which FDA operates. An article in interstate commerce is under FDA's jurisdiction if it meets the statutory definition of "food," "drug," "device," "cosmetic," "animal feed," "dietary supplement," or "tobacco product."[11] The statute does not define any of those terms to include the label or packaging of the article.

To the contrary, the statute defines "label" and "package" separately. Both definitions treat these things as discrete items, and not as "parts" of the article itself. "Label" is defined as "a display of written, printed, or graphic matter *upon the immediate container of any article*,"[12] thus making clear that a label is something affixed to the container in which an article is sold, not part of the article itself. Similarly, "package" is defined as the "pack, box, carton, or container … [or] wrapping … *in which a tobacco product* is offered for sale, sold, or otherwise distributed to consumers."[13] This obviously means that a package is external to, and not a part of, the tobacco product.[14] Both definitions preclude the Agency's interpretation in the Draft FAQ.

Moreover, the definition of "tobacco product" itself precludes the Agency's interpretation. The statute defines a "tobacco product" as having three elements: (1) a "product" that (2) is "made or derived from tobacco" and (3) is "intended for human consumption."[15] All three elements must exist to meet the definition, because the definition is conjunctive. Applying this definition makes clear that labels and packaging are not "tobacco products" because they are neither "made or derived from tobacco" nor "intended for human consumption."

Further, the Agency's position is inconsistent with the plain meaning of the word "part"[16] because "part" is generally understood to refer to a portion or subdivision of a larger whole, not something external to it.[17] Thus, "parts" of a tobacco product must be portions of something made or derived from tobacco that is intended for human consumption.

Other definitions in the statute confirm the error of the Agency's reliance on the word "part." For example, the definition of "new tobacco product," includes "part" in a list of terms that refer

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[11] 21 U.S.C. §§ 321(f), 321(g)(1), 321(h), 321(i), 321(w), 321(ff)(3), 321(rr).

[12] *Id.* § 321(k) (emphasis added).

[13] *Id.* § 387(13) (emphasis added).

[14] "Package" is also defined under the Federal Cigarette Labeling and Advertising Act using almost identical wording but with reference to the sale of "cigarettes." 15 U.S.C. § 1332(4). Cigarettes are defined as the "roll of tobacco" itself and not the packaging. *Id.* § 1332(1). Congress, by using the same definition of package under the FSPTCA, is presumed to have intended for the provisions to be interpreted in parallel. *See, e.g.*, *Sullivan v. Stroop*, 496 U.S. 478 (1990).

[15] 21 U.S.C. § 321(rr)(1).

[16] Draft FAQ § II(A).

[17] *See* http://www.merriam-webster.com/dictionary/part (defining "part" as "a constituent member of a machine or other apparatus"); Webster's Third New International Dictionary (Unabridged) (1993) (defining "part" as "one of the equal or unequal portions into which something is or is regarded as divided").

to specific physical changes to the tobacco product,[18] and Section 904(a)(1) includes the phrase "other part" at the end of a list including tobacco, papers, and filters.[19] Under well-settled canons of statutory construction, the word "part" must draw its meaning from the terms around it and thus should be read to refer to a physical element of the tobacco product, such as tobacco, papers, or filters.[20] Similarly, the definition of "characteristics" demonstrates that Congress did not intend to make labels or packaging part of substantial equivalence review. "Characteristics" is defined to include "the materials, ingredients, design, composition, heating source, or other features of a tobacco product."[21] Labels and packaging cannot fit comfortably within that definition.[22]

Finally, at numerous other places in the statute, Congress indicated that a tobacco product's label and packaging are different from, rather than a "part" of, the product. For example, Section 902 contains separate provisions deeming a tobacco product adulterated based on the presence of any "poisonous or deleterious substance" in the product itself *or in its packaging*; and Section 301(qq) prohibits the creation of counterfeit tobacco products by placing an identification device such as a "label ... upon any tobacco product or container *or labeling thereof*."

2. The Draft FAQ Conflicts with the Basic Structure of the Statute.

The Draft FAQ conflicts with the basic structure of the statute, which provides FDA authority to regulate labels and packaging that is wholly separate from the regulation of new tobacco products. Under FDCA provisions applicable to other product categories, labels and packaging are regulated directly, not by implication. For example, FDA regulation of labels and packaging for drug products is based on the statute's general misbranding and new drug approval provisions.[23] The FSPTCA applies that same framework to tobacco products,[24] and absent contrary legislative intent, labels and packaging under the FSPTCA should be treated consistently.

For example, Section 905 requires every manufacturer to register its establishments with FDA and submit a listing of each tobacco product in commercial distribution. This submission

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[18] *See id.* § 387j(a)(1) ("change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient").

[19] 21 U.S.C. § 387d(a)(1) (a manufacturer must list all ingredients "added by the manufacturer to the *tobacco, paper, filter, or other part* of each tobacco product" (emphasis added)).

[20] *See, e.g., Wash. State Dep't of Soc. & Health Servs. v. Guardianship Estate of Keffeler*, 537 U.S. 371, 384 (2003) (canons of *ejusdem generis* and *noscitur a sociis* require that "general words are construed to embrace only objects similar to those enumerated by the specific words" enumerated in the same list) (internal quotation marks omitted); *see also United States v. Tinklenberg*, 131 S. Ct. 2007, 2019 (2011) (absent indication to the contrary, "[i]dentical words used in different parts of a statute are presumed to have the same meaning").

[21] 21 U.S.C. § 387j(a)(3)(B).

[22] Indeed, FDA itself implicitly recognized this difficulty when it provided guidance that the requirement to provide an ingredient list does not apply to "packaging differences that do not affect the characteristics of the product." FDA Guidance, *Guidance for Industry: Listing of Ingredients in Tobacco Products* § III(C) (Nov. 2009), *available at* http://1.usa.gov/pCVt43 (hereinafter "Listing Guidance").

[23] *See, e.g.*, 21 U.S.C. § 355(d)(7); 21 C.F.R. § 201.10.

[24] *See* 21 U.S.C. § 387c.

includes "a copy of all consumer information and other labeling for such tobacco product."[25] Section 911 authorizes FDA to review data and information relating to tobacco products "the label, labeling, or advertising of which represents" that the product presents a reduced risk or lower exposure to a substance.[26] And Section 903, the statute's misbranding provision, provides the Agency with ample tools to combat any potentially "false or misleading" statements, including names.[27] In light of these and other provisions, premarket review is simply unnecessary for changes to product labels or packaging.[28]

If the Agency's interpretation of "tobacco product" is designed to guard against the possibility that a change to a label or packaging could modify the product itself, that interpretation is unnecessary. The Agency's response to FAQ3 notes, for example, the possibility that a switch from a hard pack to a soft pack might lead to "a change in moisture content, shelf life, ingredient composition, [or] nicotine delivery." To the extent FDA has authority to require premarket review in such a case, it is not because the packaging has changed, but because there has been a change to the tobacco product. For example, "ingredients" are among the "modifications" expressly included in Section 910(a)(1)(B) and the characteristics intended to be included in substantial equivalence review.[29] There is no need for FDA to contort the definition of tobacco product to reach those situations.

Perhaps most tellingly, in Section 903(b), Congress expressly provided that FDA may "require prior approval of statements made on the label of a tobacco product"[30] only "by regulation"[31] issued "in accordance with chapter 5 of title 5, United States Code."[32] The Draft FAQ seeks effectively to "require prior approval of statements made on the label" – that is, to require prior FDA authorization of product names – without satisfying the clear and unambiguous requirement

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[25] *See* 21 U.S.C. § 321(m)(1) (the statutory term "labeling" includes "all labels and other written, printed or graphic matter … upon any article or any of its containers or wrappers"). FDA guidance states that "labeling is to be submitted as an exact, legible, full color copy." *See* FDA Guidance, *Guidance for Industry: Registration and Product Listing for Owners and Operators of Domestic Tobacco Product Establishments* (Nov. 2009), *available at* http://1.usa.gov/nDD9mU (hereinafter "Listing Guidance").

[26] *See* 21 U.S.C. § 387k(b).

[27] 21 U.S.C. § 387c(a); *cf.* 21 C.F.R. § 201.10 (regulating drug names in labeling).

[28] Significantly, Section 905(i)(3)(D) reflects a scheme in which FDA receives notification of labeling changes *after* they occur. 21 U.S.C. § 387e(i)(3)(D) (requiring the manufacturer to notify FDA of "[a]ny material change" in biannual updates). This mirrors the Agency's approach in other contexts. For example, FDA guidance regarding the labeling for OTC topical acne drug products states that "[l]abeling that is revised to meet the requirements of this rule should be submitted to FDA through the drug listing process." FDA Guidance, *Guidance for Industry: Topical Acne Drug Products for Over-the-Counter Human Use—Revision of Labeling and Classification of Benzoyl Peroxide as Safe and Effective; Small Entity Compliance Guide* (June 2011), *available at* http://1.usa.gov/pKrtrm.

[29] 21 U.S.C. §§ 387(j)(a)(1)(B), 387(a)(3)(B).

[30] *Id.* § 387c(b).

[31] *Id.*

[32] *Id.* § 387a(d).

that the Agency proceed through notice-and-comment rulemaking.[33] The Agency's use of Draft FAQ in this instance is contrary to law and invalid for this additional and independent reason.[34]

3. Treating Labels and Packaging as "Part" of the Tobacco Product Leads to Unintended Results.

The Agency's interpretation of "tobacco product" is flawed because it leads to unintended results.[35] For instance, Section 904(a)(1) requires a manufacturer to provide FDA a listing of all ingredients "added by the manufacturer to the tobacco, paper, filter, or other part of each tobacco product by brand and by quantity in each brand and subbrand." If the label and packaging were parts of the tobacco product, then a manufacturer would be required to submit a listing, by quantity, of all the ingredients added by the manufacturer to the label of its tobacco products. But it is clear that a "label" (a term that refers to "a display of written, printed, or graphic matter upon the immediate container of any article")[36] could never have "ingredients" to be listed.

The Draft FAQ itself recognizes that results not intended by Congress would follow if labels and packaging were part of the tobacco product. For example, label changes required by Section 911 (to remove descriptors) and Section 201 (to add graphic warnings) would trigger the need for premarket review.[37] To avoid this result, the Agency says it will exercise "enforcement discretion" to allow manufacturers to comply. The Agency also recognizes that its interpretation leads to the conclusion that modifications to font, ink, or color used on a tobacco product's label or packaging might transform it into a new tobacco product,[38] and it likewise relies upon enforcement discretion to the extent those changes do not raise "different questions of public health." As a legal matter, FDA cannot cure an incorrect statutory interpretation by invoking enforcement discretion. Doing so is also bad policy because it blurs the line between lawful and prohibited conduct.

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[33] Even if FDA had proceeded by regulation as described in Section 903(b), it could not have required premarket review of product names under Sections 905(j) and 910(b) because, as shown above, that interpretation is unambiguously foreclosed by other statutory provisions and the statutory context and purpose.

[34] The notion that label and packaging changes trigger premarket review under Sections 905(j) and 910(b) also cannot be reconciled with Title II of the FSPTCA, which includes specific amendments addressing many aspects of product labels. Title II delimits the scope of FDA's ability to regulate the content of product labels and also reflects Congress's intention not to empower FDA to regulate the content of labels indiscriminately. *See, e.g.*, 15 U.S.C. § 1333 (specifying warning content and format for cigarettes).

[35] *Cf. Nixon v. Missouri Mun. League*, 541 U.S. 125, 138 (2004) (explaining canon against "'construe[ing] a statute in a manner that leads to absurd or futile results'").

[36] 21 U.S.C. § 321(k).

[37] Draft FAQ § II(A), FAQ1 and FAQ2.

[38] *Id.* § II(A), FAQ4

II. FDA Should Confirm That A Product's Name Is Not "Part" Of A Tobacco Product, And That Name Changes Do Not Require Substantial Equivalence Reports or Section 910(b) Submissions.

In the Draft FAQ the Agency incorrectly asserts that any change to the name of a product after February 15, 2007 makes that product a "new tobacco product" subject to the requirements of Sections 905(j) and 910(b).[39] Nothing in the FSPTCA supports that construction. As discussed above, the word "part" must be understood to refer to a *physical* element within the tobacco product;[40] a name does not qualify. Moreover, the structure of the statute precludes construing labels and packaging (and thus, the names printed on them) to be parts of the tobacco product.[41] Likewise, there is no need to depart from the unambiguous text with respect to names.

Congress knew how to refer to product names when that was its intention. For example, Section 904 contains multiple reporting requirements—such as reporting of ingredient, nicotine, and constituent information—that require submissions to be made on a brand and subbrand basis.[42] Section 915 likewise requires the testing and reporting of constituents, ingredients, and additives for each brand and subbrand.[43] Section 301(qq) prohibits the sale of a tobacco product that misrepresents its name as that of another.[44] In addition, the relevant provisions specifically use "brand name" and related terms when Congress intended for FDA to regulate these commercial designations. There is no comparable reference to names in the definition of "tobacco product" or "new tobacco product."[45] Had Congress intended to regulate product names through these definitions, it would have said so explicitly.[46]

In addition, including a product's name in the definitions of tobacco product and new tobacco product would violate the First Amendment's Free Speech Clause. Brand names are protected as commercial speech.[47] An interpretation of the FSPTCA that would require manufacturers to obtain FDA authorization before changing the names of their products would impose a

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[39] In particular the Draft FAQ states that (1) a cigarette would be a new tobacco product "if the cigarette was marketed on February 15, 2007, but subsequently the name of the product was modified or changed," and (2) if a manufacturer markets a cigarette as "Brand X" on February 15, 2007, and, after that date, continues to market Brand X but also begins to market the identical cigarette under the additional name "Brand Y," then Brand Y "is a new tobacco product subject to the premarket review requirements."

[40] *Supra* § 1.

[41] *Supra* § 2.

[42] *See, e.g.*, 21 U.S.C. § 387d(a)(1). FDA guidance for Section 904 states that "[e]ach product for which an ingredient list is submitted is to be clearly and uniquely identified by its brand and subbrand, [as well as additional information] as needed to uniquely identify the brand and subbrand of the product." Listing Guidance § III(C)(2).

[43] 21 U.S.C. § 387o(b)(1).

[44] 21 U.S.C. § 331(qq).

[45] *E.g.*, 21 U.S.C. §§ 387(2), 387(6), 387o(b); 21 C.F.R. Part 1140.

[46] *See Whitman v. Am. Trucking Assns., Inc.*, 531 U.S. 457, 468 (2001) ("Congress . . . does not, one might say, hide elephants in mouseholes").

[47] *See, e.g., San Francisco Arts & Athletics v. United States Olympic Comm.*, 483 U.S. 522, 535 & 537 n.16 (1987) (the "Olympic" mark receives First Amendment protection as commercial speech); *Friedman v. Rogers*, 440 U.S. 1, 11 (1979) ("The use of trade names . . . is a form of commercial speech . . . .").

constitutionally suspect prior restraint.[48] Such restraints are impermissible absent procedural safeguards sufficient to protect against the "danger of suppressing constitutionally protected speech."[49]

The Draft FAQ, however, provides no information regarding the standards or procedures FDA would employ when evaluating name changes or additional names. Neither the Draft FAQ nor any other FDA pronouncement regarding Section 905(j) indicates how the Agency would intend to judge names or determine whether a "new" name is substantially equivalent. Such standardless discretion to allow or disallow otherwise lawful speech violates traditional principles of prior restraint under the First Amendment.[50]

A blanket prohibition on all new names that have not obtained FDA authorization—a process that could prevent a manufacturer from engaging in speech for a period of months or years (if the speech is allowed at all)—would also clearly violate the *Central Hudson* test for assessing the constitutionality of restrictions on commercial speech.[51] Such a prohibition would bar speech regarding lawful products and applies to all names without regard to whether they are misleading or not. Moreover, it is unnecessary to advance any governmental interest in ensuring that names comply with the provisions of the FSPTCA because, as explained above, other provisions of the statute provide FDA with the tools it needs to advance this interest in a less restrictive way.[52]

At the very least, the Agency's interpretation raises sufficiently grave constitutional questions that a reviewing court would construe the statute to exclude names from the definitions of "tobacco product" and "new tobacco product."[53] Because the interpretation proposed in the

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[48] *See, e.g.*, *Southeastern Promotions, Ltd. v. Conrad*, 420 U.S. 546, 558 (1975) ("Any system of prior restraint . . . comes to this Court bearing a heavy presumption against its constitutional validity.") (internal quotation marks omitted); *New York Magazine v. MTA*, 136 F.3d 123, 131-32 (2d Cir. 1998) (affirming injunction of prior restraint on commercial speech).

[49] *Freedman v. Maryland*, 380 U.S. 51, 58 (1965) (A system of prior restraint "avoids constitutional infirmity only if it takes place under procedural safeguards designed to obviate the dangers of a censorship system."). Congress's sensitivity to this issue is reflected in the requirement in Section 903(b) that any requirement for prior approval of label statements be established by regulation only after notice-and-comment procedures.

[50] *Shuttlesworth v. Birmingham*, 394 U.S. 147, 150-51 (1969) ("[A] law subjecting the exercise of First Amendment freedoms to the prior restraint of a license, without narrow, objective, and definite standards to guide the licensing authority, is unconstitutional."). In addition, the absence of a fixed deadline by which FDA must make a substantial equivalence determination weighs heavily against the constitutionality of the proposed interpretation. *Cf. Nutritional Health Alliance v. Shalala*, 144 F.3d 220, 228 (2d Cir. 1998) (upholding FDA review of dietary supplement labels on the basis of a statutory deadline for completion of such review).

[51] *Central Hudson Gas & Electric Corp. v. Public Service Commission*, 447 U.S. 557 (1980).

[52] For example, manufacturers could notify FDA of name changes by updating their ingredient submissions under Section 904, or through regular product listing submissions. *See supra* notes 28 and 42.

[53] As noted, the text, context, and structure of the statute unambiguously foreclose the interpretation in the Draft FAQ under which FDA could require a Section 905(j) or a Section 910(b) submission for a change to the label or packaging of a tobacco product. Even if the statute were ambiguous, however, the ambiguity would have to be resolved against the speech-restrictive interpretation under the avoidance canon. *Edward J. DeBartolo Corp. v. Fla. Gulf Coast Bldg. & Constr. Trades Council*, 485 U.S. 568, 575 (1988) ("[W]here an otherwise acceptable construction of a statute would raise serious constitutional problems, the Court will construe the statute to avoid such problems unless such construction is plainly contrary to the intent of Congress.").

Draft FAQ is plainly not required by the statute, (and, indeed is contrary to it), these constitutional infirmities must be avoided in the Final Guidance.

III. FDA Should Confirm That Actions That Do Not Change The Finished Tobacco Product Are Not Modifications Within The Meaning of 910(a)(1)(B) And Do Not Require A Substantial Equivalence Report Or A 910(b) Submission.

In a number of instances, the Draft FAQ indicates that manufacturer actions that do not change the finished tobacco product may nonetheless constitute "modifications" that require a substantial equivalence report or a 910(b) submission. As explained below, these statements are inconsistent with the statute, which imposes premarket review obligations only upon modifications "of a tobacco product."[54] These aspects of the Draft FAQ should therefore be removed from the Final Guidance.

A. FDA Should Affirm That Tightening The Range For A Tobacco Product Additive Is Not A Modification Within The Meaning of 910(a)(1)(B).

FDA should affirm that a manufacturer's decision to make the specification range for a product additive more precise, but still within the previously reported range, does not constitute a modification that would trigger premarket review. The Draft FAQ currently takes the opposite view. FDA's response to FAQ9 states that "[a]ny modification made to the level of an additive" would require premarket clearance. This interpretation is overbroad.

We agree that a change to a static specification (*e.g.,* from 0.003 to 0.005) or expanding a range specification for tobacco product additive (*e.g.,* from 0.003-0.005 to 0.003-0.007) will likely result in a modification to the finished product triggering the need for premarket review. Tightening the range for an additive (*e.g.,* from 0.003-0.005 to 0.003-0.004), however, is different. In such cases, the "new" product by definition will fall within the permissible range of the "old" product. FDA should clarify that, in such situations, the finished product is not modified such that it requires premarket clearance.

Otherwise, the Agency will use valuable resources reviewing substantial equivalence reports for products that have not actually been modified. Assuming the only change between two products is a narrowed range for an additive, the new and predicate products would necessarily share the same characteristics and thus be substantially equivalent.[55] In addition, requiring premarket review in these circumstances would discourage manufacturers from continuing to refine and improve their manufacturing processes and controls. FDA should avoid these problems by making clear in the Final Guidance that increasing the precision of an additive specification within a preexisting range does not constitute a modification of a tobacco product.[56]

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[54] 21 U.S.C. § 387j(a)(1)(B).

[55] 21 U.S.C. § 387j(a)(3)(A)(i).

[56] As we previously noted, FDA's support for the concept of "design space" in the pharmaceutical industry counsels against the view that increasing the precision of a specification range constitutes a product modification. *See* 905(j) Comments at n.11 ("'Working within the design space is not considered as a change. Movement out of the design space is considered to be a change and would normally initiate a regulatory postapproval change process.'" (quoting

B. A Change In A Processing Aid That Does Not Have An Identifiable Effect On The Tobacco Product Is Not A Modification Within The Meaning of 910(a)(1)(B).

The statutory definition of new tobacco product is only triggered by an actual "modification" of "a tobacco product."[57] The statute refers to "any modification (including a change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient)."[58] This statutory language clearly does not reach changes in manufacturing processes unless they result in an identifiable change to the product (or the components, parts, or constituents thereof).

Nevertheless, in response to Question 11, the Agency states that premarket review would be required if a supplier begins using a new processing aid for a subcomponent of a tobacco product even if any resulting change "is so minor that it is not even capable of being quantified in the finished product." The Agency's apparent reasoning is that even if no quantifiable change has been made to the finished product, the switch in a subcomponent processing aid "may" nevertheless "have an impact on other characteristics within the tobacco product."

The Agency's response reflects a flawed analysis that is inconsistent with the statute. If Congress had intended to require premarket review solely on the basis of a change in manufacturing process, it would have said so.[59] In the final guidance, FDA should clarify that, absent an identifiable change to the resulting product, there is no modification within the meaning of Section 910(a)(1)(B).[60]

FDA Guidance For Industry: Q8 Pharmaceutical Development, at 2 (May 2006), available at http://1.usa.gov/pJpK2N)).

[57] 21 U.S.C. § 387(a)(1)(B).

[58] *Id.*

[59] Other provisions of the FSPTCA support this conclusion. "[R]aw materials used in manufacturing a component, part, or accessory of a tobacco product" are excluded from the statutory definition of "tobacco product." *See* 21 U.S.C. § 321(rr)(1). A change in raw material therefore cannot amount to a modification of a tobacco product unless the change results in identifiable alteration of the finished product. The same logic should apply to manufacturing processes, which are not mentioned in the tobacco product definition and are regulated under different provisions of the FSPTCA that direct FDA to establish manufacturing controls through regulations. *See* 21 U.S.C. § 387f(e)(1)(A). Moreover, in light of the explicit statutory requirement to include information about the manufacturing process in a Section 910 application, *see id.* § 387j(b)(1)(C), the absence of any specific requirement to include that information in a substantial equivalence report indicates that Congress did not view a change in the manufacturing process alone as triggering premarket review.

[60] At a minimum, FDA should clarify that the *possibility* of an unquantifiable change is not a modification. The response to FAQ11 justifies its conclusion by noting that a change in processing aid "*may* have an impact on other characteristics within the tobacco product (e.g., *may* alter chemical reactions and create a new ingredient, additive, or constituent)." (Emphases added). Such speculation is inconsistent with the premise of the question (that there was no quantifiable change to the finished product) and, in all events, is no basis for expanding the scope of the FSPTCA's premarket review requirements.

C. Adjustments Made To Ensure Product Consistency Are Not Modifications Within The Meaning Of 910(a)(1)(B).

We previously asked the Agency to confirm that the frequent adjustments a manufacturer must make to maintain consistent product characteristics are not "modifications" within the meaning of Section 910(a)(1)(B).[61] FAQ8 provides a partial response by stating that FDA will use its "enforcement discretion" to allow "tobacco blending changes required to address the natural variation of tobacco." While we agree that consistency-maintaining changes are permissible, we do not agree that such changes implicate FDA's enforcement discretion. Rather, adjustments made by a manufacturer to maintain consistent product characteristics are not modifications within the meaning of Section 910(a)(1)(B). In the final guidance, FDA should acknowledge that Section 910 does not apply in this scenario.

IV. FDA Should Provide Guidance Regarding The Level Of Specificity Needed In Substantial Equivalence Reports Regarding Tobacco Product Additives.

In response to requests that FDA identify the level of specificity required for 905(j) reports when reporting the amounts and levels of additives in products, FAQ 13 says that it is the manufacturer's responsibility to "present the data in a form that will provide the basis for" substantial equivalence review. It is unrealistic to expect stakeholders to predict in advance the level of the specificity that the Agency will require. Moreover, the Agency's failure to provide more specificity could lead to inconsistent applications from manufacturers and to inconsistent reviews within the Center for Tobacco Products. FDA should, therefore, provide a substantive response to FAQ13 and reopen public comment to provide an opportunity for meaningful public participation.

V. New Requirements For Substantial Equivalence Reporting Should Not Be Added in This FAQ Document.

A. Substantial Equivalence Reports Should Not Require Reporting On Harmful Or Potentially Harmful Constituents.

We urge the Agency to reconsider its response to FAQ17 that manufacturers "provide information regarding harmful or potentially harmful constituents ("HPHC") as appropriate to demonstrate that the new tobacco product is substantially equivalent to the predicate product."[62] In its Final Guidance the Agency should state that HPHC data will not be required in Section 905(j) reports.

Any requirement that substantial equivalence reports contain HPHC data would be contrary to the FSPTCA. Substantial equivalence review is based on a comparison of the "characteristics"

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[61] 905(j) Comments at 3.

[62] ALCS previously provided comments on the 905(j) Guidance stating that substantial equivalence review should not require HPHC reporting. *See* 905(j) Comments at 7-8; *cf.* 905(j) Guidance at 11 ("For all products, you should report levels of all HPHC in tabular format, with a side-by-side comparison with the predicate tobacco product and, where applicable, to a grandfathered tobacco product.").

of the new and predicate products.[63] The statute defines the term "characteristics" to mean "the materials, ingredients, design, composition, heating source, or other features of a tobacco product."[64] Constituents are thus not included in the list of characteristics that are part of substantial equivalence review. Nor can the trailing phrase "other features of a tobacco product" be read to include constituents. The FSPTCA specifically defines the term "smoke constituent,"[65] and constituents are expressly regulated throughout the statute.[66] Moreover, the different schedules for reporting ingredients and constituents make clear that the statutory term "ingredient" does not include constituents.[67] Had Congress meant to include constituents as part of substantial equivalence review, it would have done so expressly.

The Agency's position that substantial equivalence reports must contain HPHC data also raise practical difficulties that further indicate that Congress did not intend this requirement. Manufacturers were required to file initial 905(j) reports by March 2011, well before the Agency's April 2012 deadline to publish a list of HPHCs and the April 2013 deadline to promulgate regulations for testing and reporting.[68] Obviously, manufacturers cannot test against a list that does not exist. Moreover, the current pending 905(j) reports generally rely on tobacco products that were on the market as of February 15, 2007 as predicates for the substantial equivalence comparison. Given the passage of time, it is unlikely that cigarettes and smokeless tobacco products that were on the market as of February 15, 2007 still exist in quantities sufficient to enable the testing necessary to generate HPHC data for most, if not all, predicate products.[69]

Thus, a requirement that HPHC reporting be included in 905(j) reports is contrary to law and creates substantial practical difficulties. The Agency's Final Guidance should make clear that reporting on HPHCs is not required as part of substantial equivalence review.

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[63] *See* 21 U.S.C. § 387j(a)(3)(A).

[64] 21 U.S.C. § 387j(a)(3)(B).

[65] 21 U.S.C. § 387(22).

[66] *See, e.g.*, 21 U.S.C. §§ 387g(a)(4)(A)(ii), 387g(a)(4)(B)(i) (FDA has authority to promulgate tobacco product standards addressing constituents); *id.* § 387o(b)(1) (directing FDA to promulgate regulations for the "testing and reporting of tobacco product constituents, ingredients, and additives"). *See also* Altria Client Services, Inc., R.J. Reynolds Tobacco Co., and Lorillard Tobacco Company, Comments dated October 11, 2011, Docket ID No. FDA-2011-N-0271, at 1 & n.5 (hereinafter, "2011 HPHC Comments").

[67] *See* 21 U.S.C. §§ 387d(a)(1), 387d(a)(3); *see also id.* §§ 387g(a)(1)(A), 387g(a)(3)(B)(ii) (indicating that "constituents" and "additives" are conceptually distinct categories under the FSPTCA).

[68] *See* 21 U.S.C. §§ 387d(d)(1), 387d(e), 387(o)(b)(1).

[69] For a fuller discussion related to HPHCs, we refer the Agency to previous submissions in which we discuss our experience with tobacco constituent testing and evaluation of such data as part of our ingredient testing program. *See* Altria Client Services, Inc., Comments dated August 23, 2010, Docket ID No. FDA-2010-D-0281-0003.1, *available at* http://1.usa.gov/oLwObl; *see also* 2011 HPHC Comments.

B. FDA Should Exempt Substantial Equivalence Reports From The Environmental Assessment Requirement.

In response to Question 18, FDA states that all Section 905(j) reports must include environmental assessments under 21 C.F.R. § 25.15(a). This requirement is new and was not stated or implied in the final 905(j) Guidance FDA published in January 2011.[70] In fact, this new requirement was not announced until almost six months *after* manufacturers submitted their initial 905(j) reports in March 2011. This new requirement is thus procedurally improper with respect to reports previously submitted by manufacturers and, at a minimum, the Agency should clarify that this newly stated requirement does not apply to them. It would make no sense to apply the requirement to these reports because they pertained to products that were on the market in March 2011. The intent of these reports is to obtain an agency determination that such products are substantially equivalent to one or more predicate products that were on the market on or before February 15, 2007. In other words, the only requested agency action is to maintain the status quo—not the type of agency action that requires an environmental review.

More fundamentally, substantial equivalence reports for tobacco products are not included among the agency actions for which an environmental assessment is necessary under 21 C.F.R. § 25.20. To the extent the Agency wishes to amend Part 25 to include tobacco products, it must do so through formal notice and comment rulemaking.[71]

Requiring environmental assessments for substantial equivalence is also substantively unjustified, and FDA should establish a categorical exemption from the environmental assessment for all 905(j) reports. Essentially every other FDA-regulated industry benefits from a categorical exemption for agency actions similar to substantial equivalence determinations. In each of these industries, FDA has taken the position that environmental assessments are not necessary if the requested agency action does not increase overall use of the product type.[72] Section 905(j) reports seek only an agency determination that a given product is equivalent to, and thus likely to compete with or replace, products that already are or have been on the market. Therefore, 905(j) reports should be categorically exempt from the environmental assessment requirement.

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[70] The Preface of the 905(j) Guidance states that the Agency's intent in promulgating the guidance was to clarify "FDA's expectations regarding 905(j) reports" in "sufficient time" for stakeholders to prepare submissions prior to March 2011. The guidance specifically represented that it included a list of "the information [FDA] believes a typical 905(j) report may need to include." 905(j) Guidance at 7.

[71] When the Agency has expanded the scope of other preexisting regulations to include tobacco products, it has done so by amendment to the regulation. *See, e.g.*, 76 Fed. Reg. 20,901 (Apr. 14, 2011). From both a consistency and an administrative law perspective, *see supra* note 5. FDA should take the same approach here and undertake notice-and-comment rulemaking before substantively amending Part 25.

[72] *See, e.g.*, 21 C.F.R. §§ 25.15(c) (agency actions that "do not significantly affect the quality of the human environment" are ordinarily excluded), 25.30(k) (labeling changes that do not affect levels of use); 25.31(a) (new drug approval applications that will not "increase the use of the active moiety"), 25.31(g) (bioequivalence determinations for human drugs and comparability determinations for biologics), 25.32(f) (determinations that food is GRAS if it is already marketed for the proposed use), 25.33(a) (new animal drug approval applications that will not increase use), 25.34(b) (device classification determinations that will not increase or expand the use of the device), 25.34(d) (class III medical device approvals if the device is of the same type and use of a previously approved device), 25.34(f) (restricted device regulations that will not expand or increase the use of the product).

* * * * *

We appreciate the opportunity to submit these comments and urge the Agency to revise the Draft FAQ as described above. We look forward to further opportunities to provide comments to the Agency as its thinking on substantial equivalence continues to evolve.

Sincerely,

James E. Dillard III

Altria
Altria Client Services

James E. Dillard III
Senior Vice President
Regulatory Affairs

June 14, 2013

Division of Dockets Management (HFA305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Response to "Comments in Response to Submissions of Other Parties on Demonstrating Substantial Equivalence for Tobacco Products"

Altria Client Services ("ALCS"), on behalf of Philip Morris USA ("PM USA") and U.S. Smokeless Tobacco Company ("USSTC"),[1] submits these comments in response to the above referenced docket submission ("Submission") by the Cancer Action Network, American Heart Association, American Lung Association, Legacy and the Campaign for Tobacco-Free Kids.[2] The Submission raises issue with our and other manufacturers' docket submissions on FDA's tobacco product pathways.

We provide these comments to ensure that FDA understands our perspective on important Section 905(j) premarket review issues. This response addresses two points:

- *First*, Congress intended that manufacturers be able to bring products to market through the substantial equivalence pathway, a pathway with different requirements than the new tobacco product application pathway.

- *Second*, the Submission's statutory interpretations would nullify the Section 905(j) pathway.

[1] PM USA and USSTC are wholly-owned subsidiaries of Altria Group, Inc. ("Altria"). ALCS provides certain services, including regulatory affairs, to the Altria family of companies. "We" and "our" are used throughout to refer to PM USA and USSTC.

[2] The Submission is available at http://www.regulations.gov/#!documentDetail;D=FDA-2010-D-0635-0021.

Altria Client Services Inc.
2325 Bells Road
Richmond, Virginia 23234
(804) 335-2679
James.E.Dillard@altria.com

I. Congress Intended to Provide Alternative Pathways for New and Modified Tobacco Products to Come to the Market.

The "Purpose" section of the Family Smoking Prevention and Tobacco Control Act (FSPTCA) states that the legislation is intended to "continue to permit the sale of tobacco products . . . ." To that end, Congress created distinct regulatory pathways allowing manufacturers to bring tobacco products to the market.

Congress set forth in great detail how tobacco manufacturers can bring new or modified tobacco products to market:

- Manufacturers may submit a Section 905(j) substantial equivalence report if they believe the product either has the same characteristics[3] as a predicate tobacco product, or has different characteristics but "does not raise different questions of public health" when compared to the predicate product.
- Manufacturers may also seek a substantial equivalence exemption if the product is a minor modification (such as the addition or deletion of an existing additive) to another tobacco product.
- Manufacturers must submit a Premarket Tobacco Product Application (Section 910) if a new tobacco product does not meet the substantial equivalence criteria.[4]

Congress modeled the Section 905(j) substantial equivalence concept after Section 510(k) premarket notification for medical devices. In creating the Section 905(j) pathway, Congress recognized that not all tobacco products should or would require the extensive review the statute mandates for a Section 910 application. FDA acknowledged this when it recently stated, "[s]ubstantial equivalence is an alternative pathway to the new product submission."[5]

II. The Submission Seeks to Nullify the Section 905(j) Substantial Equivalence Pathway.

The Submission, if adopted by FDA, would minimize any meaningful distinction between the Section 905(j) substantial equivalence pathway and the premarket application pathway of Section 910. It would effectively write Section 905(j) out of the statute, in clear derogation of Congress's intent.

Below we address some of the specific points raised in the Submission.

A. The Submission Negates Section 905(j) Review.

The Submission suggests that the only tobacco product eligible for "same characteristics" review under Section 905(j) would be one that was exactly the same as a predicate product but with a

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[3] The FSTPCA defines characteristics as "the materials, ingredients, design, composition, heating source, or other features of a tobacco product."

[4] A manufacturer can also seek approval for a modified risk tobacco product claim for a reduced harm tobacco product (Section 911).

[5] *See* comments by Cristi Stark on the April 2013 FDA Tobacco Compliance Webinar "Substantial Equivalence: An Update."

different label or packaging. The Submission would also require manufacturers to submit research proving that the label or packaging change does not encourage initiation.[6] This interpretation contravenes Congressional intent.

Requiring that a product have the exact same characteristics as the predicate product would, by definition, mean that the product is not modified, and therefore is not "new." Such an interpretation would also render the "same characteristics" test meaningless, as any new or modified product that is different in any way from the predicate product would automatically be reviewed to determine whether the product raises "different questions of public health."[7] As described above, Congress created the Section 905(j) review process as an "alternative" path to bring new and modified tobacco products to the market for adult tobacco consumers.

The Submission incorrectly suggests that virtually any label or packaging change triggers a Section 905(j) or Section 910 review, on the theory that a label or packaging change transforms a tobacco product into a "new tobacco product" requiring premarket submission by a manufacturer. In creating a substantial equivalence pathway to bring tobacco products to market, Congress never intended to create a backhanded mechanism to require premarket approval for all label or packaging changes.

Any interpretation that a change in a label or packaging transforms a tobacco product into a "new tobacco product" is foreclosed by the text, context and purpose of the FSPTCA. The FSPTCA is clear that a manufacturer must obtain FDA authorization to market a "tobacco product" only if the product is a "new tobacco product," meaning either that it was not commercially marketed as of February 15, 2007, or is a "modification" of a "tobacco product" and commercially marketed after that date. The FSPTCA does not define "tobacco product" to include the label or packaging of the product. Indeed, the statute defines "label" and package" separately and as discrete items, not as "parts" of the article itself.[8] Moreover, the definition of "tobacco product" itself excludes any interpretation that the label or packaging are part of the "tobacco product."[9] Congress authorized such advance scrutiny of labeling only under Section 911 for modified risk products and under Section 903(b) by notice and comment rulemaking.

There is no statutory basis for the Submission's suggestion that FDA's review of a label or packaging change under Section 905(j) would need to take "into account the impact of its name

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[6] *See* page 35 of *"Comments in Response to Submissions of Other Parties on Demonstrating Substantial Equivalence for Tobacco Products"* which states: "Contrary to the arguments made by the tobacco product manufacturers, the requirement that characteristics be 'the same' does not render the standard meaningless. A product that is physically the same as a predicate product maybe rebranded with a new name. As the FDA has noted, offering the product with a new name renders it a new product, but the same physical characteristics would mean that it would qualify for review as 'substantially equivalent' taking into account the impact of its name change, new packaging and marketing in terms of appeal to non-tobacco users."

[7] *See* ALCS comments "*Comments on the Guidance for Industry and FDA Staff, Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products*," Docket No. FDA-2010-D-0635 (76 Fed. Reg. 789 (Jan. 6, 2011)) which we incorporate herein.

[8] The FSPTCA defines "label" as "a display of written, printed, or graphic matter upon the immediate container of any article." "Package" is defined as the "pack, box, carton, or container. . . [or] . . . wrapping . . . in which a tobacco product is offered for sale, sold, or otherwise distributed to consumers."

[9] The FSPTCA defines "tobacco product" as having three elements: (1) a "product" that (2) is "made or derived from tobacco" and (3) is "intended for human consumption."

change, new packaging and marketing in terms of appeal to non-tobacco users." In trying to inject this new test into every assessment of substantial equivalence, the Submission confuses statutory requirements for Section 910 with requirements for Section 905(j). The assessment of a new product application under Section 910 expressly includes consideration of "the increased or decreased likelihood that existing users of tobacco products will stop using such products," and "the increased or decreased likelihood that those who do not use tobacco products will start using such products." Congress did not include any such consideration of these behavioral effects in the streamlined assessment of substantial equivalence under Section 910(a), or in the reporting required under Section 905(j).[10]

To subject all changes in the label or name of a product to premarket review would also raise serious First Amendment concerns. The Submission argues that requiring a substantial equivalence review for a change in the name of a tobacco product does not implicate First Amendment interests, because the same review would be required if there was a physical change in the product. This argument is inconsistent with the intent of the statute. The name, label or packaging of a product communicates information. It is *speech* about a product. The Submission would regulate this speech by prohibiting it unless, and until, FDA finds the product itself and the associated speech of the name or other communications on the label or packaging substantially equivalent to those of a predecessor. The proponent of any such limitation on speech must, at the very least, satisfy the standards set forth in *Central Hudson Gas & Elec. Corp. v. Pub. Serv. Comm.*, 447 U.S. 557 (1980), governing restrictions on commercial speech. The Submission has to demonstrate that its proposed approach would directly advance a substantial government interest, and would be no more extensive than necessary to do so. The Submission did not attempt to make such a showing.

The Submission urges that the restraint on speech would operate as a "*prior* restraint" on protected speech. As a matter of logic, such a prohibition pending review of a label and packaging is no less of a prior restraint just because a similar review precedes some other change that does not involve speech. The law is clear that FDA may not adopt such a prior restraint of speech without providing clear standards as to when label changes trigger, and when they satisfy, the substantial equivalence test, nor without procedural safeguards sufficient to protect against the "danger of suppressing constitutionally protected speech."[11] As there are no statutory provisions here permitting such limitations on speech, Congress included no clear standards or procedural protections, and FDA has provided none.[12]

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[10] A well-accepted canon of statutory interpretation is that "where 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." *Keene Corp. v. United States*, 508 U.S. 200, 208 (1993) (quoting *Russello v. United States*, 464 U.S. 16, 23 (1983)). See also *Bailey v. United States*, 516 U.S. 137, 146 (1995) (distinction in one provision between "used" and "intended to be used" creates implications that related provision's reliance on "use" alone refers to actual and not intended use); *Bates v. United States*, 522 U.S. 23, 29 (1997) (inclusion of "intent to defraud" language in one provision and exclusion in a parallel provision indicated intent to defraud was not an element of the offense of knowingly and willingly misappropriating student loan funds).

[11] *Freedman v. Maryland*, 380 U.S. 51, 58 (1965) (A system of prior restraint "avoids constitutional infirmity only if it takes place under procedural safeguards designed to obviate the dangers of a censorship system."). Congress's sensitivity to this issue is reflected in the requirement in Section 903(b) that any requirement for prior approval of label statements be established by regulation only after notice-and-comment procedures.

[12] In previous submissions, we have raised additional concerns with FDA about its interpretation regarding packaging variations and its relevance to substantial equivalence evaluations. These concerns include the fact that FDA's

B. The Submission Incorrectly Rules Out Valid Predicates for the Substantial Equivalence Analysis.

The Submission would further impede Congressional intent by limiting those products that could serve as predicate tobacco products for the purposes of Section 905(j) review.[13]

The Submission's assertion that a tobacco product must be found substantially equivalent to a single predicate product conflicts with previous FDA statements.[14] FDA's August 2012 webinar titled "*Reports on Substantial Equivalence (905(j)(1)(A)(i) Reports): An Update*" clearly stated that multiple predicate products are acceptable for Section 905(j) submissions.[15] FDA's statement aligns with how the Agency treats substantial equivalence for other regulated industries.

C. The Submission Incorrectly Includes HPHCs in the Substantial Equivalence Analysis.

The Submission incorrectly states that comparisons of harmful or potentially harmful constituents ("HPHCs") or smoke constituents must be part of the substantial equivalence process.[16] As stated in our February 8, 2011 filing, for the purposes of defining substantial equivalence, "the term 'characteristics' means the materials ingredients, design, composition, heating source, or other features of a tobacco product."[17] It does not include "constituents." When Congress wanted to address "constituents" in the FSPTCA, it did so explicitly (*e.g.*, the establishment and publishing of a HPHC list under Section 904(d) & (e); manufacturer testing and reporting of tobacco product constituents under regulations to be promulgated by FDA under Section 915). Congress did not include constituents in the context of substantial equivalence reports, meaning that Congress did not intend to require comparison of constituents in a 905(j) submission. The timing of key requirements within the Act also supports this point. Congress required substantial equivalence reports by March 22, 2011, almost a full year before the deadline Congress imposed for FDA to identify and publish its list of HPHCs, by April 1, 2012.

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interpretation is articulated only in draft guidance documents that are marked "not for implementation," and FDA has not yet finalized the documents or responded to the comments submitted. We also note that CTP's interpretation is inconsistent with its previous statements in its November 2009 *Guidance for Industry: Registration and Product Listing for Owners and Operators of Domestic Tobacco Product Establishments*[12] and November 2009 *Guidance for Industry: Listing of Ingredients in Tobacco Products*[12] and is internally inconsistent within its September 2011 *Draft Guidance for Industry and FDA Staff: Demonstrating the Substantial Equivalence of a New Tobacco Product: Responses to Frequently Asked Questions*. We attach our November 8, 2011 submission to FDA which addresses all these issues in greater depth.

[13] FDA has defined a predicate product *as "one that was commercially marketed (other than in a test market) as of February 15, 2007 or a product previously found to be substantially equivalent by the FDA and in compliance with the requirements of the FD&C Act."*

[14] *See* discussion beginning on page 50 of *"Comments in Response to Submissions of Other Parties on Demonstrating Substantial Equivalence for Tobacco Products."*

[15] *See* webinar slide 23 "Predicate Product" which states "Multiple predicates allowed."

[16] *See* discussion beginning on page 35 of *"Comments in Response to Submissions of Other Parties on Demonstrating Substantial Equivalence for Tobacco Products."*

[17] 21 U.S.C. § 387(a)(3).

Further, it is highly unlikely that cigarettes and smokeless tobacco products on the market on or before February 15, 2007, still exist, let alone in quantities sufficient to satisfy FDA's future testing requirements. The fact that manufacturers did not conduct testing against an as-yet-to-be-defined constituent list or that manufacturers do not have sufficient quantity to conduct such tests more than six years later should not -- and cannot -- foreclose the use of predicate products as the Submission suggests.[18]

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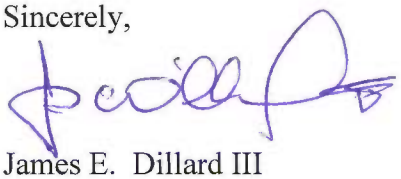
We appreciate the opportunity to share again our perspective with FDA on these important topics. As always, we would be happy to discuss further this response with FDA.

Sincerely,



James E. Dillard III

[18] *See* page 75 of *"Comments in Response to Submissions of Other Parties on Demonstrating Substantial Equivalence for Tobacco Products"* which states: "Products as to which insufficient samples exist to permit adequate testing cannot be predicate products."

Altria Client Services

James E. Dillard III
Senior Vice President
Regulatory Affairs

November 8, 2011

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. FDA-2011-D-0147 (76 Fed. Reg. 55,927 (Sept. 9, 2011)) – Comments on the "Draft Guidance for Industry and FDA Staff: Demonstrating the Substantial Equivalence of a New Tobacco Product: Responses to Frequently Asked Questions"

Altria Client Services ("ALCS") Inc., on behalf of Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC"),[1] submits these comments on the above-captioned draft frequently asked questions document ("Draft FAQ").

First, the Draft FAQ inappropriately announces for the first time FDA's interpretations of key statutory terms. While FAQ documents can be useful in responding to common questions, they should not be used to advance interpretations of key statutory terms or attempt to establish new legal norms.[2]

Second, the Draft FAQ contains serious substantive flaws. It sets forth, without adequate explanation or support, incorrect interpretations of the Family Smoking Prevention and Tobacco Control Act ("FSPTCA"); raises serious constitutional issues; and reflects policy judgments that merit reconsideration. As discussed in greater detail below, in its Final Guidance FDA should:

- delete any suggestion that the definition of "tobacco product" includes the product's label or packaging and acknowledge that a substantial equivalence report or a 910(b) submission is not required based on a label or packaging change that does not modify the product itself;

[1] PM USA and USSTC are wholly-owned subsidiaries of Altria Group, Inc. ALCS provides certain services, including regulatory affairs, to the Altria family of companies. "We" and "our" are used throughout these comments to refer collectively to PM USA and USSTC.

[2] *See* 21 C.F.R. § 10.115(d). An FAQ document by its very nature is not reasonably expected to include new regulatory requirements or novel statutory interpretations, and it is therefore less likely to be among the key resources stakeholders consult in assessing their compliance responsibilities.

Altria Client Services Inc.
2325 Bells Road
Richmond, Virginia 23234
(804) 335-2679
James.E.Dillard@altria.com

- confirm that a change in the name of a tobacco product is not a modification of the tobacco product and does not require a substantial equivalence report or a 910(b) submission;

- confirm that actions that do not change the finished tobacco product, including (1) tightening the range for a tobacco product additive, (2) changing processing aids, or (3) ensuring product consistency, are not modifications of the tobacco product and do not require a substantial equivalence report or a 910(b) submission;

- provide guidance regarding the level of specificity needed in substantial equivalence reports regarding tobacco product additives; and

- delete newly stated requirements that substantial equivalence reports include reports on harmful or potentially harmful constituents and environmental assessments.

I. The Agency Should Delete From The Draft FAQ Any Suggestion That The Statutory Definition Of "Tobacco Product" Includes The Product's Label Or Packaging And Acknowledge That A Substantial Equivalence Report Or Section 910(b) Submission Is Not Required Based On A Label Or Packaging Change That Does Not Modify The Product Itself.

The Draft FAQ asserts, without explanation or support, that "[t]he label and packaging is part of a tobacco product."[3] The Draft FAQ thus concludes that any change to the label or packaging of a tobacco product that occurs after February 15, 2007 makes that product a "new tobacco product" subject to the requirements of Sections 905(j) and 910(b).[4] However, that interpretation is foreclosed by the text, context and purpose of the statute. Furthermore, the Draft FAQ violates administrative law principles,[5] represents a clear break from FDA's previous statements

[3] Draft FAQ § II; *see id.* § II(A) ("The label and packaging of a tobacco product is considered a 'part' of that product.").

[4] *Id.* § II(A), FAQ1 ("[W]e do not intend to enforce the premarket requirements of sections 905(j) and 910 ... for modifications to product packaging or labels to remove the descriptors 'light', 'mild', or 'low' or similar descriptors to comply with section 911 ...."); *id.* at FAQ2 ("We do not intend to enforce the premarket requirements of sections 905(j) and 910 ... for a tobacco product that was commercially marketed in the United States on February 15, 2007, and that had no modifications ... other than to comply with the graphic warning requirements of section 201 ...."); *id.* at FAQ3 ("[If] the package was changed from a soft pack to a hard pack (or from a hard pack to a soft pack) after February 15, 2007, and this change did not modify the tobacco product in any other way (e.g., a change in moisture content, shelf life, ingredient composition, nicotine delivery, harmful/potentially harmful constituents), and no other modifications were made ... then we do not intend to enforce the premarket requirements of sections 905(j) and 910 ...."); *id.* at FAQ4 ("[If] a modification to font size, ink color, or background color was made to the packaging or labels after February 15, 2007 and no other modifications were made to the tobacco product after February 15, 2007, then we do not intend to enforce the premarket requirements of sections 905(j) and 910 ... for this type of modification, provided the modification does not raise different questions of public health ... and you are in compliance with all other statutory labeling and packaging requirements ....").

[5] The lack of explanation provides a separate ground on which to conclude that the interpretation in the document is invalid. *See, e.g., Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983) (An agency must "articulate a satisfactory explanation for its action including a 'rational connection between the facts found and the choice made.'") (quoting *Burlington Truck Lines, Inc. v. United States*, 371 U.S. 156, 168 (1962)). There is yet another reason to reject the interpretation in the Draft Guidance: it imposes binding legal requirements without

regarding Sections 905(j) and 910,[6] and does not help achieve the legitimate policy goals underlying the statute, which are amply served by other provisions.

A. A Requirement That Manufacturers Make Premarket Submissions For Label and Packaging Changes Would Be Contrary To The Statute.

A label or packaging change does not transform a tobacco product into a "new tobacco product" that requires premarket submissions by a manufacturer. Under the FSPTCA, a manufacturer must obtain FDA authorization to market a "tobacco product" only if the product is a "new tobacco product," meaning either that it was not commercially marketed as of February 15, 2007 or is a "modification" of a "tobacco product" and commercially marketed after that date.[7] After March 22, 2011, the manufacturer of a "new tobacco product" must submit either (1) a report under Section 905(j) seeking an order that the product is "substantially equivalent," or (2) an application for premarket authorization under Section 910.[8]

Due to the major consequences that flow from "new tobacco product" status, we have urged the Agency to confirm our interpretation of the statute.[9] FDA, however, has stated that further elaboration is unnecessary because the meaning of the statute is clear.[10] That certainly is correct in the statute's treatment of the label and packaging issues addressed in the Draft FAQ. However, the Draft FAQ position that altering a product's label or packaging transforms it into a "new tobacco product" by modifying "part" of the tobacco product has no basis in the statute and is utterly inconsistent with it.

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notice-and-comment rulemaking. *See Appalachian Power Co. v. EPA*, 208 F.3d 1015, 1024 (D.C. Cir. 2000); *Paralyzed Veterans of Am. v. D.C. Arena L.P.*, 117 F.3rd 579, 588 (D.C. Cir. 1997).

[6] The definitions FDA set out in its guidance on demonstrating substantial equivalence tracked the statutory language and gave no indication that FDA would view a product's name, label, or packaging to be part of the tobacco product itself. *See* FDA Guidance, *Guidance for Industry and Food and Drug Administration Staff; Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products* (Jan. 5, 2011) at 4, *available at* http://1.usa.gov/pCVt43 (hereinafter, "905(j) Guidance"). The Agency adopted the same definitions in its newly released guidance on premarket review applications under Section 910. *See* FDA Draft Guidance, *Guidance for Industry; Applications for Premarket Review of New Tobacco Products*, at 3 (Sept. 2011), *available at* http://1.usa.gov/pCVt43.

[7] 21 U.S.C. § 387(a)(1).

[8] *See Id.* §§ 387e(j)(1), 387j(a)(2). *See also* 905(j) Guidance at 5 (explaining that the manufacturer of a tobacco product introduced after February 15, 2007, and prior to March 22, 2011, and who submits a report under Section 905(j) prior to March 23, 2011, may continue to market the product unless or until FDA issues an order that the product is not substantially equivalent). In addition, FDA promulgated regulations describing the process for exempting minor changes in tobacco additives from the premarket review requirements. *See* 21 C.F.R. Pt. 1107.

[9] ALCS, Comments dated February 8, 2011, Docket ID No. FDA-2010-D-0635-0005, at 3, *available at* http://1.usa.gov/pwbTbr (hereinafter, "905(j) Comments"); *see also* ALCS, Comments dated March 22, 2011, Docket ID No. FDA-2010-N-0646-0011, at 1 ("We reiterate that there are numerous sources of variability inherent in tobacco products that should not constitute a 'modification.'"), *available at* http://1.usa.gov/nwfDPk.

[10] *See* 76 Fed. Reg. 38,961, 38,962 (July 5, 2011) ("FDA disagrees with the suggestion in the comments that the term 'new tobacco product' has not been sufficiently defined" in the statute.).

1. *The label and packaging of a tobacco product are not "part" of the tobacco product.*

The Agency's assertion that the label and packaging of a tobacco product are "part" of the tobacco product is inconsistent with the statutory scheme under which FDA operates. An article in interstate commerce is under FDA's jurisdiction if it meets the statutory definition of "food," "drug," "device," "cosmetic," "animal feed," "dietary supplement," or "tobacco product."[11] The statute does not define any of those terms to include the label or packaging of the article.

To the contrary, the statute defines "label" and "package" separately. Both definitions treat these things as discrete items, and not as "parts" of the article itself. "Label" is defined as "a display of written, printed, or graphic matter *upon the immediate container of any article*,"[12] thus making clear that a label is something affixed to the container in which an article is sold, not part of the article itself. Similarly, "package" is defined as the "pack, box, carton, or container … [or] wrapping … *in which a tobacco product* is offered for sale, sold, or otherwise distributed to consumers."[13] This obviously means that a package is external to, and not a part of, the tobacco product.[14] Both definitions preclude the Agency's interpretation in the Draft FAQ.

Moreover, the definition of "tobacco product" itself precludes the Agency's interpretation. The statute defines a "tobacco product" as having three elements: (1) a "product" that (2) is "made or derived from tobacco" and (3) is "intended for human consumption."[15] All three elements must exist to meet the definition, because the definition is conjunctive. Applying this definition makes clear that labels and packaging are not "tobacco products" because they are neither "made or derived from tobacco" nor "intended for human consumption."

Further, the Agency's position is inconsistent with the plain meaning of the word "part"[16] because "part" is generally understood to refer to a portion or subdivision of a larger whole, not something external to it.[17] Thus, "parts" of a tobacco product must be portions of something made or derived from tobacco that is intended for human consumption.

Other definitions in the statute confirm the error of the Agency's reliance on the word "part." For example, the definition of "new tobacco product," includes "part" in a list of terms that refer

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[11] 21 U.S.C. §§ 321(f), 321(g)(1), 321(h), 321(i), 321(w), 321(ff)(3), 321(rr).

[12] *Id.* § 321(k) (emphasis added).

[13] *Id.* § 387(13) (emphasis added).

[14] "Package" is also defined under the Federal Cigarette Labeling and Advertising Act using almost identical wording but with reference to the sale of "cigarettes." 15 U.S.C. § 1332(4). Cigarettes are defined as the "roll of tobacco" itself and not the packaging. *Id.* § 1332(1). Congress, by using the same definition of package under the FSPTCA, is presumed to have intended for the provisions to be interpreted in parallel. *See, e.g.*, *Sullivan v. Stroop*, 496 U.S. 478 (1990).

[15] 21 U.S.C. § 321(rr)(1).

[16] Draft FAQ § II(A).

[17] *See* http://www.merriam-webster.com/dictionary/part (defining "part" as "a constituent member of a machine or other apparatus"); Webster's Third New International Dictionary (Unabridged) (1993) (defining "part" as "one of the equal or unequal portions into which something is or is regarded as divided").

to specific physical changes to the tobacco product,[18] and Section 904(a)(1) includes the phrase "other part" at the end of a list including tobacco, papers, and filters.[19] Under well-settled canons of statutory construction, the word "part" must draw its meaning from the terms around it and thus should be read to refer to a physical element of the tobacco product, such as tobacco, papers, or filters.[20] Similarly, the definition of "characteristics" demonstrates that Congress did not intend to make labels or packaging part of substantial equivalence review. "Characteristics" is defined to include "the materials, ingredients, design, composition, heating source, or other features of a tobacco product."[21] Labels and packaging cannot fit comfortably within that definition.[22]

Finally, at numerous other places in the statute, Congress indicated that a tobacco product's label and packaging are different from, rather than a "part" of, the product. For example, Section 902 contains separate provisions deeming a tobacco product adulterated based on the presence of any "poisonous or deleterious substance" in the product itself *or in its packaging*; and Section 301(qq) prohibits the creation of counterfeit tobacco products by placing an identification device such as a "label ... upon any tobacco product or container *or labeling thereof*."

2. The Draft FAQ Conflicts with the Basic Structure of the Statute.

The Draft FAQ conflicts with the basic structure of the statute, which provides FDA authority to regulate labels and packaging that is wholly separate from the regulation of new tobacco products. Under FDCA provisions applicable to other product categories, labels and packaging are regulated directly, not by implication. For example, FDA regulation of labels and packaging for drug products is based on the statute's general misbranding and new drug approval provisions.[23] The FSPTCA applies that same framework to tobacco products,[24] and absent contrary legislative intent, labels and packaging under the FSPTCA should be treated consistently.

For example, Section 905 requires every manufacturer to register its establishments with FDA and submit a listing of each tobacco product in commercial distribution. This submission

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[18] *See id.* § 387j(a)(1) ("change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient").

[19] 21 U.S.C. § 387d(a)(1) (a manufacturer must list all ingredients "added by the manufacturer to the *tobacco, paper, filter, or other part* of each tobacco product" (emphasis added)).

[20] *See, e.g., Wash. State Dep't of Soc. & Health Servs. v. Guardianship Estate of Keffeler*, 537 U.S. 371, 384 (2003) (canons of *ejusdem generis* and *noscitur a sociis* require that "general words are construed to embrace only objects similar to those enumerated by the specific words" enumerated in the same list) (internal quotation marks omitted); *see also United States v. Tinklenberg*, 131 S. Ct. 2007, 2019 (2011) (absent indication to the contrary, "[i]dentical words used in different parts of a statute are presumed to have the same meaning").

[21] 21 U.S.C. § 387j(a)(3)(B).

[22] Indeed, FDA itself implicitly recognized this difficulty when it provided guidance that the requirement to provide an ingredient list does not apply to "packaging differences that do not affect the characteristics of the product." FDA Guidance, *Guidance for Industry: Listing of Ingredients in Tobacco Products* § III(C) (Nov. 2009), *available at* http://1.usa.gov/pCVt43 (hereinafter "Listing Guidance").

[23] *See, e.g.*, 21 U.S.C. § 355(d)(7); 21 C.F.R. § 201.10.

[24] *See* 21 U.S.C. § 387c.

includes "a copy of all consumer information and other labeling for such tobacco product."[25] Section 911 authorizes FDA to review data and information relating to tobacco products "the label, labeling, or advertising of which represents" that the product presents a reduced risk or lower exposure to a substance.[26] And Section 903, the statute's misbranding provision, provides the Agency with ample tools to combat any potentially "false or misleading" statements, including names.[27] In light of these and other provisions, premarket review is simply unnecessary for changes to product labels or packaging.[28]

If the Agency's interpretation of "tobacco product" is designed to guard against the possibility that a change to a label or packaging could modify the product itself, that interpretation is unnecessary. The Agency's response to FAQ3 notes, for example, the possibility that a switch from a hard pack to a soft pack might lead to "a change in moisture content, shelf life, ingredient composition, [or] nicotine delivery." To the extent FDA has authority to require premarket review in such a case, it is not because the packaging has changed, but because there has been a change to the tobacco product. For example, "ingredients" are among the "modifications" expressly included in Section 910(a)(1)(B) and the characteristics intended to be included in substantial equivalence review.[29] There is no need for FDA to contort the definition of tobacco product to reach those situations.

Perhaps most tellingly, in Section 903(b), Congress expressly provided that FDA may "require prior approval of statements made on the label of a tobacco product"[30] only "by regulation"[31] issued "in accordance with chapter 5 of title 5, United States Code."[32] The Draft FAQ seeks effectively to "require prior approval of statements made on the label" – that is, to require prior FDA authorization of product names – without satisfying the clear and unambiguous requirement

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[25] *See* 21 U.S.C. § 321(m)(1) (the statutory term "labeling" includes "all labels and other written, printed or graphic matter … upon any article or any of its containers or wrappers"). FDA guidance states that "labeling is to be submitted as an exact, legible, full color copy." *See* FDA Guidance, *Guidance for Industry: Registration and Product Listing for Owners and Operators of Domestic Tobacco Product Establishments* (Nov. 2009), *available at* http://1.usa.gov/nDD9mU (hereinafter "Listing Guidance").

[26] *See* 21 U.S.C. § 387k(b).

[27] 21 U.S.C. § 387c(a); *cf.* 21 C.F.R. § 201.10 (regulating drug names in labeling).

[28] Significantly, Section 905(i)(3)(D) reflects a scheme in which FDA receives notification of labeling changes *after* they occur. 21 U.S.C. § 387e(i)(3)(D) (requiring the manufacturer to notify FDA of "[a]ny material change" in biannual updates). This mirrors the Agency's approach in other contexts. For example, FDA guidance regarding the labeling for OTC topical acne drug products states that "[l]abeling that is revised to meet the requirements of this rule should be submitted to FDA through the drug listing process." FDA Guidance, *Guidance for Industry: Topical Acne Drug Products for Over-the-Counter Human Use—Revision of Labeling and Classification of Benzoyl Peroxide as Safe and Effective; Small Entity Compliance Guide* (June 2011), *available at* http://1.usa.gov/pKrtrm.

[29] 21 U.S.C. §§ 387(j)(a)(1)(B), 387(a)(3)(B).

[30] *Id.* § 387c(b).

[31] *Id.*

[32] *Id.* § 387a(d).

that the Agency proceed through notice-and-comment rulemaking.[33] The Agency's use of Draft FAQ in this instance is contrary to law and invalid for this additional and independent reason.[34]

3. *Treating Labels and Packaging as "Part" of the Tobacco Product Leads to Unintended Results.*

The Agency's interpretation of "tobacco product" is flawed because it leads to unintended results.[35] For instance, Section 904(a)(1) requires a manufacturer to provide FDA a listing of all ingredients "added by the manufacturer to the tobacco, paper, filter, or other part of each tobacco product by brand and by quantity in each brand and subbrand." If the label and packaging were parts of the tobacco product, then a manufacturer would be required to submit a listing, by quantity, of all the ingredients added by the manufacturer to the label of its tobacco products. But it is clear that a "label" (a term that refers to "a display of written, printed, or graphic matter upon the immediate container of any article")[36] could never have "ingredients" to be listed.

The Draft FAQ itself recognizes that results not intended by Congress would follow if labels and packaging were part of the tobacco product. For example, label changes required by Section 911 (to remove descriptors) and Section 201 (to add graphic warnings) would trigger the need for premarket review.[37] To avoid this result, the Agency says it will exercise "enforcement discretion" to allow manufacturers to comply. The Agency also recognizes that its interpretation leads to the conclusion that modifications to font, ink, or color used on a tobacco product's label or packaging might transform it into a new tobacco product,[38] and it likewise relies upon enforcement discretion to the extent those changes do not raise "different questions of public health." As a legal matter, FDA cannot cure an incorrect statutory interpretation by invoking enforcement discretion. Doing so is also bad policy because it blurs the line between lawful and prohibited conduct.

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[33] Even if FDA had proceeded by regulation as described in Section 903(b), it could not have required premarket review of product names under Sections 905(j) and 910(b) because, as shown above, that interpretation is unambiguously foreclosed by other statutory provisions and the statutory context and purpose.

[34] The notion that label and packaging changes trigger premarket review under Sections 905(j) and 910(b) also cannot be reconciled with Title II of the FSPTCA, which includes specific amendments addressing many aspects of product labels. Title II delimits the scope of FDA's ability to regulate the content of product labels and also reflects Congress's intention not to empower FDA to regulate the content of labels indiscriminately. *See, e.g.*, 15 U.S.C. § 1333 (specifying warning content and format for cigarettes).

[35] *Cf. Nixon v. Missouri Mun. League*, 541 U.S. 125, 138 (2004) (explaining canon against "'construe[ing] a statute in a manner that leads to absurd or futile results'").

[36] 21 U.S.C. § 321(k).

[37] Draft FAQ § II(A), FAQ1 and FAQ2.

[38] *Id.* § II(A), FAQ4

II. FDA Should Confirm That A Product's Name Is Not "Part" Of A Tobacco Product, And That Name Changes Do Not Require Substantial Equivalence Reports or Section 910(b) Submissions.

In the Draft FAQ the Agency incorrectly asserts that any change to the name of a product after February 15, 2007 makes that product a "new tobacco product" subject to the requirements of Sections 905(j) and 910(b).[39] Nothing in the FSPTCA supports that construction. As discussed above, the word "part" must be understood to refer to a *physical* element within the tobacco product;[40] a name does not qualify. Moreover, the structure of the statute precludes construing labels and packaging (and thus, the names printed on them) to be parts of the tobacco product.[41] Likewise, there is no need to depart from the unambiguous text with respect to names.

Congress knew how to refer to product names when that was its intention. For example, Section 904 contains multiple reporting requirements—such as reporting of ingredient, nicotine, and constituent information—that require submissions to be made on a brand and subbrand basis.[42] Section 915 likewise requires the testing and reporting of constituents, ingredients, and additives for each brand and subbrand.[43] Section 301(qq) prohibits the sale of a tobacco product that misrepresents its name as that of another.[44] In addition, the relevant provisions specifically use "brand name" and related terms when Congress intended for FDA to regulate these commercial designations. There is no comparable reference to names in the definition of "tobacco product" or "new tobacco product."[45] Had Congress intended to regulate product names through these definitions, it would have said so explicitly.[46]

In addition, including a product's name in the definitions of tobacco product and new tobacco product would violate the First Amendment's Free Speech Clause. Brand names are protected as commercial speech.[47] An interpretation of the FSPTCA that would require manufacturers to obtain FDA authorization before changing the names of their products would impose a

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[39] In particular the Draft FAQ states that (1) a cigarette would be a new tobacco product "if the cigarette was marketed on February 15, 2007, but subsequently the name of the product was modified or changed," and (2) if a manufacturer markets a cigarette as "Brand X" on February 15, 2007, and, after that date, continues to market Brand X but also begins to market the identical cigarette under the additional name "Brand Y," then Brand Y "is a new tobacco product subject to the premarket review requirements."

[40] *Supra* § 1.

[41] *Supra* § 2.

[42] *See, e.g.*, 21 U.S.C. § 387d(a)(1). FDA guidance for Section 904 states that "[e]ach product for which an ingredient list is submitted is to be clearly and uniquely identified by its brand and subbrand, [as well as additional information] as needed to uniquely identify the brand and subbrand of the product." Listing Guidance § III(C)(2).

[43] 21 U.S.C. § 387o(b)(1).

[44] 21 U.S.C. § 331(qq).

[45] *E.g.*, 21 U.S.C. §§ 387(2), 387(6), 387o(b); 21 C.F.R. Part 1140.

[46] *See Whitman v. Am. Trucking Assns., Inc.*, 531 U.S. 457, 468 (2001) ("Congress . . . does not, one might say, hide elephants in mouseholes").

[47] *See, e.g., San Francisco Arts & Athletics v. United States Olympic Comm.*, 483 U.S. 522, 535 & 537 n.16 (1987) (the "Olympic" mark receives First Amendment protection as commercial speech); *Friedman v. Rogers*, 440 U.S. 1, 11 (1979) ("The use of trade names . . . is a form of commercial speech . . . .").

constitutionally suspect prior restraint.[48] Such restraints are impermissible absent procedural safeguards sufficient to protect against the "danger of suppressing constitutionally protected speech."[49]

The Draft FAQ, however, provides no information regarding the standards or procedures FDA would employ when evaluating name changes or additional names. Neither the Draft FAQ nor any other FDA pronouncement regarding Section 905(j) indicates how the Agency would intend to judge names or determine whether a "new" name is substantially equivalent. Such standardless discretion to allow or disallow otherwise lawful speech violates traditional principles of prior restraint under the First Amendment.[50]

A blanket prohibition on all new names that have not obtained FDA authorization—a process that could prevent a manufacturer from engaging in speech for a period of months or years (if the speech is allowed at all)—would also clearly violate the *Central Hudson* test for assessing the constitutionality of restrictions on commercial speech.[51] Such a prohibition would bar speech regarding lawful products and applies to all names without regard to whether they are misleading or not. Moreover, it is unnecessary to advance any governmental interest in ensuring that names comply with the provisions of the FSPTCA because, as explained above, other provisions of the statute provide FDA with the tools it needs to advance this interest in a less restrictive way.[52]

At the very least, the Agency's interpretation raises sufficiently grave constitutional questions that a reviewing court would construe the statute to exclude names from the definitions of "tobacco product" and "new tobacco product."[53] Because the interpretation proposed in the

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[48] *See, e.g.*, *Southeastern Promotions, Ltd. v. Conrad*, 420 U.S. 546, 558 (1975) ("Any system of prior restraint . . . comes to this Court bearing a heavy presumption against its constitutional validity.") (internal quotation marks omitted); *New York Magazine v. MTA*, 136 F.3d 123, 131-32 (2d Cir. 1998) (affirming injunction of prior restraint on commercial speech).

[49] *Freedman v. Maryland*, 380 U.S. 51, 58 (1965) (A system of prior restraint "avoids constitutional infirmity only if it takes place under procedural safeguards designed to obviate the dangers of a censorship system."). Congress's sensitivity to this issue is reflected in the requirement in Section 903(b) that any requirement for prior approval of label statements be established by regulation only after notice-and-comment procedures.

[50] *Shuttlesworth v. Birmingham*, 394 U.S. 147, 150-51 (1969) ("[A] law subjecting the exercise of First Amendment freedoms to the prior restraint of a license, without narrow, objective, and definite standards to guide the licensing authority, is unconstitutional."). In addition, the absence of a fixed deadline by which FDA must make a substantial equivalence determination weighs heavily against the constitutionality of the proposed interpretation. *Cf. Nutritional Health Alliance v. Shalala*, 144 F.3d 220, 228 (2d Cir. 1998) (upholding FDA review of dietary supplement labels on the basis of a statutory deadline for completion of such review).

[51] *Central Hudson Gas & Electric Corp. v. Public Service Commission*, 447 U.S. 557 (1980).

[52] For example, manufacturers could notify FDA of name changes by updating their ingredient submissions under Section 904, or through regular product listing submissions. *See supra* notes 28 and 42.

[53] As noted, the text, context, and structure of the statute unambiguously foreclose the interpretation in the Draft FAQ under which FDA could require a Section 905(j) or a Section 910(b) submission for a change to the label or packaging of a tobacco product. Even if the statute were ambiguous, however, the ambiguity would have to be resolved against the speech-restrictive interpretation under the avoidance canon. *Edward J. DeBartolo Corp. v. Fla. Gulf Coast Bldg. & Constr. Trades Council*, 485 U.S. 568, 575 (1988) ("[W]here an otherwise acceptable construction of a statute would raise serious constitutional problems, the Court will construe the statute to avoid such problems unless such construction is plainly contrary to the intent of Congress.").

Draft FAQ is plainly not required by the statute, (and, indeed is contrary to it), these constitutional infirmities must be avoided in the Final Guidance.

III. FDA Should Confirm That Actions That Do Not Change The Finished Tobacco Product Are Not Modifications Within The Meaning of 910(a)(1)(B) And Do Not Require A Substantial Equivalence Report Or A 910(b) Submission.

In a number of instances, the Draft FAQ indicates that manufacturer actions that do not change the finished tobacco product may nonetheless constitute "modifications" that require a substantial equivalence report or a 910(b) submission. As explained below, these statements are inconsistent with the statute, which imposes premarket review obligations only upon modifications "of a tobacco product."[54] These aspects of the Draft FAQ should therefore be removed from the Final Guidance.

A. FDA Should Affirm That Tightening The Range For A Tobacco Product Additive Is Not A Modification Within The Meaning of 910(a)(1)(B).

FDA should affirm that a manufacturer's decision to make the specification range for a product additive more precise, but still within the previously reported range, does not constitute a modification that would trigger premarket review. The Draft FAQ currently takes the opposite view. FDA's response to FAQ9 states that "[a]ny modification made to the level of an additive" would require premarket clearance. This interpretation is overbroad.

We agree that a change to a static specification (*e.g.*, from 0.003 to 0.005) or expanding a range specification for tobacco product additive (*e.g.*, from 0.003-0.005 to 0.003-0.007) will likely result in a modification to the finished product triggering the need for premarket review. Tightening the range for an additive (*e.g.*, from 0.003-0.005 to 0.003-0.004), however, is different. In such cases, the "new" product by definition will fall within the permissible range of the "old" product. FDA should clarify that, in such situations, the finished product is not modified such that it requires premarket clearance.

Otherwise, the Agency will use valuable resources reviewing substantial equivalence reports for products that have not actually been modified. Assuming the only change between two products is a narrowed range for an additive, the new and predicate products would necessarily share the same characteristics and thus be substantially equivalent.[55] In addition, requiring premarket review in these circumstances would discourage manufacturers from continuing to refine and improve their manufacturing processes and controls. FDA should avoid these problems by making clear in the Final Guidance that increasing the precision of an additive specification within a preexisting range does not constitute a modification of a tobacco product.[56]

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[54] 21 U.S.C. § 387j(a)(1)(B).

[55] 21 U.S.C. § 387j(a)(3)(A)(i).

[56] As we previously noted, FDA's support for the concept of "design space" in the pharmaceutical industry counsels against the view that increasing the precision of a specification range constitutes a product modification. *See* 905(j) Comments at n.11 ("'Working within the design space is not considered as a change. Movement out of the design space is considered to be a change and would normally initiate a regulatory postapproval change process.'" (quoting

B. A Change In A Processing Aid That Does Not Have An Identifiable Effect On The Tobacco Product Is Not A Modification Within The Meaning of 910(a)(1)(B).

The statutory definition of new tobacco product is only triggered by an actual "modification" of "a tobacco product."[57] The statute refers to "any modification (including a change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient)."[58] This statutory language clearly does not reach changes in manufacturing processes unless they result in an identifiable change to the product (or the components, parts, or constituents thereof).

Nevertheless, in response to Question 11, the Agency states that premarket review would be required if a supplier begins using a new processing aid for a subcomponent of a tobacco product even if any resulting change "is so minor that it is not even capable of being quantified in the finished product." The Agency's apparent reasoning is that even if no quantifiable change has been made to the finished product, the switch in a subcomponent processing aid "may" nevertheless "have an impact on other characteristics within the tobacco product."

The Agency's response reflects a flawed analysis that is inconsistent with the statute. If Congress had intended to require premarket review solely on the basis of a change in manufacturing process, it would have said so.[59] In the final guidance, FDA should clarify that, absent an identifiable change to the resulting product, there is no modification within the meaning of Section 910(a)(1)(B).[60]

FDA Guidance For Industry: Q8 Pharmaceutical Development, at 2 (May 2006), available at http://1.usa.gov/pJpK2N)).

[57] 21 U.S.C. § 387(a)(1)(B).

[58] *Id.*

[59] Other provisions of the FSPTCA support this conclusion. "[R]aw materials used in manufacturing a component, part, or accessory of a tobacco product" are excluded from the statutory definition of "tobacco product." *See* 21 U.S.C. § 321(rr)(1). A change in raw material therefore cannot amount to a modification of a tobacco product unless the change results in identifiable alteration of the finished product. The same logic should apply to manufacturing processes, which are not mentioned in the tobacco product definition and are regulated under different provisions of the FSPTCA that direct FDA to establish manufacturing controls through regulations. *See* 21 U.S.C. § 387f(e)(1)(A). Moreover, in light of the explicit statutory requirement to include information about the manufacturing process in a Section 910 application, *see id.* § 387j(b)(1)(C), the absence of any specific requirement to include that information in a substantial equivalence report indicates that Congress did not view a change in the manufacturing process alone as triggering premarket review.

[60] At a minimum, FDA should clarify that the *possibility* of an unquantifiable change is not a modification. The response to FAQ11 justifies its conclusion by noting that a change in processing aid "*may* have an impact on other characteristics within the tobacco product (e.g., *may* alter chemical reactions and create a new ingredient, additive, or constituent)." (Emphases added). Such speculation is inconsistent with the premise of the question (that there was no quantifiable change to the finished product) and, in all events, is no basis for expanding the scope of the FSPTCA's premarket review requirements.

C. Adjustments Made To Ensure Product Consistency Are Not Modifications Within The Meaning Of 910(a)(1)(B).

We previously asked the Agency to confirm that the frequent adjustments a manufacturer must make to maintain consistent product characteristics are not "modifications" within the meaning of Section 910(a)(1)(B).[61] FAQ8 provides a partial response by stating that FDA will use its "enforcement discretion" to allow "tobacco blending changes required to address the natural variation of tobacco." While we agree that consistency-maintaining changes are permissible, we do not agree that such changes implicate FDA's enforcement discretion. Rather, adjustments made by a manufacturer to maintain consistent product characteristics are not modifications within the meaning of Section 910(a)(1)(B). In the final guidance, FDA should acknowledge that Section 910 does not apply in this scenario.

IV. FDA Should Provide Guidance Regarding The Level Of Specificity Needed In Substantial Equivalence Reports Regarding Tobacco Product Additives.

In response to requests that FDA identify the level of specificity required for 905(j) reports when reporting the amounts and levels of additives in products, FAQ 13 says that it is the manufacturer's responsibility to "present the data in a form that will provide the basis for" substantial equivalence review. It is unrealistic to expect stakeholders to predict in advance the level of the specificity that the Agency will require. Moreover, the Agency's failure to provide more specificity could lead to inconsistent applications from manufacturers and to inconsistent reviews within the Center for Tobacco Products. FDA should, therefore, provide a substantive response to FAQ13 and reopen public comment to provide an opportunity for meaningful public participation.

V. New Requirements For Substantial Equivalence Reporting Should Not Be Added in This FAQ Document.

A. Substantial Equivalence Reports Should Not Require Reporting On Harmful Or Potentially Harmful Constituents.

We urge the Agency to reconsider its response to FAQ17 that manufacturers "provide information regarding harmful or potentially harmful constituents ("HPHC") as appropriate to demonstrate that the new tobacco product is substantially equivalent to the predicate product."[62] In its Final Guidance the Agency should state that HPHC data will not be required in Section 905(j) reports.

Any requirement that substantial equivalence reports contain HPHC data would be contrary to the FSPTCA. Substantial equivalence review is based on a comparison of the "characteristics"

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[61] 905(j) Comments at 3.

[62] ALCS previously provided comments on the 905(j) Guidance stating that substantial equivalence review should not require HPHC reporting. *See* 905(j) Comments at 7-8; *cf.* 905(j) Guidance at 11 ("For all products, you should report levels of all HPHC in tabular format, with a side-by-side comparison with the predicate tobacco product and, where applicable, to a grandfathered tobacco product.").

of the new and predicate products.[63] The statute defines the term "characteristics" to mean "the materials, ingredients, design, composition, heating source, or other features of a tobacco product."[64] Constituents are thus not included in the list of characteristics that are part of substantial equivalence review. Nor can the trailing phrase "other features of a tobacco product" be read to include constituents. The FSPTCA specifically defines the term "smoke constituent,"[65] and constituents are expressly regulated throughout the statute.[66] Moreover, the different schedules for reporting ingredients and constituents make clear that the statutory term "ingredient" does not include constituents.[67] Had Congress meant to include constituents as part of substantial equivalence review, it would have done so expressly.

The Agency's position that substantial equivalence reports must contain HPHC data also raise practical difficulties that further indicate that Congress did not intend this requirement. Manufacturers were required to file initial 905(j) reports by March 2011, well before the Agency's April 2012 deadline to publish a list of HPHCs and the April 2013 deadline to promulgate regulations for testing and reporting.[68] Obviously, manufacturers cannot test against a list that does not exist. Moreover, the current pending 905(j) reports generally rely on tobacco products that were on the market as of February 15, 2007 as predicates for the substantial equivalence comparison. Given the passage of time, it is unlikely that cigarettes and smokeless tobacco products that were on the market as of February 15, 2007 still exist in quantities sufficient to enable the testing necessary to generate HPHC data for most, if not all, predicate products.[69]

Thus, a requirement that HPHC reporting be included in 905(j) reports is contrary to law and creates substantial practical difficulties. The Agency's Final Guidance should make clear that reporting on HPHCs is not required as part of substantial equivalence review.

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[63] *See* 21 U.S.C. § 387j(a)(3)(A).

[64] 21 U.S.C. § 387j(a)(3)(B).

[65] 21 U.S.C. § 387(22).

[66] *See, e.g.*, 21 U.S.C. §§ 387g(a)(4)(A)(ii), 387g(a)(4)(B)(i) (FDA has authority to promulgate tobacco product standards addressing constituents); *id.* § 387o(b)(1) (directing FDA to promulgate regulations for the "testing and reporting of tobacco product constituents, ingredients, and additives"). *See also* Altria Client Services, Inc., R.J. Reynolds Tobacco Co., and Lorillard Tobacco Company, Comments dated October 11, 2011, Docket ID No. FDA-2011-N-0271, at 1 & n.5 (hereinafter, "2011 HPHC Comments").

[67] *See* 21 U.S.C. §§ 387d(a)(1), 387d(a)(3); *see also id.* §§ 387g(a)(1)(A), 387g(a)(3)(B)(ii) (indicating that "constituents" and "additives" are conceptually distinct categories under the FSPTCA).

[68] *See* 21 U.S.C. §§ 387d(d)(1), 387d(e), 387(o)(b)(1).

[69] For a fuller discussion related to HPHCs, we refer the Agency to previous submissions in which we discuss our experience with tobacco constituent testing and evaluation of such data as part of our ingredient testing program. *See* Altria Client Services, Inc., Comments dated August 23, 2010, Docket ID No. FDA-2010-D-0281-0003.1, *available at* http://1.usa.gov/oLwObl; *see also* 2011 HPHC Comments.

B. FDA Should Exempt Substantial Equivalence Reports From The Environmental Assessment Requirement.

In response to Question 18, FDA states that all Section 905(j) reports must include environmental assessments under 21 C.F.R. § 25.15(a). This requirement is new and was not stated or implied in the final 905(j) Guidance FDA published in January 2011.[70] In fact, this new requirement was not announced until almost six months *after* manufacturers submitted their initial 905(j) reports in March 2011. This new requirement is thus procedurally improper with respect to reports previously submitted by manufacturers and, at a minimum, the Agency should clarify that this newly stated requirement does not apply to them. It would make no sense to apply the requirement to these reports because they pertained to products that were on the market in March 2011. The intent of these reports is to obtain an agency determination that such products are substantially equivalent to one or more predicate products that were on the market on or before February 15, 2007. In other words, the only requested agency action is to maintain the status quo—not the type of agency action that requires an environmental review.

More fundamentally, substantial equivalence reports for tobacco products are not included among the agency actions for which an environmental assessment is necessary under 21 C.F.R. § 25.20. To the extent the Agency wishes to amend Part 25 to include tobacco products, it must do so through formal notice and comment rulemaking.[71]

Requiring environmental assessments for substantial equivalence is also substantively unjustified, and FDA should establish a categorical exemption from the environmental assessment for all 905(j) reports. Essentially every other FDA-regulated industry benefits from a categorical exemption for agency actions similar to substantial equivalence determinations. In each of these industries, FDA has taken the position that environmental assessments are not necessary if the requested agency action does not increase overall use of the product type.[72] Section 905(j) reports seek only an agency determination that a given product is equivalent to, and thus likely to compete with or replace, products that already are or have been on the market. Therefore, 905(j) reports should be categorically exempt from the environmental assessment requirement.

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[70] The Preface of the 905(j) Guidance states that the Agency's intent in promulgating the guidance was to clarify "FDA's expectations regarding 905(j) reports" in "sufficient time" for stakeholders to prepare submissions prior to March 2011. The guidance specifically represented that it included a list of "the information [FDA] believes a typical 905(j) report may need to include." 905(j) Guidance at 7.

[71] When the Agency has expanded the scope of other preexisting regulations to include tobacco products, it has done so by amendment to the regulation. *See, e.g.*, 76 Fed. Reg. 20,901 (Apr. 14, 2011). From both a consistency and an administrative law perspective, *see supra* note 5. FDA should take the same approach here and undertake notice-and-comment rulemaking before substantively amending Part 25.

[72] *See, e.g.*, 21 C.F.R. §§ 25.15(c) (agency actions that "do not significantly affect the quality of the human environment" are ordinarily excluded), 25.30(k) (labeling changes that do not affect levels of use); 25.31(a) (new drug approval applications that will not "increase the use of the active moiety"), 25.31(g) (bioequivalence determinations for human drugs and comparability determinations for biologics), 25.32(f) (determinations that food is GRAS if it is already marketed for the proposed use), 25.33(a) (new animal drug approval applications that will not increase use), 25.34(b) (device classification determinations that will not increase or expand the use of the device), 25.34(d) (class III medical device approvals if the device is of the same type and use of a previously approved device), 25.34(f) (restricted device regulations that will not expand or increase the use of the product).

* * * * *

We appreciate the opportunity to submit these comments and urge the Agency to revise the Draft FAQ as described above. We look forward to further opportunities to provide comments to the Agency as its thinking on substantial equivalence continues to evolve.

Sincerely,

James E. Dillard III

Altria
Altria Client Services

James E. Dillard III
Senior Vice President
Regulatory Affairs

February 18, 2014

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. FDA-2013-N-1588 (78 Fed. Reg. 76838 (December 19, 2013)) "Comments on Agency Information Collection Activities; Proposed Collection; Comment Request; Tobacco Products, Exemptions From Substantial Equivalence"

Altria Client Services Inc. ("ALCS"), on behalf of Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC"),[1] submits these comments in response to the above-referenced docket and December 19, 2013, Federal Register notice (the "Notice").[2] The Notice seeks input on FDA's collection of information regarding exemptions from substantial equivalence requirements for tobacco products under the Federal Food, Drug, and Cosmetic Act ("FDCA" or "the Act").

In the Notice, FDA seeks comments on "ways to enhance the quality, utility, and clarity of the information to be collected." These comments will cover two issues related to the clarity of the information to be collected. First, PM USA and USSTC again urge FDA to clarify and revise its rule for exemptions from substantial equivalence requirements in several ways as set forth in our previously submitted comments on the proposed rule "Tobacco Products, Exemption from Substantial Equivalence Requirements" and "Guidance for Industry and FDA Staff, Section 905(j) Reports: Demonstrating Substantial

[1] PM USA and USSTC are wholly-owned subsidiaries of Altria Group, Inc. ALCS provides certain services, including regulatory affairs, to the Altria family of companies. "We" and "our" are used throughout these comments to refer collectively to PM USA and USSTC.
[2] 78 Fed. Reg. 76838 (Dec. 19, 2013).

Altria Client Services Inc.
2325 Bells Road
Richmond, Virginia 23234
(804) 335-2679
James.E.Dillard@altria.com

Equivalence for Tobacco Products" which are referenced and incorporated in these comments.[3] Second, PM USA and USSTC urge FDA to clarify that substantial equivalence exemptions for new tobacco products apply to minor modifications of any tobacco product that is lawfully marketed.

Also in the Notice, FDA seeks comments on "ways to minimize the burden of the collection of information on respondents . . .." To further this goal, PM USA and USSTC urge FDA to revise its National Environmental Policy Act (NEPA) implementing regulations to provide categorical exclusion regulations for actions related to substantial equivalence exemptions.

A. FDA Should Clarify and Revise its Rule on Exemptions from Substantial Equivalence Requirements to Enhance the Quality, Utility, and Clarity of the Information to be Collected

PM USA and USSTC previously filed comments on the proposed rule "Tobacco Products, Exemption from Substantial Equivalence Requirements" and "Guidance for Industry and FDA Staff, Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products" which are referenced and incorporated in these comments.[4] As stated in those comments, we again urge FDA to:

- clarify its definition of a "new tobacco product" and provide additional guidance about what constitutes a "modification;"
- eliminate any requirements regarding behavioral types of effects from the categories of data required for a substantial equivalence exemption; [5]
- establish a categorical exemption for a range of levels applicable to all similar products that include a particular additive for which the FDA grants an exemption request;
- establish a 90 day review period for exemption requests and to deem minor modifications notified;
- establish an exemption for additive modifications that are part or the result of blend maintenance;
- allow an exemption request to cover an entire category of products and allow for modifications within a requested range; and
- allow exemptions for non-additive modifications.

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[3] *See* Attachment A. Letter from James E. Dillard III to Division of Dockets Management re: Docket No. FDA-2010-N-0646 (76 Fed. Reg. 737 (Jan. 6, 2011)) "Tobacco Products, Exemptions from Substantial Equivalence Requirements" (Mar. 22, 2011); Letter from James E. Dillard III to Division of Dockets Management re: Docket No. FDA-2010-D-0635 (76 Fed. Reg. 789 (Jan. 6, 2011)) – Comments on the "Guidance for Industry and FDA Staff, Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products" (Feb. 8, 2011).

[4] *Id.*

[5] *See* 21 C.F.R. § 1107.1(b)(7) (requiring a certification summarizing the evidence and reasons why "the modification does not increase the tobacco product's appeal to or use by minors, toxicity, addictiveness, or abuse liability" to support a substantial equivalence exemption request).

B. Substantial Equivalence Exemptions Apply to Provisional Tobacco Products

A subset of new tobacco products are certain post-February 15, 2007, products introduced to the market in the statutory period after February 15, 2007, and before March 22, 2011. Referred to as "provisional tobacco products," these products required submission of a substantial equivalence report by March 22, 2011.[6] A premarket approval application and order are not required for a provisional tobacco product to be sold unless (1) a substantial equivalence report was not submitted to FDA by the statutory deadline, or (2) the FDA issues an order that the product is not substantially equivalent.[7] Provisional tobacco products meeting these criteria are lawfully marketed tobacco products.

Notwithstanding the statutory text, FDA has communicated to PM USA its erroneous position that a substantial equivalence exemption is not permitted for a provisional tobacco product unless FDA has issued a finding of substantial equivalence for that product. Stated another way, it is the agency's position that manufacturers may only submit substantial equivalence exemption requests for minor modifications to "grandfathered products" or products that already have been found substantially equivalent to an appropriate predicate product. FDA's interpretation is clearly incorrect.

1. Under the Act, Congress directly addressed the application of substantial equivalence exemptions to provisional tobacco products.

The statutory provisions for substantial equivalence exemptions cover all lawfully marketed tobacco products, including provisional tobacco products. The plain language of the Act provides for a substantial equivalence exemption for "a modification of a tobacco product *that can be sold under this Act*."[8] Congress has unambiguously addressed whether the statutory provisions for substantial equivalence exemptions cover provisional tobacco products. Absent two circumstances (described above), provisional tobacco products "can be sold" to adult tobacco consumers.

Even if the statutory language were not clear, the legislative history of the Act confirms that the substantial equivalence exemption provision is intended to encompass all tobacco products that can be lawfully marketed under the Act. Congress rejected statutory language that could have limited the scope of products eligible for an exemption from substantial

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[6] FDCA § 905(j)(2); 21 U.S.C. § 387e(j)(2).

[7] FDCA § 910(a)(2)(B); 21 U.S.C. § 387j(a)(2)(B); *see also* FDA Guidance for Industry and FDA Staff – Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products (January 2011), *available at* http://www.fda.gov/TobaccoProducts/Labeling/TobaccoProductReviewEvaluation/NewTobaccoProductReviewandEvaluation/SubstantialEquivalence/default.htm.

[8] FDCA § 905(j)(3)(A)(1); 21 U.S.C. § 387e(j)(3)(A)(i) (emphasis added).

equivalence requirements. In a congressional bill introduced in 2007, a provision would have limited the exemption to a minor modification of "a tobacco product *authorized for sale* under this Act."[10] The phrase "authorized for sale," which presupposes an affirmative authorization beyond what is required for provisional tobacco products, was replaced with the phrase "that can be sold" during the markup of the bill in 2008. The bill was later reintroduced with the same language and passed by Congress in 2009 as the Act.

Additionally, if Congress had intended to limit application of the substantial equivalence exemption, it would have done so by the express terms of the provision, as it did in other statutory provisions in the Act.[11] For example, if Congress had intended to exclude provisional tobacco products from consideration for substantial equivalence exemptions it would have drafted Section 905(j)(3)(i) to include language similar to that in Section 905(j)(1) limiting the scope and application of substantial equivalence reports.[12]

Finally, the Act must be read in the context of the entire statutory scheme.[13] The statutory scheme demonstrates that Congress did not intend to exclude provisional tobacco products from exemptions authorized by Section 905(j)(3). To determine that Section 905(j)(3) excludes provisional tobacco products from its scope requires a conclusion that provisional tobacco products are unlawful under the Act. That conclusion is contrary to the Act which, as noted, includes specific provisions establishing the legal marketing of a provisional tobacco product in the absence of an FDA order that the product is not substantially equivalent.[14]

2. Even if the substantial equivalence exemptions provision is ambiguous, exclusion of provisional tobacco products from exemptions is an impermissible construction of the Act.

Not only does the plain language of the Act not exclude provisional tobacco products from substantial equivalence exemptions but FDA's own implementing regulations support the plain language of the Act and do not exclude provisional tobacco products. The implementing regulations provide:

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[10] *See* H.R. 11008, 110th Cong. (2007).

[11] *Franklin Nat'l Bank v. New York*, 347 U.S. 373, 378 (1954) (finding "no indication that Congress intended to make this phase of national banking subject to local restrictions, as it has done by express language in several other instances").

[12] *See* FDCA § 905(j)(1)(A)(i); 21 U.S.C. § 387e(j)(1)(A)(i) ("a tobacco product commercially marketed (other than for test marketing) in the United States as of February 15, 2007, or to a tobacco product that the Secretary has previously determined, pursuant to subsection (a)(3) of section 910, is substantially equivalent and that is in compliance with the requirements of this Act.").

[13] *Catawba County N.C. v. EPA*, 571 F.3d 20, 35 (D.C. Cir. 2009) (even a textually ambiguous statute "may foreclose an agency's preferred interpretation . . . if its structure, legislative history, or purpose makes clear what its text leaves opaque"); *Sierra Club v. EPA*, 551 F.3d 1019, 1027 (D.C. Cir. 2008) ("*Chevron* step one analysis" entails "examin[ing] the meaning of certain words or phrases in context" and "exhaust[ing] the tradition tools of statutory construction").

[14] *See, e.g.*, FDCA §905(j)(2); 21 U.S.C. §387e(j)(2).

(1) Such modification would be a minor modification of a tobacco product that can be sold under the Federal Food, Drug, and Cosmetic Act (a legally marketed tobacco product).[15]

Despite the importance of defining an appropriate predicate product, the preambles to the proposed and final rules for substantial equivalence exemptions do not address the meaning or agency interpretation of "a product that can be sold under [Act]." Nevertheless, by the express terms of its own regulation, a legally marketed tobacco product may be considered for an exemption from the substantial equivalence requirements. The more limited interpretation -- that provisional tobacco products are excluded from the scope of the exemption -- results in the illogical conclusion that such products are not legally marketed products under the FDCA. Unless FDA has issued an order that it is not substantially equivalent, a provisional tobacco product can be sold under the Act. A minor modification relating to tobacco product additives renders it eligible for consideration for an exemption from substantial equivalence requirements.

C. Substantial Equivalence Exemptions Should be Categorically Excluded from NEPA.

The Notice also invites comments on "ways to minimize the burden of the collection of information on respondents . . .." PM USA and USSTC urge FDA to revise its National Environmental Policy Act (NEPA) implementing regulations to provide categorical exclusion regulations for actions related to substantial equivalence exemptions.

In Docket No. FDA-2013-N-1282: *National Environmental Policy Act; Environmental Assessments for Tobacco Products; Categorical Exclusions*, FDA proposes to amend 21 C.F.R. Part 25 to exclude certain classes of tobacco products-related actions from the requirement to prepare an environmental assessment or environmental impact statement. In its preamble to this proposed rule, the FDA provides a sound rationale for establishing these categorical exclusions that also applies to exemption requests. For example, in the preamble to the proposed rule FDA states that there are approximately 5,000 brands and subbrands currently on the market subject to its authority and, after reviewing 2011 Toxic Release Inventory National Analysis data, it concludes that the environmental effects of "keeping tobacco products on the market are individually and cumulatively trivial" when compared to total toxic releases from industrial manufacturing and existing environmental effects due to the use and disposal of tobacco products in the United States.[16] FDA estimates that it will receive exemption requests for 500 tobacco products each year that, by definition, will involve minor modifications to a fraction of the products on the market. Thus, the exemption requests will have a fraction of the environmental effect compared to those which FDA proposes to be subject to a categorical exclusion on the basis of their trivial impact on the environment.

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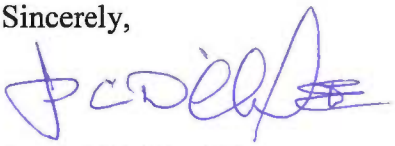
[15] *See* 21 C.F.R. §1107.1(a)(1).
[16] *Id.*

Revising 21 C.F.R. Section 1107.1(b)(9) and FDA's NEPA implementing regulations at 21 C.F.R. Part 25 to provide a categorical exclusion for exemption requests would reduce the number of environmental assessments (EAs) required by FDA. As a safeguard, FDA retains the authority to require an EA based on extraordinary circumstances for all actions that are subject to a categorical exclusion. Reducing the number of EAs to be submitted and reviewed would allow FDA to focus its attention on "proposed actions that are likely to have the potential to cause significant environmental effects . . ."[17] and would allow tobacco manufacturers to focus on other parts of the substantial equivalence exemption submission.

Conclusion

We appreciate the opportunity to submit these comments. We look forward to further opportunities to work with the FDA as it develops a process to establish exemptions from the substantial equivalence process and revise its NEPA implementing regulations to categorically exclude actions related to substantial equivalence exemptions.

Sincerely,



James E. Dillard III

Attachments

[17] 75 Fed. Reg. 75628 (Dec. 6, 2010).

Attachment A

Altria
Altria Client Services

James E. Dillard III
Senior Vice President
Regulatory Affairs
James.E.Dillard@altria.com

2325 Bells Road
Richmond, VA 23234
(804) 335-2679

March 22, 2011

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. FDA-2010-N-0646 (76 Fed. Reg. 737 (January 6, 2011))
"Tobacco Products, Exemptions from Substantial Equivalence Requirements"

Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC")[1] submit these comments on the above captioned proposed rule "Tobacco Products, Exemptions from Substantial Equivalence Requirements."

As the Agency finalizes the proposed rule, we reference and incorporate our previously filed comments to the "Guidance for Industry and FDA Staff, Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products."[2] We asked the Agency to clarify its definition of a "new tobacco product" and provide additional guidance about what constitutes a "modification." We reiterate that there are numerous sources of variability inherent in tobacco products that should not constitute a "modification." These include variations in manufacturing and differences in materials from lot-to-lot. Adjustments made in response to such variations that are necessary to maintain consistent product characteristics are also not properly considered product "modifications" under the Family Smoking Prevention and Tobacco Control Act ("the Act"). As such, these adjustments do not render a product a "new tobacco product" or require premarket review under Sections 905(j) or 910. We urge the Agency to comply with the statute as it finalizes the rule for the exemption process. If, however, the Agency does not exclude such adjustments, we believe it should consider such adjustments minor modifications exempt from substantial equivalence requirements.[3]

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[1] Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC") are wholly-owned subsidiaries of Altria Group, Inc. Altria Client Services ("ALCS") is making this submission on behalf of PM USA and USSTC. ALCS provides certain services, including regulatory affairs, to the Altria family of companies. "We" is used throughout to refer to PM USA and USSTC.

[2] *See* Attachment A.

[3] This suggestion assumes, for purposes of this submission and participation in the rulemaking process and without prejudice to the statutory interpretation noted above and in our prior comments, that such adjustments could be construed as modifications for purposes of implementing and enforcing the Act.

Congress established an exemption process in section 905(j) of the Act to provide an alternative, less burdensome process to filing a substantial equivalence report. FDA's proposed rule, however, is contrary to Congressional intent because the proposed rule imposes on both the Agency and manufacturers unnecessary and duplicative burdens. For example, the proposed rule requires a manufacturer to file an exemption request and, if the exemption is granted, to file a subsequent 90 day notification that the modification made to the product is covered by the granted exemption and is otherwise in compliance with the Act. These requirements can be met in the exemption request, thus eliminating an additional unnecessary filing. In addition, and as discussed below, the proposed rule conflicts with several provisions of the Act in conditioning exemptions on the submission of data that Congress intended to exclude from substantial equivalence determinations.

A. Analysis of Toxicity Data Should Be the Basis for Agency Decision-Making on Exemptions.

The development of tobacco regulations should be guided by science- and evidence-based decisions. As such, we support the proposed rule where it will ensure that exemption decisions are based on an analysis of changes in toxicity that could result from ingredient (used interchangeably here with "additive") changes or other minor modifications to tobacco products.

We previously described the Product Integrity evaluation process for cigarettes and smokeless tobacco products used by PM USA and USSTC to determine the suitability of materials, ingredients and product designs.[4] This process evaluates proposed materials, ingredients and product designs to assess whether ingredients and design changes could potentially increase the inherent toxicity of cigarette smoke or smokeless tobacco products. These Product Integrity processes are derived from FDA's own well-established approach for the evaluation and approval of food ingredients.[5]

In an upcoming special issue of Inhalation Toxicology (expected April 2011), ALCS will report results from a large, multi-year study designed to investigate the effects of individual ingredients on mainstream cigarette smoke toxicity. Constituents of mainstream smoke and biological studies such as genotoxicity and smoke inhalation were analyzed.

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[4] *See* Altria Client Services, Inc., Comments dated August 23, 2010, Docket ID No. FDA-2010-D-0281-0003.1, available at http://www.regulations.gov/#!documentDetail;D=FDA-2010-D-0281-0003.1. This evaluation process is also described in the ALCS Product Integrity Toxicological Framework Guideline, the ALCS Product Integrity Toxicological Guideline -- Cigarette Products and the ALCS Product Integrity Review and Toxicological Evaluation Guideline: Smokeless Tobacco Products: Test Articles, Prototypes and Products, which were submitted to FDA on April 29, 2010 as part of PM USA's Tobacco Health Documents Submission.

[5] *See* FDA, *Guidance for Indus. and Other Stakeholders: Toxicological Principles for the Safety Assessment of Food Ingredients* (2000), *available at* http://www.fda.gov/downloads/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodIngredientsandPackaging/Redbook/UCM222779.pdf.

Results indicate that tobacco itself drives the biological activity of cigarette smoke and this biological activity is not impacted by the addition of ingredients as commonly used. While occasional single point-in-time analysis of cigarette smoke may demonstrate a numerical difference between the control (without the test ingredient) and experimental cigarette (with test ingredient), such differences are the result of analytical variability and the intrinsic variability of tobacco.

To determine the acceptability of ingredients for use in smokeless tobacco products we rely on recognized processes for evaluating the safety of ingredients for use in foods.[6] A food ingredient is determined safe for use based on a reasonable certainty that a substance is not harmful under the intended conditions of use.[7] Consideration of knowledge of chemical structures and the outcomes of toxicity studies inform this determination. It is scientifically valid to apply these determinations to ingredients used in smokeless tobacco products because the route of exposure is the same as for foods; hence, an extensive testing program such as described above for cigarettes is not necessary. Overall, ingredients added to smokeless tobacco products will not alter the toxicity of the product provided ingredients are used within limitations supported by available toxicological data.

We urge the FDA to promulgate a final rule that establishes a process focused on whether the addition of, or an increase in, the amount of an additive would increase the inherent toxicity of the tobacco product. Manufacturers can provide comparative internal toxicity testing information as part of their exemption request. Toxicity information is also available in the robust body of published scientific literature that shows additives have little influence on the inherent toxicity of cigarettes[8] or, in the case of smokeless tobacco products, have been demonstrated to be safe for use in foods. Once the Agency decides to grant an exemption request for a particular additive, the Agency should establish a categorical exemption for a range of levels of that additive applicable to all similar products (*e.g.*, all cigarettes or all smokeless tobacco products).

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[6] Additives used in smokeless tobacco products are generally recognized as safe (GRAS) as food ingredients by either FDA, the Flavor and Extract Manufacturers Association, or have undergone a self-GRAS process based on available toxicity information.

[7] *See* Title 21 of the Code of Federal Regulations.

[8] *See* Baker et al., (2004) Anal App Pyrol 71:223-311; Baker et al., (2004) Food Chem Toxicol 42 Suppl:S53-S83; Carmines, (2002) Food Chem Toxicol 40:77-91; Carmines et al., (2005) Food Chem Toxicol 43:1303-1322; Carmines and Gaworski, (2005) Food Chem Toxicol 43:1521-1539; Gaworski et al., (1998) Inhal Toxicol 10:357-38; Gaworski et al., (1999) Toxicology 139:1-17; Gaworski et al., (2008) Food Chem Toxicol 46:339-351; Gaworski et al., (2010) Toxicology 269:54-66; Heck et al., (2002) Inhal Toxicol 14:1135-1152; Heck, (2010) Food Chem Toxicol 48(S2):1-38; Paschke et al., (2002) Beitr Tabakforsch Int 20:107-247; Potts et al., (2010) Exp Toxicol Pathol 62:117-126; Renne et al., (2006) Inhal Toxicol 18:685-706; Roemer et al., (2002) Food Chem Toxicol 40:105-111; Rustemeier et al., (2002) Food Chem Toxicol 40:93-104; Stavanja et al., (2003) J Toxicol Environ Health Part A 66:1453-1473; Stavanja et al., (2008) Exp Toxicol Pathol 59:339-353; Vanscheeuwijck et al., (2002) Food Chem Toxicol 40:113-131.

B. Proposed Requirements About Addictiveness and Appeal to or Use by Minors are Not Required by Statute Nor is Such Information Available.

The proposed rule would require a "certification" "providing the rationale for the official's determination that the modification will not increase the product's toxicity, addictiveness, or appeal to or use by minors . . . " As previously noted in Section VI of our comments on the substantial equivalence guidance, behavioral types of effects are not part of the statutory framework for a substantial equivalence determination. They are also not included in the statutory requirements for a minor modification exemption under 905(j)(3), and, therefore, should be eliminated from the categories of data required by the proposed rule.

The Act has different requirements for the types of data that industry must submit, or that FDA must consider, for 905(j) exemptions as compared to non-substantially equivalent new products, modified risk products or the development of product standards. For example, an evaluation of the risks and benefits to the population as a whole, including users and non users of the tobacco product, and taking into account the increased or decreased likelihood of cessation or initiation of product use, is a criteria for FDA evaluation of non-substantially equivalent new tobacco products.[9] Similar language regarding cessation or initiation effects is also included in describing the criteria for authorization of modified risk tobacco products,[10] and for the development of tobacco product standards.[11] Moreover, an application for authorization of certain types of modified risk tobacco products (*i.e.*, "reduced exposure" products) requires "testing of actual consumer perception" with respect to risks.[12]

In contrast, Congress excluded any consideration of behavioral effects from the substantial equivalence criteria. Thus, the statute precludes consideration of behavioral effects as part of the substantial equivalence evaluation or in the evaluation of minor modification exemption requests.[13]

In addition, the proposed rule's data and certification requirements pose insurmountable practical problems. Specifically, the proposed requirement that manufacturers not only produce information about addictiveness and appeal to, or use by, minors, but also make certifications based on that information, is not viable. We do not believe sufficiently

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[9] *See* 21 U.S.C. § 387j(c)(4).
[10] *See* 21 U.S.C. § 387k(g)(4)(B) & (C).
[11] *See* 21 U.S.C. § 387g(a)(3)(B)(i)(II) & (III).
[12] *See* 21 U.S.C. § 387k(g)(2)(B)(iii).
[13] A well-accepted canon of statutory interpretation is that "where 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." *Keene Corp. v. United States*, 508 U.S. 200, 208 (1993) (*quoting Russello v. United States*, 464 U.S. 16, 23 (1983)). *See also Bailey v. United States*, 516 U.S. 137, 146 (1995) (distinction in one provision between "used" and "intended to be used" creates implication that related provision's reliance on "use" alone refers to actual and not intended use); *Bates v. United States*, 522 U.S. 23, 29 (1997) (inclusion of "intent to defraud" language in one provision and exclusion in a parallel provision indicated intent to defraud was not an element of the offense of knowingly and willingly misappropriating student loan funds).

sensitive tools (with the level of accuracy, reliability, and reproducibility required to make regulatory decisions) exist to measure addictiveness or appeal to, or use by, minors. SCENIHR[14] recently evaluated the potential role of tobacco additives in the addictiveness and attractiveness of tobacco products and noted that there are no universal standards for human studies or agreement about various possible endpoints which define whether an additive or a combination of additives increases the addictive potency or attractiveness of the final tobacco product.[15] Uncertainties of testing aside, there are other issues to consider, particularly as it relates to minors. For example, as a matter of policy, PM USA and USSTC do not conduct consumer or clinical research involving tobacco products with anyone under 21 years of age. As a result, we could not provide the information requested about appeal to, or use by, minors.

Toxicity data will likely be needed to evaluate some minor modification exemption requests and that data must be presented in a truthful and balanced manner. To the extent that the Agency believes it is necessary to require a certification, however, we believe the same certification requirement that applies to a medical device substantial equivalence submission under 21 C.F.R. § 807.87(k)[16] should apply in the exemption request process. Such a certification requirement would be sufficient to alert the petitioner that it must present a truthful and balanced summary of the data on the proposed minor modification, including all material facts.

C. Decisions on 905(j)(3) Exemption Requests Should be Rendered Within 90 Days and Minor Modifications Should be "Deemed Notified" Under 905(j)(1)(A)(ii) Upon Establishment of a Categorical Exemption.

The proposed rule establishes no time period in which the FDA must respond to a 905(j)(3) request. For reasons similar to those articulated in Section I of our comments on the substantial equivalence guidance, we believe the final rule should establish a 90 day review period for 905(j)(3) exemption requests. Such a requirement is logical given the 90 day period Congress established for the FDA to conduct a premarket review of additive

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[14] SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks) is one of three independent non-food Scientific Committees providing the European Commission with the scientific advice needed when preparing policy and proposals relating to consumer safety, public health and the environment.

[15] SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks), 2010. Addictiveness and Attractiveness of Tobacco Additives. European Union, Brussels. Available at http://ec.europa.eu/health/scientific_committees/consultations/public_consultations/scenihr_cons_12_en.htm (accessed March 18, 2001). Additionally, SCENIHR found that the clinical criteria for dependence, laboratory measures of self-administration, and preference measurements in humans which indicate that tobacco has a high addictive potential "have limitations when assessing the addictiveness of individual additives in the final tobacco product." With regard to attractiveness, SCENIHR found that adult tobacco user panel studies and surveys conceivably give only limited information regarding the stimulation to use a product, and there are many other direct and indirect factors such as taste, marketing, price etc., which must also be considered. *See also* Henningfield, J.E., et. al. Conference on abuse liability and appeal of tobacco products: Conclusions and recommendations. Drug Alcohol Depend. (2011), doi:10.1016/j.drugalcdep.2010.12.009 (acknowledging the methodological issues and gaps that need to be addressed in the evaluation of tobacco products for abuse liability and product appeal).

[16] A statement that the submitter believes, to the best of his or her knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted.

additions to tobacco products.[17] Failure to establish an efficient and clear timeframe defeats the Congressional intent in the 905(j)(3) exemptions framework.

The final rule should also allow a manufacturer to provide information in the exemption request that its product is in compliance with the Act and serve as the 905(j)(1)(A)(ii) 90 day notification. Thus, the notification requirement would run concurrently with FDA's review of the exemption request and eliminate the inefficiency of requiring an Agency decision on an exemption request before a manufacturer can submit a 90 day notification to FDA under 905(j)(1)(A)(ii).

Additionally, when the FDA establishes a categorical minor modification exemption for a class of products or modifications (*e.g.*, designated additives), it should be "deemed notified" to the Agency for purposes of compliance with 905(j)(1)(A)(ii).[18] The categorical exemption itself will establish that "the modifications are covered by exemptions granted by the Secretary," and the FDA may limit the terms of the exemption to any "product that is commercially marketed and in compliance with the requirements of this Act." Thus, all of the elements of the required notification will already be known to FDA and, in the case of an additive change, the Agency would receive details regarding the modification under separate requirements, *i.e.*, section 904(c).

D. The Reduction or Elimination of an Additive Should be Categorically Exempt From Substantial Equivalence Requirements.

Sections 904(c)(3) and 905(j)(3) both address the addition or removal of tobacco additives. When a manufacturer reduces or eliminates an additive, section 904(c)(3) requires manufacturers to notify the FDA 60 days *after* entering such a modified product into interstate commerce. This requirement for notification after the fact reflects Congress' determination that premarket review by FDA is not necessary to assess the reduction or elimination of an additive prior to the manufacturer entering the modified product into interstate commerce. FDA's final rule for 905(j)(3) exemptions should be consistent with this Congressional determination and categorically exempt from the substantial equivalence requirements all modifications that reduce or eliminate an additive.

Section 904(c)(3) also requires manufacturers to notify the FDA 60 days *after* entering a product into the market when it "adds or increases an additive that has by regulation been designated by the Secretary as an additive that is not a human or animal carcinogen, or otherwise harmful to health under intended conditions of use."[19] Again, the final rule for 905(j)(3) exemptions should categorically exempt such modifications in recognition of the Congressional determination that additions or increases of "designated" additives do not require a regulatory assessment before a manufacturer enters a product into the market. In

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[17] 21 U.S.C. § 387d(c).

[18] 905(j)(1)(A)(ii) requires a notification of "the basis for such person's determination that . . . the modifications are to a product that is commercially marketed and in compliance with the requirements of this Act, and all of the modifications are covered by exemptions granted by the Secretary."

[19] 21 USC § 387d(c)(3).

addition, the final rule should merge the "designation" regulation process, when established, with the 905(j)(3) substantial equivalence exemption process.

E. Additive Modifications that are Part of Blend Maintenance or the Result of Blend Maintenance Should be Exempt from Substantial Equivalence Requirements.

FDA's Final Guidance for Industry and FDA Staff, Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products, states that "FDA does not intend to enforce the requirements of sections 910 and 905(j) for tobacco blending changes required to address the natural variation of tobacco (e.g., blending changes due to variation in growing conditions) in order to maintain a consistent product." As noted above, these types of adjustments do not constitute "modifications" within the definition of a "new tobacco product." If, however, the Agency does not exclude such adjustments, the final rule should categorically exempt blend changes and associated additive changes required to address the natural variation of tobacco.

Such changes are a practical necessity in the tobacco products industry due to crop variability and availability (beyond a manufacturer's control) to maintain a consistent tobacco product. Congress clearly did not intend that blending adjustments and accompanying changes attributable to the natural variation of an agricultural product would result in a 905(j) report or exemption request with no corresponding public health benefit.

F. The Final Rule Should Allow an Exemption Request to Cover Multiple Products or Even an Entire Category of Products and Allow for Modifications Within a Requested Range.

The Final Rule should clarify that an exemption request, once granted, may cover multiple products, or a category of products produced by a manufacturer, *e.g.*, cigarettes or smokeless tobacco products. In addition, a granted exemption should cover modifications within a requested range. For example, if supported by appropriate toxicological data, a granted exemption should allow a manufacturer to add a particular ingredient to any of its cigarette products up to a specified level, without requiring the manufacturer to file a substantial equivalence report or a duplicative exemption request for each product. Otherwise, the Agency and manufacturers will divert resources on exemption requests or substantial equivalence reports for the same additive with no corresponding public health benefit.

FDA recognizes that it may establish such exemptions in the future as it acquires more information, presumably including from the scientific literature and exemption filings, substantial equivalence reports and other information submitted by manufacturers. The Agency should establish such a pathway for these categorical exemptions in the final rule rather than in the future.

G. The Final Rule Should Provide Exemptions for Non-Additive Modifications.

As described above, the Act does not include adjustments made to maintain consistent product characteristics within the definition of a "new tobacco product." If, however, the Agency disagrees, it should also include exemptions for non-additive minor modifications in the final rule. Such exemptions could cover, for example, blend maintenance adjustments or adjustments in cigarette ventilation to maintain consistent strength of taste in response to agronomic variations. As with the blending adjustments discussed in Section E above, these types of modifications involve only a deliberate and minor "change" to maintain a consistent product.

FDA has the authority to promulgate regulations implementing exemptions for substantial equivalence for non-additive modifications under its 701(a) "authority to promulgate regulations for the efficient enforcement of this Act." As with appropriately focused regulations regarding minor modifications to additives, such regulations would promote regulatory efficiency by reducing the number of unnecessary substantial equivalence reports. FDA should, therefore, broaden the scope of minor modification exemptions in the final rule by allowing for exemptions for non-additive modifications.

Conclusion

We appreciate the opportunity to submit these comments and urge the Agency to incorporate them in the final rule. We look forward to further opportunities to work with the FDA as it develops a process to establish exemptions from the substantial equivalence process.

Sincerely,

James E. Dillard III

ATTACHMENT A

Altria
Altria Client Services

James E. Dillard III
Senior Vice President
Regulatory Affairs

February 8, 2011

Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. FDA-2010-D-0635 (76 Fed. Reg. 789 (Jan. 6, 2011)) – Comments on the "Guidance for Industry and FDA Staff, Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products"

Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC") submit these comments on the above-captioned guidance document ("Guidance").[1] We may supplement these comments at a future date as the FDA's thinking on tobacco product substantial equivalence evolves. We also plan to submit separate comments on the FDA's proposed rule on exemptions from substantial equivalence requirements.[2]

We appreciate the complexity of the issues associated with substantial equivalence reporting. We offer these comments and ask the Agency to take them into account and issue a revised Guidance.[3]

Our comments are organized into the following sections:

- The FDA's Guidance Should Address the Timing of 905(j) Decisions
- The Agency Needs to Clarify its Definition of "New Tobacco Product"
- "As of February 15, 2007" Means On or Before that Date

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[1] Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC") are wholly-owned subsidiaries of Altria Group, Inc. Altria Client Services ("ALCS") is making this submission on behalf of PM USA and USSTC. ALCS provides certain services, including regulatory affairs, to the Altria family of companies. "We" is used throughout to refer to PM USA and USSTC.

[2] *See* 76 Fed. Reg. 737 (Jan 6, 2011).

[3] FDA issued a Final Guidance in contravention to its general rule requiring "public participation" in the development of guidance documents. *See* 21 U.S.C. § 371(h)(1)(A), (C). We urge FDA to consider the public comments it receives and issue a Revised Final Guidance in a timely manner.

Altria Client Services Inc.
2325 Bells Road
Richmond, Virginia 23234
(804) 335-2679
James.E.Dillard@altria.com

- Comparison to Multiple Predicates is Consistent with the Statute and the Scientific Basis of Other FDA Regulatory Processes
- FDA Needs to Address Several Issues About What Constitutes "Same Characteristics"
- Certain of the "Additional Data" FDA Recommends Considering When Analyzing "Different Questions of Public Health" are Not Required by the Statute or Needed for Substantial Equivalence Determinations
- The Agency Needs to Provide Details About How a Manufacturer Can Demonstrate Compliance with the Requirements of the Act
- A Post-March 22, 2011 905(j) Report Should be Deemed to Satisfy the Ingredient Disclosure Requirements of 904(c)

I. The FDA's Guidance Should Address the Timing of 905(j) Decisions.

Revised Guidance should address the timing of the FDA's 905(j) decisions. For products proposed to be first commercially marketed after March 22, 2011, prompt FDA decisions on 905(j) reports are crucial because manufacturers cannot lawfully market such products until the FDA issues a substantial equivalence order. The Agency should establish a reasonable timeframe for its review of such submissions.

For other product submissions to the FDA, the Agency operates under either a statutory or regulatory deadline or an established "performance goal." For example, the FDA committed to issuing a decision on modified risk tobacco product applications within 360 days of receiving the application.[4] For new tobacco products under FDCA § 910, the FDA must respond "as soon as possible, but in no event later than 180 days after receipt of [the] application."[5] A 905(j) submission should require fewer Agency resources and less review time because the statutory requirements for substantial equivalence are fewer and less complex.

In the other FDA-regulated product context most analogous to 905(j) "substantial equivalence" reports—medical device 510(k) "substantial equivalence" submissions[6]—the FDA has committed to issuing a decision for 90% of medical device 510(k)s within 90

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[4] *See* FDA Draft Guidance, "Preliminary Timetable for the Review of Applications for Modified Risk Tobacco Products under the Federal Food, Drug, and Cosmetic Act" (Nov. 2009), *available at* http://www.fda.gov/downloads/TobaccoProducts/GuidanceComplianceRegulatoryInformation/UCM191915.pdf.

[5] 21 U.S.C. § 387j(c)(1).

[6] *Compare* 21 U.S.C. § 360c(i) (medical device "substantial equivalence") *to* 21 U.S.C. § 387j(a)(3) (tobacco product "substantial equivalence"). Neither provision mandates a timeframe in which the FDA must respond to a "substantial equivalence" submission.

days of receipt, and for 98% of them within 150 days.[7] FDA regulations allow 180 days for Agency review of the more complex medical device premarket approval application.[8]

The FDA should establish a "performance goal" of issuing a decision on most, if not all, 905(j) reports required for introduction of a new tobacco product within 90 days of receipt. A 90-day review deadline for 905(j) submissions is reasonable given the user fees paid by manufacturers[9] and the relatively simpler designs (compared to medical devices) that are commonly used in the vast majority of tobacco products in a particular category.

We also suggest that the FDA provide for expedited review of 905(j) reports for situations beyond a manufacturer's control in which a product change is required in a short time frame. For example, an ingredient or material may become unavailable due to uncontrollable supply chain interruptions. It would be unreasonable to require a manufacturer to discontinue production of its affected tobacco products under such circumstances while awaiting the FDA review of a 905(j) report.

II. The Agency Needs to Clarify its Definition of "New Tobacco Product."

The Agency needs to clarify the definition of "new tobacco product" by identifying the specific factors, product attributes, and other considerations that will result in a product being deemed a "new tobacco product."

There are numerous sources of variability inherent in tobacco products that should not constitute a 910(a)(1)(B) "modification." These include variations in manufacturing and differences in materials from lot-to-lot. Adjustments made in response to such variations that are necessary to maintain consistent product characteristics (*e.g.*, adjustments in ventilation parameters to maintain a consistent "tar" per puff, and therefore consistent strength of taste) also should not be considered "modifications." In fact, such adjustments are the opposite of a "modification" since they are intended to maintain a consistent product. In addition, testing variability among different analytical laboratories and (to a lesser extent) within the same laboratory can create the appearance of product variations when, in fact, none actually exists.[10] None of these inherent variations, or adjustments made in response to them, should be considered "modifications."

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[7] *See* FDA Letter to Senator Edward M. Kennedy, Chairman, Committee on Health, Education, Labor, and Pensions, U.S. Senate, Medical Device User Fee Amendments Act of 2007 (MDUFA) Performance Goals and Procedures (Sept. 27, 2007), *available at* http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/UCM109102.pdf.

[8] *See* 21 C.F.R. § 814.40; FDA, Premarket Approval (PMA), available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketApprovalPMA/default.htm.

[9] *See* 21 U.S.C. § 387s(b)(1) (Fiscal year 2009 user fees totaled $85 million; user fees increase in subsequent years until 2019 when the ongoing user fee is $712 million per fiscal year).

[10] "Determination of 'Hoffman Anayltes' in Cigarette Mainstream Smoke. The Coresta 2006 Joint Experiment" Vol. 23 #4 May 2009, p. 161 (available at www.beitraege-bti.de).

Moreover, a product should not be considered "modified" if it is produced within specifications that existed prior to February 15, 2007. For example, there may be a range in paper permeability to permit adjustments to maintain consistent product characteristics. This approach is analogous to the "design space" concept recognized in the regulation of pharmaceutical production.[11]

III. "As of February 15, 2007" Means On or Before that Date.

The phrase "as of February 15, 2007" means on or before the date February 15, 2007. There is no statutory requirement in § 910 or in § 905(j) that a manufacturer provide evidence that a predicate product was marketed nearly four years ago *on* Thursday, February 15, 2007. Such a requirement would not be reasonable or practical, especially given that the Act did not become law until more than 28 months later.

The words "as of" are used to indicate a time or date at which something begins or ends."[12] Thus, February 15, 2007 is the "end" of the period of eligible predicates and grandfathering as "non-new" tobacco products. The following day is the "beginning" of when tobacco products are no longer eligible to serve as predicates (except in the case of products previously found to be substantially equivalent) and may be "new" tobacco products.

Finally, the contrast to the language "after February 15, 2007" (*see* §§910(a)(1)(B) and (a)(2)(B)(i)) clearly indicates that "as of" was intended to mean "on or before."

IV. Comparison to Multiple Predicates is Consistent with the Statute and the Scientific Basis of Other FDA Regulatory Processes.

A multiple predicate approach is consistent with the statute and the scientific basis for FDA's historical treatment of substantial equivalence in other regulated areas. We urge the FDA to consider a "market range" approach to predicate products in which the various attributes of a "new tobacco product" are compared to the various attributes of similar tobacco products, as they existed on or before February 15, 2007.

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[11] An FDA/international regulatory document on drug development, "Guidance for Industry: Q8 Pharmaceutical Development" (May 2006), utilizes the concept of "design space." It defines this concept as: "The multidimensional combination and interaction of input variables (*e.g.*, material attributes) and process parameters that have been demonstrated to provide assurance of quality. Working within the design space is not considered as a change. Movement out of the design space is considered to be a change and would normally initiate a regulatory postapproval change process. Design space is proposed by the applicant and is subject to regulatory assessment and approval." Application of the "design space" concept to tobacco products would of course be somewhat different than it would with respect to drugs, given the differences in the nature of the products and industry design specifications, controls, etc.

[12] *See* Merriam-Webster Online Dictionary at http://www.merriam-webster.com/dictionary/as%20of.

The substantial equivalence provisions of § 910(a) are modeled on the medical device provisions of FDCA, which also refer to "a predicate" product in the singular.[13] FDA interprets this language, however, to permit a new device to be compared to more than one predicate[14] and very recently stated, in its comprehensive plan for improving the 510(k) program, that it "strongly supports the use of multiple predicates."[15] Given this analogous statutory framework, Congress's use of the term "predicate" should be read to allow for the use of multiple predicate products in a substantial equivalence evaluation.[16]

The Institute of Medicine ("IOM") also applied the logic of multiple predicates when it developed the framework for the "No increased risk" threshold in Regulatory Principle 7 "as compared to similar conventional tobacco products."[17] The IOM further noted that tobacco products without health claims should be "at least no more hazardous than in similar contemporaneously marketed products,"[18] an approach that draws from the diversity of products available in the U.S. market and does not limit review to one-to-one product comparisons.

V. FDA Needs to Address Several Issues About What Constitutes "Same Characteristics."

A. "Same Characteristics" Cannot be Interpreted to Mean Identical Characteristics.

The term "same characteristics" cannot be interpreted to mean "identical characteristics." To do so would render the "same characteristics" test meaningless because any product that is new or modified would be automatically evaluated under "different questions of public health." Also, a product that is identical to a predicate is, by definition, neither new nor modified. A basic principle of statutory interpretation is that one must "give effect, if possible, to every clause and word of a statute, avoiding, if it may be, any construction which implies that the legislature was ignorant of the meaning

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[13] *See* 21 U.S.C. § 360c(i)(1)(A) ("'substantially equivalent' ... means, with respect to a device being compared to a predicate device . . .").

[14] *See* FDA Center for Devices and Radiological Health, "Premarket Notification 510(k): Regulatory Requirements for Medical Devices," 1995 WL 17210952 (noting that a device may be compared to one or more predicate devices in claiming substantial equivalence); FDA, "Regulations Restricting the Sale and Distribution of Cigarettes and Smokeless Tobacco to Protect Children and Adolescents," 61 Fed. Reg. 44396, 44410, 1996 WL 482785 (1995) (noting that devices "may not be commercially distributed unless the Agency issues an order finding the device substantially equivalent to one or more predicate devices already legally marketed in the United States").

[15] *See* CDRH, "510(k) and Science Report Recommendations: Summary and Overview of Comments and Next Steps" at § 5.1.2.3, published Jan. 19, 2011 at http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDRH/CDRHReports/UCM239449.pdf.

[16] *Ratzlaf v. United States*, 510 U.S. 135, 143 (1994) ("A term appearing in several places in a statutory text is generally read the same way each time it appears."); *Merrill Lynch, Pierce, Fenner & Smith v. Curran*, 456 U.S. 343, 382 n.66 (1982), quoting *Lorillard v. Pons*, 434 U.S. 575, 580 (1978) ("Congress is presumed to be aware of an administrative . . . interpretation of a statute.").

[17] IOM, Clearing the Smoke: Assessing the Science Base for Tobacco Harm Reduction (2001), 222.

[18] *Id.* at 223.

of the language it employed."[19] A modern variant of this canon is that statutes must be construed "so as to avoid rendering superfluous" any statutory language.[20]

The Guidance does not clearly explain the circumstances under which a tobacco product may be "new" and yet have the "same characteristics" as a predicate(s). Nor does the Guidance explicitly define "same characteristics." The overall implication, however, is that FDA intends to take a narrow view of "same characteristics."[21] For example, it appears that ingredient substitutions that go beyond those described in section V.C of the Guidance would result in a determination that the characteristics are different and trigger an analysis under "different questions of public health." Such a narrow interpretation reads the "same characteristics" test out of the statute.

FDA recently acknowledged the importance of clarifying the criteria that trigger the different pathways of the substantial equivalence framework for medical devices.[22] It should do the same here.

New tobacco products with conventional designs comprising new combinations of ingredients, ingredient levels and materials used in marketed tobacco products would have the same characteristics as those already marketed products in terms of smoke toxicity.[23] It is important to give closer scrutiny to truly novel compositional or design features of a new tobacco product which might have the potential to alter toxicity. This approach is consistent with a reasonable interpretation of both "same characteristics" and "different questions of public health."

The Agency should adopt an interpretation of "same characteristics" that recognizes the range of characteristics on the market on or before February 15, 2007. Such an approach would align with statutory intent and relieve the FDA of the burden of conducting unnecessary reviews.

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[19] *Montclair v. Ramsdell*, 107 U.S. 147, 152 (1883).

[20] *Astoria Federal Savings & Loan Ass'n v. Solimino*, 501 U.S. 104, 112 (1991); *Sprietsma v. Mercury Marine*, 537 U.S. 51, 63 (2003) (interpreting word "law" broadly could render word "regulation" superfluous in preemption clause applicable to a state "law or regulation"). *See also Bailey v. United States*, 516 U.S. 137, 146 (1995) ("we assume that Congress used two terms because it intended each term to have a particular, nonsuperfluous meaning") (rejecting interpretation that would have made "uses" and "carries" redundant in statute penalizing using or carrying a firearm in commission of offense).

[21] *See e.g.*, Guidance section V.A (request for voluminous data to be presented as "side-by-side quantitative and qualitative comparisons of the new tobacco product with the predicate tobacco product with respect to all product characteristics"); section V.C ("same characteristics" will only be found when "a minimal number of ingredients, or materials have been substituted (substitution may include the same ingredient or material but from a different source)," and there is "documentation demonstrating that the substituted ingredient(s) or material(s) meets the required specifications for the replaced ingredient(s) or material(s).").

[22] See, *e.g.*, CDRH, "510(k) and Science Report Recommendations: Summary and Overview of Comments and Next Steps," published Jan. 19, 2011, available at http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDRH/CDRHReports/UCM239449.pdf.

[23] We alert the Agency to an upcoming special edition of *Inhalation Toxicology* in which we will discuss results from our multi-year testing program of cigarette ingredients. The program investigated dose response relationships of various chemical classes using standard toxicology endpoints that have been used to assess cigarette smoke. The results of this testing lead to the conclusion that the ingredients typically used in modern cigarettes do not substantially alter smoke toxicity.

B. The "Same Characteristics" Analysis Should Not Include a Comparison of Harmful and Potentially Harmful Constituents Between the Predicate(s) and the "New" Product.

Among the "other features" that FDA recommends including in a characteristics comparison between new and predicate tobacco products are "harmful and potentially harmful constituents" (HPHCs). FDA is directed, under §§ 904(d) & (e) of the Act, to establish and publish a list of HPHCs; no such list, however, has been published. As a result, it is unknown what constituents should be measured and reported as part of the substantial equivalence process. Until such time as a list of HPHCs is developed and published, manufacturers can provide information only about those constituents for which validated analytical methods, historical data, and ongoing testing and reporting requirements exist for marketed products, *e.g.*, information submitted to the Federal Trade Commission and the Centers for Disease Control.

For purposes of defining substantial equivalence, "the term 'characteristics' means the materials, ingredients, design, composition, heating source, or other features of a tobacco product."[24] It does not include "constituents." When Congress wanted to address constituents in the Act, it did so explicitly (*e.g.*, the establishment and publishing of a HPHC list under §§ 904(d) & (e); manufacturer testing and reporting of tobacco product constituents under regulations to be promulgated by FDA under § 915; testing and reporting of constituents for new tobacco products 90 days prior to introduction under § 904(c)(1); and FDA's authority under § 907 to establish tobacco product standards, including "for the reduction or elimination of other constituents, including smoke constituents, or harmful components of the product.").

Given this comprehensive framework, and the exclusion of constituents in the substantial equivalence context, it is clear that Congress did not intend for the FDA to require a comparison of constituents as part of a substantial equivalence report.[25] Congressional intent is further evidenced by the timing of the various provisions on constituents. Specifically, substantial equivalence reports are due by March 22, 2011, which is well before the April 1, 2012 deadline by which FDA is required to publish a list of HPHCs and promulgate regulations for testing and reporting.

Regardless of when a HPHC list becomes available, it is highly unlikely that cigarettes and smokeless tobacco products on the market on or before February 15, 2007 still exist, let alone in quantities sufficient to satisfy FDA's future testing

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[24] 21 U.S.C. § 387j(a)(3).

[25] A well-accepted canon of statutory interpretation is that "where 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." *Keene Corp. v. United States*, 508 U.S. 200, 208 (1993) (*quoting Russello v. United States*, 464 U.S. 16, 23 (1983)). *See also Bailey v. United States*, 516 U.S. 137, 146 (1995) (distinction in one provision between "used" and "intended to be used" creates implication that related provision's reliance on "use" alone refers to actual and not intended use); *Bates v. United States*, 522 U.S. 23, 29 (1997) (inclusion of "intent to defraud" language in one provision and exclusion in a parallel provision indicated intent to defraud was not an element of the offense of knowingly and willingly misappropriating student loan funds).

requirements. Therefore, it is impossible to generate constituent data for most, if not all, predicate products.[26]

In the HPHC context and others related to substantial equivalence, the Agency should make clear that roll-your-own tobacco products (RYO) and cigarette tobacco are subject to the same requirements as other cigarettes and smokeless tobacco products, and further explain how it will apply these requirements to these tobacco products. Consumers have multiple options from which to choose when combining commercially marketed RYO and cigarette tobaccos, papers, filters and other materials in different configurations. For example, when the HPHC list is published, it is unclear how such a "consumer assembled product" would be tested to determine HPHC levels. As the Agency considers these types of issues, it should follow the Act's requirement that, unless otherwise stated, the requirements applicable to cigarettes also apply to cigarette tobacco.[27]

VI. Certain of the "Additional Data" FDA Recommends Considering When Analyzing "Different Questions of Public Health" are Not Required by the Statute or Needed for Substantial Equivalence Determinations.

The "Additional Data" listed in the Guidance are not required by the statute or needed for substantial equivalence determinations.

The Guidance does not explicitly state the FDA's views about when a new tobacco product would be deemed to raise "different questions of public health." It appears, however, that the Agency believes that making such a determination could involve an assessment of the "additional data," including consumer perception studies, clinical studies, abuse liability data, and toxicological data.

This additional data is not required by the Tobacco Control Act. The various provisions of the Act have different requirements for the types of data that industry must submit, or that FDA must consider. For example, the criteria for evaluating non-substantially equivalent new tobacco products under § 910(c) of the Act require an evaluation of the risks and benefits to the population as a whole, including users and non users of the tobacco product, and taking into account the increased or decreased likelihood of cessation or initiation of product use.[28] This evaluation may include one or more clinical investigations.

Similar language regarding cessation or initiation effects is also included, *e.g.*, in criteria for authorization of modified risk tobacco products,[29] and for the development of

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[26] For a fuller discussion related to HPHCs and the development of the HPHC list, we refer the FDA to a previous submission in which we discuss our experience with tobacco constituent testing and evaluation of such data as part of our ingredient testing program. *See* Altria Client Services, Inc., Comments dated Aug. 23, 2010, Docket ID No. FDA-2010-D-0281-0003.1, available at http://www.regulations.gov/#!documentDetail;D=FDA-2010-D-0281-0003.1.

[27] *See* 21 U.S.C. § 387(4).

[28] *See* 21 U.S.C. § 387j(c)(4).

[29] *See* 21 U.S.C. § 387k(g)(4)(B) & (C).

tobacco product standards.[30] Moreover, an application for authorization of certain types of modified risk tobacco products (*i.e.*, "reduced exposure" products) requires "testing of actual consumer perception" with respect to risks.[31]

In contrast, Congress excluded from the criteria for substantial equivalence under § 910(a), and for reporting under § 905(j), any consideration of behavioral effects such as initiation or cessation, or of consumer perception studies. This absence shows Congressional intent that the criteria should *not* be considered in the substantial equivalence evaluation.[32]

This approach to addressing "different questions of public health" would be consistent with a tobacco regulatory principle proposed by the IOM, in response to a request from the FDA; *i.e.*, a "'No Increased Risk' Threshold for All Tobacco Products."

> In the absence of any claim of reduced exposure or reduced risk, manufacturers of tobacco products should be permitted to market new products or modify existing products without prior approval of the regulatory Agency after informing the Agency of the composition of the product and upon certifying that the product could not reasonably be expected to increase the risk of cancer, heart disease, pulmonary disease, adverse reproductive effects, or other adverse health effects, compared to similar conventional tobacco products, as judged on the basis of the most current toxicological and epidemiological information.[33]

We have long operated under similar principles. The ALCS Product Integrity Evaluation Guidelines establish the criteria to determine the acceptability of an ingredient or design change in cigarettes. The review process involves comparisons to currently marketed cigarettes and a tiered approach modeled after FDA guidelines for food ingredient exposure as described in FDA's "Office of Food Additive Safety Redbook 2000: Toxicological Principles for the Safety Assessment of Food Ingredients."[34] Guidelines for smokeless tobacco products apply similar principles.

Substantial equivalence evaluations under "different questions of public health" should be limited to standard safety studies; *i.e.*, toxicology and (where deemed necessary by the Secretary) clinical studies. An assessment of health effects based on a hazard evaluation grounded in sound scientific principles can be used to identify "different questions of public health" and will meet both Congressional intent and the "reasonable expectation of no increased risk" criteria proposed by the IOM.

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[30] *See* 21 U.S.C. § 387g(a)(3)(B)(i)(II) & (III).
[31] *See* 21 U.S.C. § 387k(g)(2)(B)(iii).
[32] *See* f.n. 25, *supra.*
[33] *See* IOM, Clearing the Smoke: Assessing the Science Base for Tobacco Harm Reduction (2001), 222.
[34] Although the procedure addressed in the FDA's "Redbook" is related to dietary exposure, PM USA considers its concepts of segregating subject materials by structure and anticipated exposure level into "concern levels" to be useful for the toxicologic evaluation of smoking products and their components.

If the FDA still believes it can request this information, it is not clear whether manufacturers would be expected to submit such data in the initial report or only upon request by the Agency.[35]

VII. The Agency Needs to Provide Details About How a Manufacturer Can Demonstrate Compliance with the Requirements of the Act.

FDA should provide a clear recommendation about the type and format of the information it wants manufacturers to provide to demonstrate compliance with other requirements of the Act.[36] The FDA already has access to information such as a manufacturer's registration and product listings, ingredient list filings, submission of tobacco health information, and any other required regulatory filings. Moreover, the § 905(j)(1)(B) requirement to report "action taken by such person to comply with the requirements under § 907 that are applicable to the tobacco product" seems to have little relevance to products currently on the market since the only tobacco product standard currently in effect is a ban on characterizing flavors in cigarettes other than menthol or tobacco.

If the FDA expects a manufacturer to summarize this information or provide additional information, it should provide that direction in Revised Guidance.

VIII. A Post-March 22, 2011 905(j) Report Should be Deemed to Satisfy the Ingredient Disclosure Requirements of 904(c).

FDA should allow a 905(j) report to fulfill more than one regulatory obligation. If a manufacturer includes the information recommended in the Guidance, the information submitted in its 905(j) report will include a complete disclosure of the ingredients (including additives) that are to be added to a tobacco product, or to any part thereof. As a result, the 905(j) report should simultaneously fulfill the ingredient disclosure requirements of FDCA § 904(c).[37] Moreover, a 905(j) report submitted on or after March 22, 2011 must be submitted at least 90 days before delivering the product

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[35] The Guidance states both that the "FDA may request" such data and that a 905(j) report "should include the[se] data."

[36] *See* section IV.D of the Guidance ("[i]n addition to determining that the product is substantially equivalent, FDA must also determine that the new tobacco product is in compliance with the requirements of the Act before issuing an order under section 910(a)(2)(A)(i).").

[37] 21 U.S.C. § 387d(c)(1) cross-references "the information required under subsection (a)" (which includes "a listing of all ingredients, including tobacco, substances, compounds and additives" added to each part of a tobacco product) and applies to products "not on the market on the date of enactment." A 904(c)(2) disclosure applies to modifications involving new additives or increased usage levels of existing additives, and a 904(c)(3) disclosure applies to modifications involving elimination or decreased usage of an additive, or to additive changes involving additives "designated" by FDA as not carcinogenic or otherwise harmful "under intended conditions of use."

for introduction into interstate commerce. Thus, assuming a manufacturer includes the information recommended in the Guidance, it would also satisfy the ingredient (including additive) disclosures under 904(c), which has a similar 90 days pre- (and in some cases 60 days post-) timing requirement.[38]

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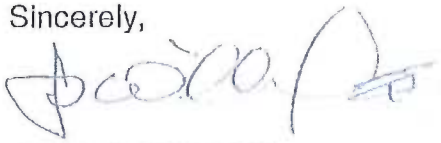
We appreciate the opportunity to submit these comments and urge the Agency to incorporate them in a Revised Guidance. We look forward to further opportunities to provide comments to the Agency as its thinking on substantial equivalence evolves.

Sincerely,



James E. Dillard III

[38] A 904(c)(1) disclosure must be made "[a]t least 90 days prior to the delivery for introduction into interstate commerce of a tobacco product not on the market on the date of enactment;" a 904(c)(2) disclosure must be made "at least 90 days prior to" the "time a tobacco product manufacturer adds to its tobacco products a new tobacco additive or increases the quantity of an existing additive;" and a 904(c)(3) disclosure must be made "within 60 days of" the "time a tobacco product manufacturer eliminates or decreases an existing additive, or adds or increases an additive that has by regulation been designated . . . ."

James E. Dillard III
Senior Vice President
Regulatory Affairs

February 25, 2014

Via Electronic Submission

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. FDA-2013-N-1558 (78 Fed. Reg. 78974 (Dec. 27, 2013)) — Comments on "Agency Information Collection Activities; Proposed Collection; Comment Request; Guidance for Industry and Food and Drug Administration Staff; Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products"

Altria Client Services Inc. ("ALCS"), on behalf of Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC"),[1] submits these comments in response to the above-captioned Federal Register notice ("Notice").

Our comments address three topics identified in the Notice:

1. "Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility;"

2. "The accuracy of the Food and Drug Administration's ("FDA's" or "the Agency's") estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used;" and

3. "Ways to enhance the quality, utility, and clarity of the information to be collected."

We recognize the magnitude of the task that FDA faces in evaluating substantial equivalence submissions, and we appreciate the opportunity to submit these comments.

[1] PM USA and USSTC are wholly-owned subsidiaries of Altria Group, Inc. ALCS provides certain services, including regulatory affairs, to the Altria family of companies. "We" and "our" are used throughout these comments to refer collectively to PM USA and USSTC.

Altria Client Services Inc.
2325 Bells Road
Richmond, Virginia 23234
(804) 335-2679
James.E.Dillard@altria.com

I. FDA overreaches by requiring information for substantial equivalence reports not required by the statute and not relevant for the proper performance of the Agency's functions.

FDA has improperly implemented the substantial equivalence provisions of the statute which is inconsistent with its plain language and its overall structure by requiring information to support 905(j) reports that are neither authorized nor relevant to a substantial equivalence determination. The following identifies examples of how the Agency's interpretation and application of the statutory requirements are inconsistent with the statute or have resulted in a substantial equivalence pathway that is unreasonable and overly burdensome.

A. A proper evaluation of substantial equivalence cannot interpret "same characteristics" to mean "identical characteristics."

Under Section 905(j), a new tobacco product is substantially equivalent to a predicate tobacco product or products if it (1) has the same characteristics as the predicate(s), or (2) has different characteristics but does not raise different questions of public health. Multiple sources reveal that FDA interprets the term "same characteristics" to mean "identical characteristics."[2] But "same" cannot mean "identical."

A product that is identical to a predicate or predicates is, by definition, neither new nor modified, and therefore is not a "new tobacco product" that must undergo premarket review by the Agency to be lawfully marketed. Under FDA's interpretation, every new or modified product automatically will be evaluated under the "different questions of public health" standard, thereby rendering the "same characteristics" test meaningless. Indeed, FDA's substantial equivalence orders to date demonstrate that the Agency has yet to find a product that satisfies the "same characteristics" test, even in cases where the product was deemed "nearly identical" to its predicate.[3] Such interpretation violates the basic principle of statutory interpretation that every word and clause in a statute must be given effect.[4] A statute must be interpreted in a way that

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[2] *See, e.g.*, FDA, *Guidance for Industry and FDA Staff, Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products* [hereinafter "*Substantial Equivalence Guidance*"], 76 Fed. Reg. 789 (Jan. 6, 2011) at § V.A (request for voluminous data to be presented as "side-by-side quantitative and qualitative comparisons of the new tobacco product with the predicate tobacco product with respect to all product characteristics"); § V.C ("same characteristics" will only be found when "a minimal number of ingredients, or materials have been substituted (substitution may include the same ingredient or material but from a different source)," and there is "documentation demonstrating that the substituted ingredient(s) or material(s) meets the required specifications for the replaced ingredient(s) or material(s).").

[3] *See, e.g.,* FDA, Technical Project ~ Lead Memorandum: SE Report SE0003730 (June 25, 2013) (stating that "The composition of the new and predicate products is nearly identical with the exception that menthol was omitted from, and fire standard compliant (FSC) paper was added to, the new product. The new and predicate products contain essentially identical tobacco blends . . .. The other ingredients and additives, including the flavors and casings, are essentially identical except for the absence of menthol and the addition of FSC banded cigarette paper and burn modifiers in FSC cigarette paper.")

[4] *See Montclair v. Ramsdell*, 107 U.S. 147, 152 (1883) (instructing that one must "give effect, if possible, to every clause and word of a statute, avoiding, if it may be, any construction which implies that the legislature was ignorant of the meaning of the language it employed.").

avoids rendering any of the statute's language superfluous.[5] Interpreting "same" to mean "identical" renders the "same characteristics" test superfluous.

In the other FDA-regulated product context most analogous to 905(j) "substantial equivalence" reports -- medical device 510(k) "substantial equivalence" submissions[6] -- Congress did not envision and FDA correctly does not interpret "same" to mean "identical." Indeed, the substantial equivalence provisions of § 910(a) are modeled on the medical device provisions of the Federal Food, Drug, and Cosmetic Act ("FDCA" or "the Act").[7] Under Section 510(k) of the Act, a medical device is substantially equivalent to its predicate(s) if it (1) has the *same* technological *characteristics* as the predicate(s) or (2) has different characteristics, is as safe and effective as the predicate(s), and does not raise different questions of safety and effectiveness.[8] Within the 510(k) context, FDA does not interpret "same" to mean "identical" and has found non-identical characteristics to be the "same."[9] By using the 510(k) model, Congress intended to incorporate the streamlined process used for medical devices. To follow a different approach for tobacco products is inconsistent with that intent.

Based on its interpretation that "same" means "identical" for purposes of substantial equivalence for tobacco products, FDA is requiring manufacturers to submit data and other information to show that their new products do not raise different questions of public health compared to predicate products, even when the new products should be considered to have the "same characteristics" as their predicates. Moreover, the amount and scope of data and information that FDA is requiring to show that a new tobacco product does not raise "different questions of public health" far exceeds that which is necessary to demonstrate that products share the same characteristics. FDA's erroneous interpretation of the word "same," particularly when coupled with its unnecessarily cumbersome approach regarding "different questions of public health," is causing FDA to request and review data and information that is not necessary to discharging its statutory obligation in determining substantial equivalence.

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[5] *Astoria Federal Savings & Loan Ass'n v. Solimino*, 501 U.S. 104, 112 (1991); *Sprietsma v. Mercury Marine*, 537 U.S. 51, 63 (2003) (using a broad interpretation of the word "law" could render the word "regulation" superfluous as used in a preemption clause that applied to a state "law or regulation"). *See also Bailey v. United States*, 516 U.S. 137, 146 (1995) ("we assume that Congress used two terms because it intended each term to have a particular, nonsuperfluous meaning") (rejecting interpretation that would have made "uses" and "carries" redundant in statute penalizing using or carrying a firearm in commission of an offense).

[6] *Compare* 21 U.S.C. § 360c(i) (medical device "substantial equivalence") *to* 21 U.S.C. § 387j(a)(3) (tobacco product "substantial equivalence").

[7] *See, e.g.,* U.S. Senate Committee on Commerce, Science, and Transportation. *National Tobacco Policy and Youth Smoking Act: Report Together with Additional Views* (to accompany S. 1415) (S.Rpt. 105-180), at 23-24, Washington: Government Printing Office, 1998 (stating "Sections 905(j) and 910 adopt the substantial equivalence provisions of [the Medical Device Amendments] sections 510(k), 513(I) and 515(b), with certain modifications").

[8] 21 U.S.C. § 360c(i)(1)(A).

[9] *See, e.g., FDA, Medical Devices—Premarket Notification (510k)* ("A claim of substantial equivalence does not mean the new and predicate devices must be identical"), *available at* http://www.fda.gov/medicaldevices/deviceregulationandguidance/howtomarketyourdevice/premarketsubmissions/premarketnotification510k/default.htm; FDA, *Medical Devices—How to Find a Predicate Device* ("A claim of substantial equivalence does not mean the device(s) must be identical"), *available at* http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/ucm134571.htm.

Instead of equating "same" with "identical," the Agency must adopt an interpretation of "same characteristics" that recognizes the ranges of characteristics of tobacco products on the market on or before February 15, 2007. This approach is consistent with a reasonable interpretation of both "same characteristics" and "different questions of public health" and results in the collection of only the information that is necessary to assess substantial equivalence, consistent with the less cumbersome procedure that Congress intended.

B. Behavioral evidence should not be required to support substantial equivalence reports.

FDA has erroneously determined that behavioral evidence, including consumer perception studies and abuse liability data, is required in substantial equivalence reports to demonstrate that a new product with different characteristics does not raise different questions of public health. As previously noted in ALCS' comments on the Guidance for Industry and FDA Staff, Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products ("Substantial Equivalence Guidance")[10] and the proposed rule for Tobacco Products, Exemption from Substantial Equivalence ("Substantial Equivalence Exemptions Proposed Rule"),[11] behavioral types of effects are not part of the statutory framework for a substantial equivalence determination. Accordingly, the collection of behavioral evidence is not necessary or appropriate to the proper performance of the Agency's review of 905(j) reports. Including this requirement both complicates the substantial equivalence process and, more generally, signals that FDA has interpreted the process beyond what Congress intended. The various premarket authorization provisions of the Act have different requirements for the types of data that industry must submit, or that FDA must consider. For example, the criteria for evaluating non-substantially equivalent new tobacco products under Section 910(c) of the Act require an evaluation of the risks and benefits to the population as a whole, including users and non-users of the tobacco product, and taking into account the increased or decreased likelihood of cessation or initiation of product use.[12] Similar language regarding cessation or initiation effects is also included, for example, in criteria for authorization of modified risk tobacco products,[13] and for the development of tobacco product standards.[14] Moreover, an application for authorization of certain types of modified risk tobacco products (*i.e.,* "reduced exposure" products) requires "testing of actual consumer perception" with respect to risks.[15]

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[10] *See* Attachment A. Letter from James E. Dillard III to Division of Dockets Management re: Docket No. FDA-2010-D-0635 (76 Fed. Reg. 789 (Jan. 6, 2011)) – Comments on the "Guidance for Industry and FDA Staff, Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products" (Feb. 8, 2011).

[11] *See* Attachment B. Letter from James E. Dillard III to Division of Dockets Management re: Docket No. FDA-210-N-0646 (76 Fed. Reg. 737 (January 6, 2011)) Tobacco Products, Exemption from Substantial Equivalence (March 22, 2011).

[12] *See* 21 U.S.C. § 387j(c)(4).

[13] *See id.* § 387k(g)(4)(B) & (C).

[14] *See id.* § 387g(a)(3)(B)(i)(II) & (III).

[15] *See id.* § 387k(g)(2)(B)(iii).

In contrast, Congress excluded from the criteria for substantial equivalence under Section 910(a), and for reporting under Section 905(j), any consideration of behavioral effects such as initiation or cessation, or of consumer perception studies. This absence shows Congress' intent that the criteria should *not* be considered in the substantial equivalence evaluation.[16] Thus, substantial equivalence evaluations under "different questions of public health" should be limited to standard safety studies; *i.e.*, toxicology and (where deemed necessary by the Secretary) clinical studies, without any additional requirement or consideration of behavioral effects.

C. Packaging and labeling are not "characteristics" nor are they "part" of a tobacco product.

FDA has taken the position that 905(j) submissions must include packaging and labeling information for both new and predicate products.[17] FDA also has taken the position that any change to the label or packaging of a tobacco product that occurs after February 15, 2007 makes that product a "new tobacco product" subject to the requirements of Sections 905(j) and 910(b).[18] Both of these positions are erroneous, and they further complicate the substantial equivalence process, departing from Congressional intent.

1. Packaging and labeling are not "characteristics" reviewed as part of a substantial equivalence determination.

Section 910's definition of "characteristics" demonstrates that Congress did not intend for FDA to consider product labeling or packaging when analyzing substantial equivalence. Section 910 defines the term "characteristics" to mean "the materials, ingredients, design, composition, heating source, or other features of a tobacco product."[19] Product labels and packaging do not fit within this definition. Indeed, FDA itself has recognized that packaging is not a "characteristic" of a tobacco product.[20]

Moreover, substantial equivalence is a *premarket* review process, whereas the statute provides for *postmarket* review of product labeling absent notice-and-comment rulemaking or a Section 911 claim of modified risk.[21] Section 903(a) empowers the Agency to seize a marketed tobacco product if it determines that the product's labeling contains "false or misleading" statements, including a misleading product name.[22] While Section 903(b) authorizes premarket review of

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[16] A well-accepted canon of statutory interpretation is that "where 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." *Keene Corp. v. United States*, 508 U.S. 200, 208 (1993) (*quoting Russello v. United States*, 464 U.S. 16, 23 (1983)); s*ee also, e.g., Bates v. United States*, 522 U.S. 23, 29 (1997) (inclusion of "intent to defraud" language in one provision and exclusion in a parallel provision indicated intent to defraud was not an element of the offense of knowingly and willingly misappropriating student loan funds).

[17] *See, e.g.,* FDA, *Draft Guidance for Industry and FDA Staff -- Demonstrating the Substantial Equivalence of a New Tobacco Product: Responses to Frequently Asked Questions* (Nov. 8, 2011) [hereinafter "*Substantial Equivalence FAQs*"].

[18] *Id.* at 3.

[19] 21 U.S.C. § 387j(a)(3)(B).

[20] *See* FDA, *Guidance for Industry -- Listing of Ingredients in Tobacco Products* § III.C (Nov. 2009) [hereinafter "*Listing of Ingredients in Tobacco Products Guidance*"] (stating that the requirement to provide an ingredient list does not apply to "packaging differences that do not affect the characteristics of the product").

[21] Congress also authorized premarket review of labeling under Section 911, but that section is not relevant to substantial equivalence.

[22] 21 U.S.C. § 387c(a); *cf.* 21 C.F.R. § 201.10 (regulating drug names in labeling).

product labeling, it provides that the Agency may do so *only* through regulation, and such a regulation has not been promulgated. Even if FDA were to promulgate such a regulation, it would be separate and apart from the requirements of Section 905(j). It is neither appropriate nor necessary for FDA to engage in premarket review of product labeling as part of the substantial equivalence process.

If FDA has any authority to require premarket review of packaging changes, it is only to the extent that the new packaging causes a change in the characteristics of the tobacco product itself. For example, FDA may require a 905(j) report for a packaging change that leads to a change in the ingredient composition of the tobacco product in the package, because "ingredients" are among the "modifications" expressly included in Section 910(a)(1)(B), as well as the "characteristics" that are subject to substantial equivalence review.[23]

2. Changes to labels and packaging do not create a "new tobacco product" subject to premarket authorization.

FDA's position is that any change to the label or packaging of a tobacco product that occurs after February 15, 2007, makes that product a "new tobacco product" subject to the requirements of Sections 905(j) and 910(b). However, as we have described in detail previously,[24] that interpretation is foreclosed by the text, context and purpose of the statute. In addition, as we also have described in detail previously,[25] including a product's name in the definitions of tobacco product and new tobacco product would violate the First Amendment's Free Speech Clause. Brand names are protected as commercial speech. An interpretation of the FSPTCA that would require manufacturers to obtain FDA authorization before changing the names of their products would impose a constitutionally suspect prior restraint. Such restraints are impermissible absent procedural safeguards sufficient to protect against the "danger of suppressing constitutionally protected speech."[26] To treat changes in labeling and packaging as creating a new tobacco product multiplies the number of substantial equivalence filings, compounding the burdens imposed by FDA's overreaching in the implementation of the process itself.

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[23] 21 U.S.C. §§ 387j(a)(1)(B), 387(a)(3)(B).

[24] *See* Attachment C. Letter from James E. Dillard III to Division of Dockets Management re: Docket No. FDA-2011-D-0147 (76 Fed. Reg. 55,927 (Sept. 9, 2011)) – Comments on the "Draft Guidance for Industry and FDA Staff -- Demonstrating the Substantial Equivalence of a New Tobacco Product: Responses to Frequently Asked Questions" (Nov. 8, 2011).

[25] *Id.*

[26] *Southeastern Promotions, Ltd. v. Conrad*, 420 U.S. 546 (1975).

D. The statute did not intend the submission of Harmful and Potentially Harmful Constituent ("HPHC") data as part of substantial equivalence evaluations.

FDA appears to have taken the position that 905(j) submissions must include HPHC[27] data for new and predicate products.[28] Adding this extra requirement further complicates and overloads the substantial equivalence process in ways Congress clearly did not intend.

Substantial equivalence is established based on a comparison of the "characteristics" of the new and predicate products.[29] The statute defines the term "characteristics" to mean "the materials, ingredients, design, composition, heating source, or other features of a tobacco product."[30] The definition does not include "constituents," and the term "ingredients" cannot be read to encompass constituents.[31] Moreover, the term "other features of a tobacco product" cannot be read to encompass constituents. If Congress had intended to include constituents as part of the substantial equivalence review process, it would have referred to "constituents" explicitly as it did in numerous other sections of the statute.[32] Congress did not include constituents in the context of substantial equivalence reports, meaning that Congress did not intend to require comparison of constituents in a 905(j) submission.[33]

The Agency's position that substantial equivalence reports must contain HPHC data also raises practical difficulties that further indicate that Congress did not intend to interject this requirement into what was supposed to be a simplified process. First, Congress required substantial equivalence reports to be submitted by March 22, 2011, long before FDA's April 2012 deadline for identifying and publishing a list of HPHCs and its April 2013 deadline for promulgating regulations for testing and reporting.[34] Congress therefore could not have intended to require FDA to consider HPHC data when evaluating substantial equivalence. Second, HPHC testing was not required as of February 15, 2007, yet products that existed on or before that date serve as predicates for the substantial equivalence analysis. It is highly unlikely that cigarettes and

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[27] "Harmful and potentially harmful constituent" has been defined, in relevant part, to include "any chemical or chemical compound in a tobacco product or in tobacco smoke: a) that is or potentially is inhaled, ingested, or absorbed into the body; and b) that causes or has the potential to cause direct or indirect harm to users or non-users of tobacco products." FDA, *Guidance for Industry and FDA Staff -- "Harmful and Potentially Harmful Constituents" in Tobacco Products as Used in Section 904(e) of the Federal Food, Drug, and Cosmetic Act*, at 2 (Jan. 2011), *available at* http://www.fda.gov/downloads/TobaccoProducts/GuidanceComplianceRegulatoryInformation/UCM241352.pdf.

[28] *See, e.g., Substantial Equivalence Guidance, supra* note 2.

[29] *See* 21 U.S.C. § 387j(a)(3)(A).

[30] *Id.* § 387j(a)(3)(B).

[31] *See id.* §§ 387d(a)(1), 387d(a)(3); *see also id.* §§ 387g(a)(l)(A), 387g(a)(3)(B)(ii) (indicating that "constituents" and "additives" are conceptually distinct categories under the FSPTCA).

[32] *See , e.g.*, Definition of "smoke constituent" in § 900(17); establishment and publishing of an HPHC list under §§ 904(d) and (e); manufacturer testing and reporting of tobacco product constituents under regulations to be promulgated by FDA under § 915; testing and reporting of constituents for new tobacco products 90 days prior to introduction under § 904(c)(1); FDA's authority under § 907 to establish tobacco product standards, including "for the reduction or elimination of other constituents, including smoke constituents, or harmful components of the product."

[33] *See supra*, note 16 (regarding well-accepted canons of statutory construction).

[34] *See* 21 U.S.C. §§ 387d(d)(1), 387d(e), 387(o)(b)(l).

smokeless tobacco products on the market on or before February 15, 2007 - at least *seven* years ago - still exist, let alone in quantities sufficient to satisfy FDA's testing requirements. Therefore, it is impossible to generate constituent data for most, if not all, "grandfathered" predicate products.[35] The inability to generate HPHC data for predicate products cannot foreclose a finding of substantial equivalence, as FDA's position suggests.

E. Substantial equivalence reports should be exempt from environmental assessment requirements.

The Agency recently proposed a rule amending 21 C.F.R. Part 25 to exclude certain classes of tobacco-related actions from the requirement to prepare an environmental assessment or an environmental impact statement (referred to as "categorical exclusions").[36] This proposed rule exempts Section 905(j) reports for tobacco products under Section 910(a)(2)(B) as well as certain FDA actions related to premarket approval of tobacco products.

In the preamble to the proposed rule, the Agency provides a sound rationale for establishing these new categorical exclusions. The Agency, however, failed to include categorical exclusions for all Section 905(j) reports, although the rationale provided by the Agency supports a broader exclusion. In the preamble to the proposed rule, the Agency considered the manufacturing effects on the environment ("trivial" when compared to the total impact by all industries) and the effects on the environment due to the use and disposal of the new products. In evaluating the latter, the Agency concluded that "any new tobacco products that receive marketing authorization through the available pathways would have less or no more environmental impact than that of tobacco products currently on the market."[37] Furthermore, nearly every other FDA-regulated industry benefits from a categorical exemption for agency actions similar to substantial equivalence determinations. In each of these industries, FDA has taken the position that environmental assessments are not necessary if the requested agency action does not increase overall use of the product type.[38] If FDA adopts a broader categorical exclusion for all Section 905(j) reports, FDA could still require an environmental assessment based on extraordinary circumstances. Accordingly, the Agency should reconsider a categorical exclusion for all substantial equivalence

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[35] For a fuller discussion related to HPHCs and the development of the HPHC list, we refer the FDA to a previous submission in which we discuss our experience with tobacco constituent testing and evaluation of such data as part of our ingredient testing program. *See* letter from James E. Dillard III to Division of Dockets Management re: Docket No. FDA-2010-D-0281 - Comments on the "Draft Guidance for Industry and FDA Staff: 'Harmful and Potentially Harmful Constituents' in Tobacco Products as Used in Section 904(e) of the Federal Food, Drug, and Cosmetic Act" (Aug. 23, 2010), *available at* http://www.regulations.gov/#!documentDetail;D=FDA-2010-D-0281-0003.

[36] FDA, *National Environmental Policy Act; Environmental Assessments for Tobacco Products; Categorical Exclusions*, Proposed Rule, 79 Fed. Reg. 3742 (Jan. 23, 2014) (proposing to require an environmental assessment for any order finding a tobacco product substantially equivalent except orders issued under section 910(a)(2)(B) for provisional tobacco products).

[37] *Id.* at 3745

[38] *See, e.g.*, 21 C.F.R. §§ 25.15(c) (agency actions that "do not significantly affect the quality of the human environment" are ordinarily excluded), 25.30(k) (labeling changes that do not affect levels of use); 25.31(a) (new drug approval applications that will not "increase the use of the active moiety"), 25.31(g) (bioequivalence determinations for human drugs and comparability determinations for biologics), 25.32(f) (determinations that food is GRAS if it is already marketed for the proposed use), 25.33(a) (new animal drug approval applications that will not increase use), 25.34(b) (device classification determinations that will not increase or expand the use of the device), 25.34(d) (class III medical device approvals if the device is of the same type and use of a previously approved device), 25.34(f) (restricted device regulations that will not expand or increase the use of the product).

determinations, consistent with the Congressional intent to make the substantial equivalence process simple and streamlined. Requiring environmental assessments makes FDA's estimate of the burdens of the current process even more unrealistic.

F. FDA's failure to recognize and account for the inherent variability in laboratory assays, manufacturing processes and in tobacco itself, results in the collection of information that is not necessary to the proper performance of a substantial equivalence determination.

First, as an agricultural product, tobacco naturally varies from crop to crop, plant to plant, leaf to leaf within the same plant, and even within a single leaf. For this reason, test results for product characteristics even within a single package can vary, a fact that FDA must account for when reviewing the data submitted in a 905(j) report.

The Agency has acknowledged that tobacco's natural variability may require adjustments to tobacco blends to maintain a consistent product.[39] But FDA's position does not go far enough. Due to crop-to-crop variations and associated tobacco supply, it may not only be necessary to adjust tobacco blends but also to adjust other product characteristics, such as inclusion levels of particular ingredients, in order to maintain a consistent product. These variations are directly tied to tobacco's inherent variability and FDA should recognize that such variations do not cause a new product to have "different characteristics" from its predicate(s).

Second, testing variability among different analytical laboratories and, to a lesser extent, within the same laboratory can create the appearance of product variations when in fact no such variations exist.[40] In general, product parameters that are measured in large quantities (e.g., parameters measured in milligrams per product unit) are easier to adjust statistically to account for assay variability. As a result, these parameters are more suitable for evaluating whether two tobacco products are substantially equivalent. Conversely, as the unit of measure of a product parameter becomes smaller (e.g., moving from milligrams to micrograms, or to nanograms or smaller), it becomes progressively less feasible to use statistics to moderate and quantify the variability and, therefore, the less suitable the parameter is for evaluating substantial equivalence. Nonetheless, FDA appears to take the position that all product parameters, regardless of magnitude, must be identical to establish that the products have the "same characteristics." As discussed above, this position improperly bypasses the "same characteristics" examination and proceeds directly to the more intensive analysis of whether a new tobacco product raises "different questions of public health."

G. Shelf life data should not be required for substantial equivalence determinations.

FDA has taken the position that 905(j) submissions must contain shelf life data for new and predicate products.[41] The definition of "characteristics," however, does not include shelf life. The *Substantial Equivalence Guidance*, which lists the information that should be submitted in a

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[39] *Substantial Equivalence Guidance, supra* note 2 at § III.D ("At this time FDA does not intend to enforce the requirements of sections 910 and 905(j) for tobacco blending changes required to address the natural variation of tobacco (e.g., blending changes due to variation in growing conditions) in order to maintain a consistent product.").

[40] "Determination of 'Hoffman Analytes' in Cigarette Mainstream Smoke. The Coresta 2006 Joint Experiment" Vol. 23, No. 4 at 161 (May 2009), *available at* ww.beitraege-bti.de.

[41] *Substantial Equivalence FAQs, supra* note 17, at FAQ 3.

905(j) report, makes no mention of shelf life. Accordingly, the Agency has previously acknowledged that shelf life data is not necessary for evaluating substantial equivalence.[42] Adding this requirement further inflates the substantial equivalence process beyond the statutory requirements and beyond what Congress intended.

II. FDA's estimate of the burden of the proposed collection of information is not accurate and significantly underestimates the time required to prepare a substantial equivalence report.

ALCS previously submitted comments on FDA's guidance documents on substantial equivalence[43] and proposed rule for exemptions from substantial equivalence requirements.[44] As described in our past comments, which are referenced and incorporated here, and in Part I above, FDA has adopted erroneous interpretations of the Family Smoking Prevention and Tobacco Control Act ("FSPTCA") leading to overly burdensome reporting requirements on manufacturers far beyond what Congress intended. In addition, in some instances, FDA has failed to clarify in a meaningful way the Agency's position and specific requirements for substantial equivalence reports. In light of FDA's approach, the Agency's estimates of the burdens imposed by the Guidance for Industry and FDA Staff, Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products ("Substantial Equivalence Guidance") are mistaken.[45]

When first estimating the annual reporting burden for substantial equivalence reports, FDA anticipated receiving a mere 150 reports per year.[46] Upon consideration that this estimate was "far too low," FDA subsequently revised its estimate to 1,000 reports per year,[47] which is a more reasonable estimate. Whether the current estimate accurately accounts for the number of substantial equivalence reports the Agency will receive each year remains to be seen; however, there remains a possibility that the annual estimate is too low.

FDA has also estimated on several occasions that an average of 360 hours will be required to prepare a substantial equivalence report. This estimate is not consistent with the industry's experience or with the burdens FDA has imposed through the substantial equivalence process, and significantly underestimates the time required to prepare a report. A recent report by the Government Accountability Office ("GAO") confirms that industry representatives have indicated that the time required to prepare a substantial equivalence report exceeds FDA's estimate of 360 hours.[48] We urge the Agency to rethink its interpretation of the Act and the amount and types of information and data it requires in a 905(j) submission to achieve the

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[42] *Substantial Equivalence Guidance, supra* note 2, at 7-11.
[43] *See* Attachment A, *supra* note 10; Attachment C, *supra* note 24.
[44] *See* Attachment B, *supra* note 11.
[45] *Substantial Equivalence Guidance, supra* note 2.
[46] *See* FDA, Notice, *Agency Information Collection Activities; Proposed Collection; Comment Request; Guidance for Industry and Food and Drug Administration Staff; Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products*, 76 Fed. Reg. 4116, 4117 (Jan. 24, 2011).
[47] *See* FDA, Notice, *Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Guidance for Industry and Food and Drug Administration Staff; Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products*, 76 Fed. Reg. 24888, 24889 (May 3, 2011).
[48] GAO, *Report to the Ranking member, Subcomm. on Primary Health and Aging Comm. On Health, Education, Labor, and Pensions, U.S. Senate, NEW TOBACCO PRODUCTS -- FDA Needs to Set Time Frames for its Review Process* 25-26, GAO-13-723 (Sept. 2013).

streamlined process envisioned in the FSPTCA. By implementing the statute consistent with its plain language and structure, FDA's estimates would be a more accurate reflection of the actual time required to submit substantial equivalence reports.

III. Recommendations to improve the quality, utility, and clarity of substantial equivalence reports.

Among topics identified in FDA's request for comments on its information collection activities for substantial equivalence are "ways to enhance the quality, utility, and clarity of the information to be collected."[49] As discussed in Part I above, the scope of information FDA currently expects to support substantial equivalence reports is too broad, exceeding the statute's limits on required information and that which is necessary for the proper performance of FDA's review of 905(j) reports. Recognizing these limits, in addition to the specific recommendations below, will help enhance the quality, utility, and clarity of information contained in substantial equivalence reports, and will simplify the process as Congress intended.

A. FDA should clarify the definition of "new tobacco product."

One way that FDA can enhance the quality, utility, and clarity of the information it receives from manufacturers is to provide a concrete definition of "new tobacco product." Specifically, the Agency should identify the precise factors, product attributes, and other considerations that will result in a product being deemed a "new tobacco product." The deficiency of guidance in this regard creates a significant risk that manufacturers will submit unnecessary 905(j) reports, unduly increasing the burden on both manufacturers and the Agency.

B. FDA should clearly define the level of specificity required for tobacco product additives.

FDA has failed to clarify the level of specificity required in 905(j) reports for the amounts and levels of additives in tobacco products. In response to requests that the Agency clearly identify such level of specificity, FDA stated, without further clarification, that such data should be presented "in a form that will provide the basis for FDA to determine if the new tobacco product is or is not substantially equivalent to the predicate product."[50] FDA's position does not provide any meaningful direction, effectively requiring manufacturers to predict in advance the level of specificity necessary for information about product additives. The Agency's failure to provide direct guidance regarding specific information required for tobacco products additives has improperly magnified the already excessive burden on manufacturers submitting substantial equivalence reports. Clear guidance about the level of specificity required for tobacco product additives will not only assist manufacturers in preparing 905(j) reports, but will also improve the quality, utility, and clarity of the information submitted in such reports.

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[49] Notice, 78 Fed. Reg. at 78975.

[50] *Substantial Equivalence FAQs, supra* note 17.

C. The optimal way to enhance the quality, utility, and clarity of substantial equivalence reports is to engage in notice-and-comment rulemaking.

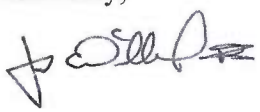
Rather than promulgating a regulation that specifies exactly the form and content required for a 905(j) submission, the Agency has instead communicated its positions in a piecemeal fashion through the issuance of draft and final guidance documents and through letters to individual manufacturers, often resulting in vague, conflicting and incomprehensible direction from the Agency.[51] The best way to ensure that both FDA and stakeholders are apprised of the information that is required to prepare and evaluate substantial equivalence reports is to promulgate a regulation that has been vetted through the notice-and-comment process and sets forth the exact requirements for 905(j) submissions, and conforms those requirements to what Congress intended for the substantial equivalence process.

At a minimum, FDA should revise its guidance to include additional information it has requested from tobacco product manufacturers over the past two years. In addition, FDA should provide an e-submitter form to include all the information sought for substantial equivalence reports. With an e-submitter form, the Agency will receive consistent information from tobacco product manufacturers and eliminate the burden of asking and responding to follow up questions.

Conclusion

We appreciate the opportunity to submit these comments and share our perspective on the burden of substantial equivalence reporting requirements. As always, we would be happy to discuss further these and other ALCS comments on the *Substantial Equivalence Guidance* with FDA.

Sincerely,



James E. Dillard III

[51] As one example, two final guidance documents issued in November 2009 state that "[p]roducts that differ in any way, *other than packaging differences that do not affect characteristics of the product*, are considered to be distinct tobacco products." *Listing of Ingredients in Tobacco Products Guidance*, *supra* note 20; *see also* FDA, *Guidance for Industry -- Registration and Product Listing for Owners and Operators of Domestic Tobacco Product Establishments* (Nov. 2009) . FDA again recognized that packaging is not a "characteristic" in its *Substantial Equivalence Guidance*, which discusses the content and data that should be submitted in a substantial equivalence report and at no point mentions packaging information. Months later, in the *Substantial Equivalence FAQs*, FDA articulated a new (and erroneous) interpretation of the Act that would require a new premarket authorization submission each time a product's packaging undergoes a change.

Attachment A

Altria
Altria Client Services

James E. Dillard III
Senior Vice President
Regulatory Affairs

February 8, 2011

Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. FDA-2010-D-0635 (76 Fed. Reg. 789 (Jan. 6, 2011)) – Comments on the "Guidance for Industry and FDA Staff, Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products"

Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC") submit these comments on the above-captioned guidance document ("Guidance").[1] We may supplement these comments at a future date as the FDA's thinking on tobacco product substantial equivalence evolves. We also plan to submit separate comments on the FDA's proposed rule on exemptions from substantial equivalence requirements.[2]

We appreciate the complexity of the issues associated with substantial equivalence reporting. We offer these comments and ask the Agency to take them into account and issue a revised Guidance.[3]

Our comments are organized into the following sections:

- The FDA's Guidance Should Address the Timing of 905(j) Decisions
- The Agency Needs to Clarify its Definition of "New Tobacco Product"
- "As of February 15, 2007" Means On or Before that Date

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[1] Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC") are wholly-owned subsidiaries of Altria Group, Inc. Altria Client Services ("ALCS") is making this submission on behalf of PM USA and USSTC. ALCS provides certain services, including regulatory affairs, to the Altria family of companies. "We" is used throughout to refer to PM USA and USSTC.

[2] *See* 76 Fed. Reg. 737 (Jan 6, 2011).

[3] FDA issued a Final Guidance in contravention to its general rule requiring "public participation" in the development of guidance documents. *See* 21 U.S.C. § 371(h)(1)(A), (C). We urge FDA to consider the public comments it receives and issue a Revised Final Guidance in a timely manner.

Altria Client Services Inc.
2325 Bells Road
Richmond, Virginia 23234
(804) 335-2679
James.E.Dillard@altria.com

- Comparison to Multiple Predicates is Consistent with the Statute and the Scientific Basis of Other FDA Regulatory Processes
- FDA Needs to Address Several Issues About What Constitutes "Same Characteristics"
- Certain of the "Additional Data" FDA Recommends Considering When Analyzing "Different Questions of Public Health" are Not Required by the Statute or Needed for Substantial Equivalence Determinations
- The Agency Needs to Provide Details About How a Manufacturer Can Demonstrate Compliance with the Requirements of the Act
- A Post-March 22, 2011 905(j) Report Should be Deemed to Satisfy the Ingredient Disclosure Requirements of 904(c)

I. The FDA's Guidance Should Address the Timing of 905(j) Decisions.

Revised Guidance should address the timing of the FDA's 905(j) decisions. For products proposed to be first commercially marketed after March 22, 2011, prompt FDA decisions on 905(j) reports are crucial because manufacturers cannot lawfully market such products until the FDA issues a substantial equivalence order. The Agency should establish a reasonable timeframe for its review of such submissions.

For other product submissions to the FDA, the Agency operates under either a statutory or regulatory deadline or an established "performance goal." For example, the FDA committed to issuing a decision on modified risk tobacco product applications within 360 days of receiving the application.[4] For new tobacco products under FDCA § 910, the FDA must respond "as soon as possible, but in no event later than 180 days after receipt of [the] application."[5] A 905(j) submission should require fewer Agency resources and less review time because the statutory requirements for substantial equivalence are fewer and less complex.

In the other FDA-regulated product context most analogous to 905(j) "substantial equivalence" reports—medical device 510(k) "substantial equivalence" submissions[6]—the FDA has committed to issuing a decision for 90% of medical device 510(k)s within 90

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[4] *See* FDA Draft Guidance, "Preliminary Timetable for the Review of Applications for Modified Risk Tobacco Products under the Federal Food, Drug, and Cosmetic Act" (Nov. 2009), *available at* http://www.fda.gov/downloads/TobaccoProducts/GuidanceComplianceRegulatoryInformation/UCM191915.pdf.

[5] 21 U.S.C. § 387j(c)(1).

[6] *Compare* 21 U.S.C. § 360c(i) (medical device "substantial equivalence") *to* 21 U.S.C. § 387j(a)(3) (tobacco product "substantial equivalence"). Neither provision mandates a timeframe in which the FDA must respond to a "substantial equivalence" submission.

days of receipt, and for 98% of them within 150 days.[7] FDA regulations allow 180 days for Agency review of the more complex medical device premarket approval application.[8]

The FDA should establish a "performance goal" of issuing a decision on most, if not all, 905(j) reports required for introduction of a new tobacco product within 90 days of receipt. A 90-day review deadline for 905(j) submissions is reasonable given the user fees paid by manufacturers[9] and the relatively simpler designs (compared to medical devices) that are commonly used in the vast majority of tobacco products in a particular category.

We also suggest that the FDA provide for expedited review of 905(j) reports for situations beyond a manufacturer's control in which a product change is required in a short time frame. For example, an ingredient or material may become unavailable due to uncontrollable supply chain interruptions. It would be unreasonable to require a manufacturer to discontinue production of its affected tobacco products under such circumstances while awaiting the FDA review of a 905(j) report.

II. The Agency Needs to Clarify its Definition of "New Tobacco Product."

The Agency needs to clarify the definition of "new tobacco product" by identifying the specific factors, product attributes, and other considerations that will result in a product being deemed a "new tobacco product."

There are numerous sources of variability inherent in tobacco products that should not constitute a 910(a)(1)(B) "modification." These include variations in manufacturing and differences in materials from lot-to-lot. Adjustments made in response to such variations that are necessary to maintain consistent product characteristics (*e.g.*, adjustments in ventilation parameters to maintain a consistent "tar" per puff, and therefore consistent strength of taste) also should not be considered "modifications." In fact, such adjustments are the opposite of a "modification" since they are intended to maintain a consistent product. In addition, testing variability among different analytical laboratories and (to a lesser extent) within the same laboratory can create the appearance of product variations when, in fact, none actually exists.[10] None of these inherent variations, or adjustments made in response to them, should be considered "modifications."

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[7] *See* FDA Letter to Senator Edward M. Kennedy, Chairman, Committee on Health, Education, Labor, and Pensions, U.S. Senate, Medical Device User Fee Amendments Act of 2007 (MDUFA) Performance Goals and Procedures (Sept. 27, 2007), *available at* http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/UCM109102.pdf.

[8] *See* 21 C.F.R. § 814.40; FDA, Premarket Approval (PMA), available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketApprovalPMA/default.htm.

[9] *See* 21 U.S.C. § 387s(b)(1) (Fiscal year 2009 user fees totaled $85 million; user fees increase in subsequent years until 2019 when the ongoing user fee is $712 million per fiscal year).

[10] "Determination of 'Hoffman Anayltes' in Cigarette Mainstream Smoke. The Coresta 2006 Joint Experiment" Vol. 23 #4 May 2009, p. 161 (available at www.beitraege-bti.de).

Moreover, a product should not be considered "modified" if it is produced within specifications that existed prior to February 15, 2007. For example, there may be a range in paper permeability to permit adjustments to maintain consistent product characteristics. This approach is analogous to the "design space" concept recognized in the regulation of pharmaceutical production.[11]

III. "As of February 15, 2007" Means On or Before that Date.

The phrase "as of February 15, 2007" means on or before the date February 15, 2007. There is no statutory requirement in § 910 or in § 905(j) that a manufacturer provide evidence that a predicate product was marketed nearly four years ago *on* Thursday, February 15, 2007. Such a requirement would not be reasonable or practical, especially given that the Act did not become law until more than 28 months later.

The words "as of" are used to indicate a time or date at which something begins or ends."[12] Thus, February 15, 2007 is the "end" of the period of eligible predicates and grandfathering as "non-new" tobacco products. The following day is the "beginning" of when tobacco products are no longer eligible to serve as predicates (except in the case of products previously found to be substantially equivalent) and may be "new" tobacco products.

Finally, the contrast to the language "after February 15, 2007" (*see* §§910(a)(1)(B) and (a)(2)(B)(i)) clearly indicates that "as of" was intended to mean "on or before."

IV. Comparison to Multiple Predicates is Consistent with the Statute and the Scientific Basis of Other FDA Regulatory Processes.

A multiple predicate approach is consistent with the statute and the scientific basis for FDA's historical treatment of substantial equivalence in other regulated areas. We urge the FDA to consider a "market range" approach to predicate products in which the various attributes of a "new tobacco product" are compared to the various attributes of similar tobacco products, as they existed on or before February 15, 2007.

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[11] An FDA/international regulatory document on drug development, "Guidance for Industry: Q8 Pharmaceutical Development" (May 2006), utilizes the concept of "design space." It defines this concept as: "The multidimensional combination and interaction of input variables (*e.g.*, material attributes) and process parameters that have been demonstrated to provide assurance of quality. Working within the design space is not considered as a change. Movement out of the design space is considered to be a change and would normally initiate a regulatory postapproval change process. Design space is proposed by the applicant and is subject to regulatory assessment and approval." Application of the "design space" concept to tobacco products would of course be somewhat different than it would with respect to drugs, given the differences in the nature of the products and industry design specifications, controls, etc.

[12] *See* Merriam-Webster Online Dictionary at http://www.merriam-webster.com/dictionary/as%20of.

The substantial equivalence provisions of § 910(a) are modeled on the medical device provisions of FDCA, which also refer to "a predicate" product in the singular.[13] FDA interprets this language, however, to permit a new device to be compared to more than one predicate[14] and very recently stated, in its comprehensive plan for improving the 510(k) program, that it "strongly supports the use of multiple predicates."[15] Given this analogous statutory framework, Congress's use of the term "predicate" should be read to allow for the use of multiple predicate products in a substantial equivalence evaluation.[16]

The Institute of Medicine ("IOM") also applied the logic of multiple predicates when it developed the framework for the "No increased risk" threshold in Regulatory Principle 7 "as compared to similar conventional tobacco products."[17] The IOM further noted that tobacco products without health claims should be "at least no more hazardous than in similar contemporaneously marketed products,"[18] an approach that draws from the diversity of products available in the U.S. market and does not limit review to one-to-one product comparisons.

V. FDA Needs to Address Several Issues About What Constitutes "Same Characteristics."

A. "Same Characteristics" Cannot be Interpreted to Mean Identical Characteristics.

The term "same characteristics" cannot be interpreted to mean "identical characteristics." To do so would render the "same characteristics" test meaningless because any product that is new or modified would be automatically evaluated under "different questions of public health." Also, a product that is identical to a predicate is, by definition, neither new nor modified. A basic principle of statutory interpretation is that one must "give effect, if possible, to every clause and word of a statute, avoiding, if it may be, any construction which implies that the legislature was ignorant of the meaning

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[13] *See* 21 U.S.C. § 360c(i)(1)(A) ("'substantially equivalent' ... means, with respect to a device being compared to a predicate device . . .").

[14] *See* FDA Center for Devices and Radiological Health, "Premarket Notification 510(k): Regulatory Requirements for Medical Devices," 1995 WL 17210952 (noting that a device may be compared to one or more predicate devices in claiming substantial equivalence); FDA, "Regulations Restricting the Sale and Distribution of Cigarettes and Smokeless Tobacco to Protect Children and Adolescents," 61 Fed. Reg. 44396, 44410, 1996 WL 482785 (1995) (noting that devices "may not be commercially distributed unless the Agency issues an order finding the device substantially equivalent to one or more predicate devices already legally marketed in the United States").

[15] *See* CDRH, "510(k) and Science Report Recommendations: Summary and Overview of Comments and Next Steps" at § 5.1.2.3, published Jan. 19, 2011 at http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDRH/CDRHReports/UCM239449.pdf.

[16] *Ratzlaf v. United States*, 510 U.S. 135, 143 (1994) ("A term appearing in several places in a statutory text is generally read the same way each time it appears."); *Merrill Lynch, Pierce, Fenner & Smith v. Curran*, 456 U.S. 343, 382 n.66 (1982), quoting *Lorillard v. Pons*, 434 U.S. 575, 580 (1978) ("Congress is presumed to be aware of an administrative . . . interpretation of a statute.").

[17] IOM, Clearing the Smoke: Assessing the Science Base for Tobacco Harm Reduction (2001), 222.

[18] *Id.* at 223.

of the language it employed."[19] A modern variant of this canon is that statutes must be construed "so as to avoid rendering superfluous" any statutory language.[20]

The Guidance does not clearly explain the circumstances under which a tobacco product may be "new" and yet have the "same characteristics" as a predicate(s). Nor does the Guidance explicitly define "same characteristics." The overall implication, however, is that FDA intends to take a narrow view of "same characteristics."[21] For example, it appears that ingredient substitutions that go beyond those described in section V.C of the Guidance would result in a determination that the characteristics are different and trigger an analysis under "different questions of public health." Such a narrow interpretation reads the "same characteristics" test out of the statute.

FDA recently acknowledged the importance of clarifying the criteria that trigger the different pathways of the substantial equivalence framework for medical devices.[22] It should do the same here.

New tobacco products with conventional designs comprising new combinations of ingredients, ingredient levels and materials used in marketed tobacco products would have the same characteristics as those already marketed products in terms of smoke toxicity.[23] It is important to give closer scrutiny to truly novel compositional or design features of a new tobacco product which might have the potential to alter toxicity. This approach is consistent with a reasonable interpretation of both "same characteristics" and "different questions of public health."

The Agency should adopt an interpretation of "same characteristics" that recognizes the range of characteristics on the market on or before February 15, 2007. Such an approach would align with statutory intent and relieve the FDA of the burden of conducting unnecessary reviews.

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[19] *Montclair v. Ramsdell*, 107 U.S. 147, 152 (1883).

[20] *Astoria Federal Savings & Loan Ass'n v. Solimino*, 501 U.S. 104, 112 (1991); *Sprietsma v. Mercury Marine*, 537 U.S. 51, 63 (2003) (interpreting word "law" broadly could render word "regulation" superfluous in preemption clause applicable to a state "law or regulation"). *See also Bailey v. United States*, 516 U.S. 137, 146 (1995) ("we assume that Congress used two terms because it intended each term to have a particular, nonsuperfluous meaning") (rejecting interpretation that would have made "uses" and "carries" redundant in statute penalizing using or carrying a firearm in commission of offense).

[21] *See e.g.*, Guidance section V.A (request for voluminous data to be presented as "side-by-side quantitative and qualitative comparisons of the new tobacco product with the predicate tobacco product with respect to all product characteristics"); section V.C ("same characteristics" will only be found when "a minimal number of ingredients, or materials have been substituted (substitution may include the same ingredient or material but from a different source)," and there is "documentation demonstrating that the substituted ingredient(s) or material(s) meets the required specifications for the replaced ingredient(s) or material(s).").

[22] See, *e.g.*, CDRH, "510(k) and Science Report Recommendations: Summary and Overview of Comments and Next Steps," published Jan. 19, 2011, available at http://www.fda.gov/downloads/AboutFDA/CentersOfffices/CDRH/CDRHReports/UCM239449.pdf.

[23] We alert the Agency to an upcoming special edition of *Inhalation Toxicology* in which we will discuss results from our multi-year testing program of cigarette ingredients. The program investigated dose response relationships of various chemical classes using standard toxicology endpoints that have been used to assess cigarette smoke. The results of this testing lead to the conclusion that the ingredients typically used in modern cigarettes do not substantially alter smoke toxicity.

B. The "Same Characteristics" Analysis Should Not Include a Comparison of Harmful and Potentially Harmful Constituents Between the Predicate(s) and the "New" Product.

Among the "other features" that FDA recommends including in a characteristics comparison between new and predicate tobacco products are "harmful and potentially harmful constituents" (HPHCs). FDA is directed, under §§ 904(d) & (e) of the Act, to establish and publish a list of HPHCs; no such list, however, has been published. As a result, it is unknown what constituents should be measured and reported as part of the substantial equivalence process. Until such time as a list of HPHCs is developed and published, manufacturers can provide information only about those constituents for which validated analytical methods, historical data, and ongoing testing and reporting requirements exist for marketed products, *e.g.*, information submitted to the Federal Trade Commission and the Centers for Disease Control.

For purposes of defining substantial equivalence, "the term 'characteristics' means the materials, ingredients, design, composition, heating source, or other features of a tobacco product."[24] It does not include "constituents." When Congress wanted to address constituents in the Act, it did so explicitly (*e.g.*, the establishment and publishing of a HPHC list under §§ 904(d) & (e); manufacturer testing and reporting of tobacco product constituents under regulations to be promulgated by FDA under § 915; testing and reporting of constituents for new tobacco products 90 days prior to introduction under § 904(c)(1); and FDA's authority under § 907 to establish tobacco product standards, including "for the reduction or elimination of other constituents, including smoke constituents, or harmful components of the product.").

Given this comprehensive framework, and the exclusion of constituents in the substantial equivalence context, it is clear that Congress did not intend for the FDA to require a comparison of constituents as part of a substantial equivalence report.[25] Congressional intent is further evidenced by the timing of the various provisions on constituents. Specifically, substantial equivalence reports are due by March 22, 2011, which is well before the April 1, 2012 deadline by which FDA is required to publish a list of HPHCs and promulgate regulations for testing and reporting.

Regardless of when a HPHC list becomes available, it is highly unlikely that cigarettes and smokeless tobacco products on the market on or before February 15, 2007 still exist, let alone in quantities sufficient to satisfy FDA's future testing

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[24] 21 U.S.C. § 387j(a)(3).

[25] A well-accepted canon of statutory interpretation is that "where 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." *Keene Corp. v. United States*, 508 U.S. 200, 208 (1993) (*quoting Russello v. United States*, 464 U.S. 16, 23 (1983)). *See also Bailey v. United States*, 516 U.S. 137, 146 (1995) (distinction in one provision between "used" and "intended to be used" creates implication that related provision's reliance on "use" alone refers to actual and not intended use); *Bates v. United States*, 522 U.S. 23, 29 (1997) (inclusion of "intent to defraud" language in one provision and exclusion in a parallel provision indicated intent to defraud was not an element of the offense of knowingly and willingly misappropriating student loan funds).

requirements. Therefore, it is impossible to generate constituent data for most, if not all, predicate products.[26]

In the HPHC context and others related to substantial equivalence, the Agency should make clear that roll-your-own tobacco products (RYO) and cigarette tobacco are subject to the same requirements as other cigarettes and smokeless tobacco products, and further explain how it will apply these requirements to these tobacco products. Consumers have multiple options from which to choose when combining commercially marketed RYO and cigarette tobaccos, papers, filters and other materials in different configurations. For example, when the HPHC list is published, it is unclear how such a "consumer assembled product" would be tested to determine HPHC levels. As the Agency considers these types of issues, it should follow the Act's requirement that, unless otherwise stated, the requirements applicable to cigarettes also apply to cigarette tobacco.[27]

VI. Certain of the "Additional Data" FDA Recommends Considering When Analyzing "Different Questions of Public Health" are Not Required by the Statute or Needed for Substantial Equivalence Determinations.

The "Additional Data" listed in the Guidance are not required by the statute or needed for substantial equivalence determinations.

The Guidance does not explicitly state the FDA's views about when a new tobacco product would be deemed to raise "different questions of public health." It appears, however, that the Agency believes that making such a determination could involve an assessment of the "additional data," including consumer perception studies, clinical studies, abuse liability data, and toxicological data.

This additional data is not required by the Tobacco Control Act. The various provisions of the Act have different requirements for the types of data that industry must submit, or that FDA must consider. For example, the criteria for evaluating non-substantially equivalent new tobacco products under § 910(c) of the Act require an evaluation of the risks and benefits to the population as a whole, including users and non users of the tobacco product, and taking into account the increased or decreased likelihood of cessation or initiation of product use.[28] This evaluation may include one or more clinical investigations.

Similar language regarding cessation or initiation effects is also included, *e.g.*, in criteria for authorization of modified risk tobacco products,[29] and for the development of

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[26] For a fuller discussion related to HPHCs and the development of the HPHC list, we refer the FDA to a previous submission in which we discuss our experience with tobacco constituent testing and evaluation of such data as part of our ingredient testing program. *See* Altria Client Services, Inc., Comments dated Aug. 23, 2010, Docket ID No. FDA-2010-D-0281-0003.1, available at http://www.regulations.gov/#!documentDetail;D=FDA-2010-D-0281-0003.1.

[27] *See* 21 U.S.C. § 387(4).

[28] *See* 21 U.S.C. § 387j(c)(4).

[29] *See* 21 U.S.C. § 387k(g)(4)(B) & (C).

tobacco product standards.[30] Moreover, an application for authorization of certain types of modified risk tobacco products (*i.e.*, "reduced exposure" products) requires "testing of actual consumer perception" with respect to risks.[31]

In contrast, Congress excluded from the criteria for substantial equivalence under § 910(a), and for reporting under § 905(j), any consideration of behavioral effects such as initiation or cessation, or of consumer perception studies. This absence shows Congressional intent that the criteria should *not* be considered in the substantial equivalence evaluation.[32]

This approach to addressing "different questions of public health" would be consistent with a tobacco regulatory principle proposed by the IOM, in response to a request from the FDA; *i.e.*, a "'No Increased Risk' Threshold for All Tobacco Products."

> In the absence of any claim of reduced exposure or reduced risk, manufacturers of tobacco products should be permitted to market new products or modify existing products without prior approval of the regulatory Agency after informing the Agency of the composition of the product and upon certifying that the product could not reasonably be expected to increase the risk of cancer, heart disease, pulmonary disease, adverse reproductive effects, or other adverse health effects, compared to similar conventional tobacco products, as judged on the basis of the most current toxicological and epidemiological information.[33]

We have long operated under similar principles. The ALCS Product Integrity Evaluation Guidelines establish the criteria to determine the acceptability of an ingredient or design change in cigarettes. The review process involves comparisons to currently marketed cigarettes and a tiered approach modeled after FDA guidelines for food ingredient exposure as described in FDA's "Office of Food Additive Safety Redbook 2000: Toxicological Principles for the Safety Assessment of Food Ingredients."[34] Guidelines for smokeless tobacco products apply similar principles.

Substantial equivalence evaluations under "different questions of public health" should be limited to standard safety studies; *i.e.*, toxicology and (where deemed necessary by the Secretary) clinical studies. An assessment of health effects based on a hazard evaluation grounded in sound scientific principles can be used to identify "different questions of public health" and will meet both Congressional intent and the "reasonable expectation of no increased risk" criteria proposed by the IOM.

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[30] *See* 21 U.S.C. § 387g(a)(3)(B)(i)(II) & (III).
[31] *See* 21 U.S.C. § 387k(g)(2)(B)(iii).
[32] *See* f.n. 25, *supra*.
[33] *See* IOM, Clearing the Smoke: Assessing the Science Base for Tobacco Harm Reduction (2001), 222.
[34] Although the procedure addressed in the FDA's "Redbook" is related to dietary exposure, PM USA considers its concepts of segregating subject materials by structure and anticipated exposure level into "concern levels" to be useful for the toxicologic evaluation of smoking products and their components.

If the FDA still believes it can request this information, it is not clear whether manufacturers would be expected to submit such data in the initial report or only upon request by the Agency.[35]

VII. The Agency Needs to Provide Details About How a Manufacturer Can Demonstrate Compliance with the Requirements of the Act.

FDA should provide a clear recommendation about the type and format of the information it wants manufacturers to provide to demonstrate compliance with other requirements of the Act.[36] The FDA already has access to information such as a manufacturer's registration and product listings, ingredient list filings, submission of tobacco health information, and any other required regulatory filings. Moreover, the § 905(j)(1)(B) requirement to report "action taken by such person to comply with the requirements under § 907 that are applicable to the tobacco product" seems to have little relevance to products currently on the market since the only tobacco product standard currently in effect is a ban on characterizing flavors in cigarettes other than menthol or tobacco.

If the FDA expects a manufacturer to summarize this information or provide additional information, it should provide that direction in Revised Guidance.

VIII. A Post-March 22, 2011 905(j) Report Should be Deemed to Satisfy the Ingredient Disclosure Requirements of 904(c).

FDA should allow a 905(j) report to fulfill more than one regulatory obligation. If a manufacturer includes the information recommended in the Guidance, the information submitted in its 905(j) report will include a complete disclosure of the ingredients (including additives) that are to be added to a tobacco product, or to any part thereof. As a result, the 905(j) report should simultaneously fulfill the ingredient disclosure requirements of FDCA § 904(c).[37] Moreover, a 905(j) report submitted on or after March 22, 2011 must be submitted at least 90 days before delivering the product

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[35] The Guidance states both that the "FDA may request" such data and that a 905(j) report "should include the[se] data."

[36] *See* section IV.D of the Guidance ("[i]n addition to determining that the product is substantially equivalent, FDA must also determine that the new tobacco product is in compliance with the requirements of the Act before issuing an order under section 910(a)(2)(A)(i).").

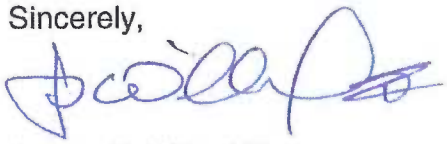
[37] 21 U.S.C. § 387d(c)(1) cross-references "the information required under subsection (a)" (which includes "a listing of all ingredients, including tobacco, substances, compounds and additives" added to each part of a tobacco product) and applies to products "not on the market on the date of enactment." A 904(c)(2) disclosure applies to modifications involving new additives or increased usage levels of existing additives, and a 904(c)(3) disclosure applies to modifications involving elimination or decreased usage of an additive, or to additive changes involving additives "designated" by FDA as not carcinogenic or otherwise harmful "under intended conditions of use."

for introduction into interstate commerce. Thus, assuming a manufacturer includes the information recommended in the Guidance, it would also satisfy the ingredient (including additive) disclosures under 904(c), which has a similar 90 days pre- (and in some cases 60 days post-) timing requirement.[38]

* * * * *

We appreciate the opportunity to submit these comments and urge the Agency to incorporate them in a Revised Guidance. We look forward to further opportunities to provide comments to the Agency as its thinking on substantial equivalence evolves.

Sincerely,



James E. Dillard III

[38] A 904(c)(1) disclosure must be made "[a]t least 90 days prior to the delivery for introduction into interstate commerce of a tobacco product not on the market on the date of enactment;" a 904(c)(2) disclosure must be made "at least 90 days prior to" the "time a tobacco product manufacturer adds to its tobacco products a new tobacco additive or increases the quantity of an existing additive;" and a 904(c)(3) disclosure must be made "within 60 days of" the "time a tobacco product manufacturer eliminates or decreases an existing additive, or adds or increases an additive that has by regulation been designated . . . ."

Attachment B

Altria Client Services

James E. Dillard III
Senior Vice President
Regulatory Affairs
James.E.Dillard@altria.com

2325 Bells Road
Richmond, VA 23234
(804) 335-2679

March 22, 2011

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. FDA-2010-N-0646 (76 Fed. Reg. 737 (January 6, 2011))
"Tobacco Products, Exemptions from Substantial Equivalence Requirements"

Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC")[1] submit these comments on the above captioned proposed rule "Tobacco Products, Exemptions from Substantial Equivalence Requirements."

As the Agency finalizes the proposed rule, we reference and incorporate our previously filed comments to the "Guidance for Industry and FDA Staff, Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products."[2] We asked the Agency to clarify its definition of a "new tobacco product" and provide additional guidance about what constitutes a "modification." We reiterate that there are numerous sources of variability inherent in tobacco products that should not constitute a "modification." These include variations in manufacturing and differences in materials from lot-to-lot. Adjustments made in response to such variations that are necessary to maintain consistent product characteristics are also not properly considered product "modifications" under the Family Smoking Prevention and Tobacco Control Act ("the Act"). As such, these adjustments do not render a product a "new tobacco product" or require premarket review under Sections 905(j) or 910. We urge the Agency to comply with the statute as it finalizes the rule for the exemption process. If, however, the Agency does not exclude such adjustments, we believe it should consider such adjustments minor modifications exempt from substantial equivalence requirements.[3]

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[1] Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC") are wholly-owned subsidiaries of Altria Group, Inc. Altria Client Services ("ALCS") is making this submission on behalf of PM USA and USSTC. ALCS provides certain services, including regulatory affairs, to the Altria family of companies. "We" is used throughout to refer to PM USA and USSTC.

[2] *See* Attachment A.

[3] This suggestion assumes, for purposes of this submission and participation in the rulemaking process and without prejudice to the statutory interpretation noted above and in our prior comments, that such adjustments could be construed as modifications for purposes of implementing and enforcing the Act.

Congress established an exemption process in section 905(j) of the Act to provide an alternative, less burdensome process to filing a substantial equivalence report. FDA's proposed rule, however, is contrary to Congressional intent because the proposed rule imposes on both the Agency and manufacturers unnecessary and duplicative burdens. For example, the proposed rule requires a manufacturer to file an exemption request and, if the exemption is granted, to file a subsequent 90 day notification that the modification made to the product is covered by the granted exemption and is otherwise in compliance with the Act. These requirements can be met in the exemption request, thus eliminating an additional unnecessary filing. In addition, and as discussed below, the proposed rule conflicts with several provisions of the Act in conditioning exemptions on the submission of data that Congress intended to exclude from substantial equivalence determinations.

A. Analysis of Toxicity Data Should Be the Basis for Agency Decision-Making on Exemptions.

The development of tobacco regulations should be guided by science- and evidence-based decisions. As such, we support the proposed rule where it will ensure that exemption decisions are based on an analysis of changes in toxicity that could result from ingredient (used interchangeably here with "additive") changes or other minor modifications to tobacco products.

We previously described the Product Integrity evaluation process for cigarettes and smokeless tobacco products used by PM USA and USSTC to determine the suitability of materials, ingredients and product designs.[4] This process evaluates proposed materials, ingredients and product designs to assess whether ingredients and design changes could potentially increase the inherent toxicity of cigarette smoke or smokeless tobacco products. These Product Integrity processes are derived from FDA's own well-established approach for the evaluation and approval of food ingredients.[5]

In an upcoming special issue of Inhalation Toxicology (expected April 2011), ALCS will report results from a large, multi-year study designed to investigate the effects of individual ingredients on mainstream cigarette smoke toxicity. Constituents of mainstream smoke and biological studies such as genotoxicity and smoke inhalation were analyzed.

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[4] *See* Altria Client Services, Inc., Comments dated August 23, 2010, Docket ID No. FDA-2010-D-0281-0003.1, available at http://www.regulations.gov/#!documentDetail;D=FDA-2010-D-0281-0003.1. This evaluation process is also described in the ALCS Product Integrity Toxicological Framework Guideline, the ALCS Product Integrity Toxicological Guideline – Cigarette Products and the ALCS Product Integrity Review and Toxicological Evaluation Guideline: Smokeless Tobacco Products: Test Articles, Prototypes and Products, which were submitted to FDA on April 29, 2010 as part of PM USA's Tobacco Health Documents Submission.

[5] *See* FDA, *Guidance for Indus. and Other Stakeholders: Toxicological Principles for the Safety Assessment of Food Ingredients* (2000), *available at* http://www.fda.gov/downloads/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodIngredientsandPackaging/Redbook/UCM222779.pdf.

Results indicate that tobacco itself drives the biological activity of cigarette smoke and this biological activity is not impacted by the addition of ingredients as commonly used. While occasional single point-in-time analysis of cigarette smoke may demonstrate a numerical difference between the control (without the test ingredient) and experimental cigarette (with test ingredient), such differences are the result of analytical variability and the intrinsic variability of tobacco.

To determine the acceptability of ingredients for use in smokeless tobacco products we rely on recognized processes for evaluating the safety of ingredients for use in foods.[6] A food ingredient is determined safe for use based on a reasonable certainty that a substance is not harmful under the intended conditions of use.[7] Consideration of knowledge of chemical structures and the outcomes of toxicity studies inform this determination. It is scientifically valid to apply these determinations to ingredients used in smokeless tobacco products because the route of exposure is the same as for foods; hence, an extensive testing program such as described above for cigarettes is not necessary. Overall, ingredients added to smokeless tobacco products will not alter the toxicity of the product provided ingredients are used within limitations supported by available toxicological data.

We urge the FDA to promulgate a final rule that establishes a process focused on whether the addition of, or an increase in, the amount of an additive would increase the inherent toxicity of the tobacco product. Manufacturers can provide comparative internal toxicity testing information as part of their exemption request. Toxicity information is also available in the robust body of published scientific literature that shows additives have little influence on the inherent toxicity of cigarettes[8] or, in the case of smokeless tobacco products, have been demonstrated to be safe for use in foods. Once the Agency decides to grant an exemption request for a particular additive, the Agency should establish a categorical exemption for a range of levels of that additive applicable to all similar products (*e.g.*, all cigarettes or all smokeless tobacco products).

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[6] Additives used in smokeless tobacco products are generally recognized as safe (GRAS) as food ingredients by either FDA, the Flavor and Extract Manufacturers Association, or have undergone a self-GRAS process based on available toxicity information.

[7] *See* Title 21 of the Code of Federal Regulations.

[8] *See* Baker et al., (2004) Anal App Pyrol 71:223-311; Baker et al., (2004) Food Chem Toxicol 42 Suppl:S53-S83; Carmines, (2002) Food Chem Toxicol 40:77-91; Carmines et al., (2005) Food Chem Toxicol 43:1303-1322; Carmines and Gaworski, (2005) Food Chem Toxicol 43:1521-1539; Gaworski et al., (1998) Inhal Toxicol 10:357-38; Gaworski et al., (1999) Toxicology 139:1-17; Gaworski et al., (2008) Food Chem Toxicol 46:339-351; Gaworski et al., (2010) Toxicology 269:54-66; Heck et al., (2002) Inhal Toxicol 14:1135-1152; Heck, (2010) Food Chem Toxicol 48(S2):1-38; Paschke et al., (2002) Beitr Tabakforsch Int 20:107-247; Potts et al., (2010) Exp Toxicol Pathol 62:117-126; Renne et al., (2006) Inhal Toxicol 18:685-706; Roemer et al., (2002) Food Chem Toxicol 40:105-111; Rustemeier et al., (2002) Food Chem Toxicol 40:93-104; Stavanja et al., (2003) J Toxicol Environ Health Part A 66:1453-1473; Stavanja et al., (2008) Exp Toxicol Pathol 59:339-353; Vanscheeuwijck et al., (2002) Food Chem Toxicol 40:113-131.

B. Proposed Requirements About Addictiveness and Appeal to or Use by Minors are Not Required by Statute Nor is Such Information Available.

The proposed rule would require a "certification" "providing the rationale for the official's determination that the modification will not increase the product's toxicity, addictiveness, or appeal to or use by minors . . . " As previously noted in Section VI of our comments on the substantial equivalence guidance, behavioral types of effects are not part of the statutory framework for a substantial equivalence determination. They are also not included in the statutory requirements for a minor modification exemption under 905(j)(3), and, therefore, should be eliminated from the categories of data required by the proposed rule.

The Act has different requirements for the types of data that industry must submit, or that FDA must consider, for 905(j) exemptions as compared to non-substantially equivalent new products, modified risk products or the development of product standards. For example, an evaluation of the risks and benefits to the population as a whole, including users and non users of the tobacco product, and taking into account the increased or decreased likelihood of cessation or initiation of product use, is a criteria for FDA evaluation of non-substantially equivalent new tobacco products.[9] Similar language regarding cessation or initiation effects is also included in describing the criteria for authorization of modified risk tobacco products,[10] and for the development of tobacco product standards.[11] Moreover, an application for authorization of certain types of modified risk tobacco products (*i.e.*, "reduced exposure" products) requires "testing of actual consumer perception" with respect to risks.[12]

In contrast, Congress excluded any consideration of behavioral effects from the substantial equivalence criteria. Thus, the statute precludes consideration of behavioral effects as part of the substantial equivalence evaluation or in the evaluation of minor modification exemption requests.[13]

In addition, the proposed rule's data and certification requirements pose insurmountable practical problems. Specifically, the proposed requirement that manufacturers not only produce information about addictiveness and appeal to, or use by, minors, but also make certifications based on that information, is not viable. We do not believe sufficiently

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[9] *See* 21 U.S.C. § 387j(c)(4).
[10] *See* 21 U.S.C. § 387k(g)(4)(B) & (C).
[11] *See* 21 U.S.C. § 387g(a)(3)(B)(i)(II) & (III).
[12] *See* 21 U.S.C. § 387k(g)(2)(B)(iii).
[13] A well-accepted canon of statutory interpretation is that "where 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." *Keene Corp. v. United States*, 508 U.S. 200, 208 (1993) (*quoting Russello v. United States*, 464 U.S. 16, 23 (1983)). *See also Bailey v. United States*, 516 U.S. 137, 146 (1995) (distinction in one provision between "used" and "intended to be used" creates implication that related provision's reliance on "use" alone refers to actual and not intended use); *Bates v. United States*, 522 U.S. 23, 29 (1997) (inclusion of "intent to defraud" language in one provision and exclusion in a parallel provision indicated intent to defraud was not an element of the offense of knowingly and willingly misappropriating student loan funds).

sensitive tools (with the level of accuracy, reliability, and reproducibility required to make regulatory decisions) exist to measure addictiveness or appeal to, or use by, minors. SCENIHR[14] recently evaluated the potential role of tobacco additives in the addictiveness and attractiveness of tobacco products and noted that there are no universal standards for human studies or agreement about various possible endpoints which define whether an additive or a combination of additives increases the addictive potency or attractiveness of the final tobacco product.[15] Uncertainties of testing aside, there are other issues to consider, particularly as it relates to minors. For example, as a matter of policy, PM USA and USSTC do not conduct consumer or clinical research involving tobacco products with anyone under 21 years of age. As a result, we could not provide the information requested about appeal to, or use by, minors.

Toxicity data will likely be needed to evaluate some minor modification exemption requests and that data must be presented in a truthful and balanced manner. To the extent that the Agency believes it is necessary to require a certification, however, we believe the same certification requirement that applies to a medical device substantial equivalence submission under 21 C.F.R. § 807.87(k)[16] should apply in the exemption request process. Such a certification requirement would be sufficient to alert the petitioner that it must present a truthful and balanced summary of the data on the proposed minor modification, including all material facts.

C. Decisions on 905(j)(3) Exemption Requests Should be Rendered Within 90 Days and Minor Modifications Should be "Deemed Notified" Under 905(j)(1)(A)(ii) Upon Establishment of a Categorical Exemption.

The proposed rule establishes no time period in which the FDA must respond to a 905(j)(3) request. For reasons similar to those articulated in Section I of our comments on the substantial equivalence guidance, we believe the final rule should establish a 90 day review period for 905(j)(3) exemption requests. Such a requirement is logical given the 90 day period Congress established for the FDA to conduct a premarket review of additive

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[14] SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks) is one of three independent non-food Scientific Committees providing the European Commission with the scientific advice needed when preparing policy and proposals relating to consumer safety, public health and the environment.

[15] SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks), 2010. Addictiveness and Attractiveness of Tobacco Additives. European Union, Brussels. Available at http://ec.europa.eu/health/scientific_committees/consultations/public_consultations/scenihr_cons_12_en.htm (accessed March 18, 2001). Additionally, SCENIHR found that the clinical criteria for dependence, laboratory measures of self-administration, and preference measurements in humans which indicate that tobacco has a high addictive potential "have limitations when assessing the addictiveness of individual additives in the final tobacco product." With regard to attractiveness, SCENIHR found that adult tobacco user panel studies and surveys conceivably give only limited information regarding the stimulation to use a product, and there are many other direct and indirect factors such as taste, marketing, price etc., which must also be considered. *See also* Henningfield, J.E., et. al. Conference on abuse liability and appeal of tobacco products: Conclusions and recommendations. Drug Alcohol Depend. (2011), doi:10.1016/j.drugalcdep.2010.12.009 (acknowledging the methodological issues and gaps that need to be addressed in the evaluation of tobacco products for abuse liability and product appeal).

[16] A statement that the submitter believes, to the best of his or her knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted.

additions to tobacco products.[17] Failure to establish an efficient and clear timeframe defeats the Congressional intent in the 905(j)(3) exemptions framework.

The final rule should also allow a manufacturer to provide information in the exemption request that its product is in compliance with the Act and serve as the 905(j)(1)(A)(ii) 90 day notification. Thus, the notification requirement would run concurrently with FDA's review of the exemption request and eliminate the inefficiency of requiring an Agency decision on an exemption request before a manufacturer can submit a 90 day notification to FDA under 905(j)(1)(A)(ii).

Additionally, when the FDA establishes a categorical minor modification exemption for a class of products or modifications (*e.g.*, designated additives), it should be "deemed notified" to the Agency for purposes of compliance with 905(j)(1)(A)(ii).[18] The categorical exemption itself will establish that "the modifications are covered by exemptions granted by the Secretary," and the FDA may limit the terms of the exemption to any "product that is commercially marketed and in compliance with the requirements of this Act." Thus, all of the elements of the required notification will already be known to FDA and, in the case of an additive change, the Agency would receive details regarding the modification under separate requirements, *i.e.*, section 904(c).

D. The Reduction or Elimination of an Additive Should be Categorically Exempt From Substantial Equivalence Requirements.

Sections 904(c)(3) and 905(j)(3) both address the addition or removal of tobacco additives. When a manufacturer reduces or eliminates an additive, section 904(c)(3) requires manufacturers to notify the FDA 60 days *after* entering such a modified product into interstate commerce. This requirement for notification after the fact reflects Congress' determination that premarket review by FDA is not necessary to assess the reduction or elimination of an additive prior to the manufacturer entering the modified product into interstate commerce. FDA's final rule for 905(j)(3) exemptions should be consistent with this Congressional determination and categorically exempt from the substantial equivalence requirements all modifications that reduce or eliminate an additive.

Section 904(c)(3) also requires manufacturers to notify the FDA 60 days *after* entering a product into the market when it "adds or increases an additive that has by regulation been designated by the Secretary as an additive that is not a human or animal carcinogen, or otherwise harmful to health under intended conditions of use."[19] Again, the final rule for 905(j)(3) exemptions should categorically exempt such modifications in recognition of the Congressional determination that additions or increases of "designated" additives do not require a regulatory assessment before a manufacturer enters a product into the market. In

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[17] 21 U.S.C. § 387d(c).

[18] 905(j)(1)(A)(ii) requires a notification of "the basis for such person's determination that . . . the modifications are to a product that is commercially marketed and in compliance with the requirements of this Act, and all of the modifications are covered by exemptions granted by the Secretary."

[19] 21 USC § 387d(c)(3).

addition, the final rule should merge the "designation" regulation process, when established, with the 905(j)(3) substantial equivalence exemption process.

E. Additive Modifications that are Part of Blend Maintenance or the Result of Blend Maintenance Should be Exempt from Substantial Equivalence Requirements.

FDA's Final Guidance for Industry and FDA Staff, Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products, states that "FDA does not intend to enforce the requirements of sections 910 and 905(j) for tobacco blending changes required to address the natural variation of tobacco (e.g., blending changes due to variation in growing conditions) in order to maintain a consistent product." As noted above, these types of adjustments do not constitute "modifications" within the definition of a "new tobacco product." If, however, the Agency does not exclude such adjustments, the final rule should categorically exempt blend changes and associated additive changes required to address the natural variation of tobacco.

Such changes are a practical necessity in the tobacco products industry due to crop variability and availability (beyond a manufacturer's control) to maintain a consistent tobacco product. Congress clearly did not intend that blending adjustments and accompanying changes attributable to the natural variation of an agricultural product would result in a 905(j) report or exemption request with no corresponding public health benefit.

F. The Final Rule Should Allow an Exemption Request to Cover Multiple Products or Even an Entire Category of Products and Allow for Modifications Within a Requested Range.

The Final Rule should clarify that an exemption request, once granted, may cover multiple products, or a category of products produced by a manufacturer, *e.g.*, cigarettes or smokeless tobacco products. In addition, a granted exemption should cover modifications within a requested range. For example, if supported by appropriate toxicological data, a granted exemption should allow a manufacturer to add a particular ingredient to any of its cigarette products up to a specified level, without requiring the manufacturer to file a substantial equivalence report or a duplicative exemption request for each product. Otherwise, the Agency and manufacturers will divert resources on exemption requests or substantial equivalence reports for the same additive with no corresponding public health benefit.

FDA recognizes that it may establish such exemptions in the future as it acquires more information, presumably including from the scientific literature and exemption filings, substantial equivalence reports and other information submitted by manufacturers. The Agency should establish such a pathway for these categorical exemptions in the final rule rather than in the future.

G. The Final Rule Should Provide Exemptions for Non-Additive Modifications.

As described above, the Act does not include adjustments made to maintain consistent product characteristics within the definition of a "new tobacco product." If, however, the Agency disagrees, it should also include exemptions for non-additive minor modifications in the final rule. Such exemptions could cover, for example, blend maintenance adjustments or adjustments in cigarette ventilation to maintain consistent strength of taste in response to agronomic variations. As with the blending adjustments discussed in Section E above, these types of modifications involve only a deliberate and minor "change" to maintain a consistent product.

FDA has the authority to promulgate regulations implementing exemptions for substantial equivalence for non-additive modifications under its 701(a) "authority to promulgate regulations for the efficient enforcement of this Act." As with appropriately focused regulations regarding minor modifications to additives, such regulations would promote regulatory efficiency by reducing the number of unnecessary substantial equivalence reports. FDA should, therefore, broaden the scope of minor modification exemptions in the final rule by allowing for exemptions for non-additive modifications.

Conclusion

We appreciate the opportunity to submit these comments and urge the Agency to incorporate them in the final rule. We look forward to further opportunities to work with the FDA as it develops a process to establish exemptions from the substantial equivalence process.

Sincerely,

James E. Dillard III

Attachment C

Altria Client Services

James E. Dillard III
Senior Vice President
Regulatory Affairs

November 8, 2011

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. FDA-2011-D-0147 (76 Fed. Reg. 55,927 (Sept. 9, 2011)) – Comments on the "Draft Guidance for Industry and FDA Staff: Demonstrating the Substantial Equivalence of a New Tobacco Product: Responses to Frequently Asked Questions"

Altria Client Services ("ALCS") Inc., on behalf of Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC"),[1] submits these comments on the above-captioned draft frequently asked questions document ("Draft FAQ").

First, the Draft FAQ inappropriately announces for the first time FDA's interpretations of key statutory terms. While FAQ documents can be useful in responding to common questions, they should not be used to advance interpretations of key statutory terms or attempt to establish new legal norms.[2]

Second, the Draft FAQ contains serious substantive flaws. It sets forth, without adequate explanation or support, incorrect interpretations of the Family Smoking Prevention and Tobacco Control Act ("FSPTCA"); raises serious constitutional issues; and reflects policy judgments that merit reconsideration. As discussed in greater detail below, in its Final Guidance FDA should:

- delete any suggestion that the definition of "tobacco product" includes the product's label or packaging and acknowledge that a substantial equivalence report or a 910(b) submission is not required based on a label or packaging change that does not modify the product itself;

[1] PM USA and USSTC are wholly-owned subsidiaries of Altria Group, Inc. ALCS provides certain services, including regulatory affairs, to the Altria family of companies. "We" and "our" are used throughout these comments to refer collectively to PM USA and USSTC.

[2] *See* 21 C.F.R. § 10.115(d). An FAQ document by its very nature is not reasonably expected to include new regulatory requirements or novel statutory interpretations, and it is therefore less likely to be among the key resources stakeholders consult in assessing their compliance responsibilities.

Altria Client Services Inc.
2325 Bells Road
Richmond, Virginia 23234
(804) 335-2679
James.E.Dillard@altria.com

- confirm that a change in the name of a tobacco product is not a modification of the tobacco product and does not require a substantial equivalence report or a 910(b) submission;

- confirm that actions that do not change the finished tobacco product, including (1) tightening the range for a tobacco product additive, (2) changing processing aids, or (3) ensuring product consistency, are not modifications of the tobacco product and do not require a substantial equivalence report or a 910(b) submission;

- provide guidance regarding the level of specificity needed in substantial equivalence reports regarding tobacco product additives; and

- delete newly stated requirements that substantial equivalence reports include reports on harmful or potentially harmful constituents and environmental assessments.

I. The Agency Should Delete From The Draft FAQ Any Suggestion That The Statutory Definition Of "Tobacco Product" Includes The Product's Label Or Packaging And Acknowledge That A Substantial Equivalence Report Or Section 910(b) Submission Is Not Required Based On A Label Or Packaging Change That Does Not Modify The Product Itself.

The Draft FAQ asserts, without explanation or support, that "[t]he label and packaging is part of a tobacco product."[3] The Draft FAQ thus concludes that any change to the label or packaging of a tobacco product that occurs after February 15, 2007 makes that product a "new tobacco product" subject to the requirements of Sections 905(j) and 910(b).[4] However, that interpretation is foreclosed by the text, context and purpose of the statute. Furthermore, the Draft FAQ violates administrative law principles,[5] represents a clear break from FDA's previous statements

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[3] Draft FAQ § II; *see id.* § II(A) ("The label and packaging of a tobacco product is considered a 'part' of that product.").

[4] *Id.* § II(A), FAQ1 ("[W]e do not intend to enforce the premarket requirements of sections 905(j) and 910 ... for modifications to product packaging or labels to remove the descriptors 'light', 'mild', or 'low' or similar descriptors to comply with section 911 ...."); *id.* at FAQ2 ("We do not intend to enforce the premarket requirements of sections 905(j) and 910 ... for a tobacco product that was commercially marketed in the United States on February 15, 2007, and that had no modifications ... other than to comply with the graphic warning requirements of section 201 ...."); *id.* at FAQ3 ("[If] the package was changed from a soft pack to a hard pack (or from a hard pack to a soft pack) after February 15, 2007, and this change did not modify the tobacco product in any other way (e.g., a change in moisture content, shelf life, ingredient composition, nicotine delivery, harmful/potentially harmful constituents), and no other modifications were made ... then we do not intend to enforce the premarket requirements of sections 905(j) and 910 ...."); *id.* at FAQ4 ("[If] a modification to font size, ink color, or background color was made to the packaging or labels after February 15, 2007 and no other modifications were made to the tobacco product after February 15, 2007, then we do not intend to enforce the premarket requirements of sections 905(j) and 910 ... for this type of modification, provided the modification does not raise different questions of public health ... and you are in compliance with all other statutory labeling and packaging requirements ....").

[5] The lack of explanation provides a separate ground on which to conclude that the interpretation in the document is invalid. *See, e.g., Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983) (An agency must "articulate a satisfactory explanation for its action including a 'rational connection between the facts found and the choice made.'") (quoting *Burlington Truck Lines, Inc. v. United States*, 371 U.S. 156, 168 (1962)). There is yet another reason to reject the interpretation in the Draft Guidance: it imposes binding legal requirements without

regarding Sections 905(j) and 910,[6] and does not help achieve the legitimate policy goals underlying the statute, which are amply served by other provisions.

A. A Requirement That Manufacturers Make Premarket Submissions For Label and Packaging Changes Would Be Contrary To The Statute.

A label or packaging change does not transform a tobacco product into a "new tobacco product" that requires premarket submissions by a manufacturer. Under the FSPTCA, a manufacturer must obtain FDA authorization to market a "tobacco product" only if the product is a "new tobacco product," meaning either that it was not commercially marketed as of February 15, 2007 or is a "modification" of a "tobacco product" and commercially marketed after that date.[7] After March 22, 2011, the manufacturer of a "new tobacco product" must submit either (1) a report under Section 905(j) seeking an order that the product is "substantially equivalent," or (2) an application for premarket authorization under Section 910.[8]

Due to the major consequences that flow from "new tobacco product" status, we have urged the Agency to confirm our interpretation of the statute.[9] FDA, however, has stated that further elaboration is unnecessary because the meaning of the statute is clear.[10] That certainly is correct in the statute's treatment of the label and packaging issues addressed in the Draft FAQ. However, the Draft FAQ position that altering a product's label or packaging transforms it into a "new tobacco product" by modifying "part" of the tobacco product has no basis in the statute and is utterly inconsistent with it.

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notice-and-comment rulemaking. *See Appalachian Power Co. v. EPA*, 208 F.3d 1015, 1024 (D.C. Cir. 2000); *Paralyzed Veterans of Am. v. D.C. Arena L.P.*, 117 F.3rd 579, 588 (D.C. Cir. 1997).

[6] The definitions FDA set out in its guidance on demonstrating substantial equivalence tracked the statutory language and gave no indication that FDA would view a product's name, label, or packaging to be part of the tobacco product itself. *See* FDA Guidance, *Guidance for Industry and Food and Drug Administration Staff; Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products* (Jan. 5, 2011) at 4, *available at* http://1.usa.gov/pCVt43 (hereinafter, "905(j) Guidance"). The Agency adopted the same definitions in its newly released guidance on premarket review applications under Section 910. *See* FDA Draft Guidance, *Guidance for Industry; Applications for Premarket Review of New Tobacco Products*, at 3 (Sept. 2011), *available at* http://1.usa.gov/pCVt43.

[7] 21 U.S.C. § 387(a)(1).

[8] *See Id.* §§ 387e(j)(1), 387j(a)(2). *See also* 905(j) Guidance at 5 (explaining that the manufacturer of a tobacco product introduced after February 15, 2007, and prior to March 22, 2011, and who submits a report under Section 905(j) prior to March 23, 2011, may continue to market the product unless or until FDA issues an order that the product is not substantially equivalent). In addition, FDA promulgated regulations describing the process for exempting minor changes in tobacco additives from the premarket review requirements. *See* 21 C.F.R. Pt. 1107.

[9] ALCS, Comments dated February 8, 2011, Docket ID No. FDA-2010-D-0635-0005, at 3, *available at* http://1.usa.gov/pwbTbr (hereinafter, "905(j) Comments"); *see also* ALCS, Comments dated March 22, 2011, Docket ID No. FDA-2010-N-0646-0011, at 1 ("We reiterate that there are numerous sources of variability inherent in tobacco products that should not constitute a 'modification.'"), *available at* http://1.usa.gov/nwfDPk.

[10] *See* 76 Fed. Reg. 38,961, 38,962 (July 5, 2011) ("FDA disagrees with the suggestion in the comments that the term 'new tobacco product' has not been sufficiently defined" in the statute.).

1. The label and packaging of a tobacco product are not "part" of the tobacco product.

The Agency's assertion that the label and packaging of a tobacco product are "part" of the tobacco product is inconsistent with the statutory scheme under which FDA operates. An article in interstate commerce is under FDA's jurisdiction if it meets the statutory definition of "food," "drug," "device," "cosmetic," "animal feed," "dietary supplement," or "tobacco product."[11] The statute does not define any of those terms to include the label or packaging of the article.

To the contrary, the statute defines "label" and "package" separately. Both definitions treat these things as discrete items, and not as "parts" of the article itself. "Label" is defined as "a display of written, printed, or graphic matter *upon the immediate container of any article*,"[12] thus making clear that a label is something affixed to the container in which an article is sold, not part of the article itself. Similarly, "package" is defined as the "pack, box, carton, or container … [or] wrapping … *in which a tobacco product* is offered for sale, sold, or otherwise distributed to consumers."[13] This obviously means that a package is external to, and not a part of, the tobacco product.[14] Both definitions preclude the Agency's interpretation in the Draft FAQ.

Moreover, the definition of "tobacco product" itself precludes the Agency's interpretation. The statute defines a "tobacco product" as having three elements: (1) a "product" that (2) is "made or derived from tobacco" and (3) is "intended for human consumption."[15] All three elements must exist to meet the definition, because the definition is conjunctive. Applying this definition makes clear that labels and packaging are not "tobacco products" because they are neither "made or derived from tobacco" nor "intended for human consumption."

Further, the Agency's position is inconsistent with the plain meaning of the word "part"[16] because "part" is generally understood to refer to a portion or subdivision of a larger whole, not something external to it.[17] Thus, "parts" of a tobacco product must be portions of something made or derived from tobacco that is intended for human consumption.

Other definitions in the statute confirm the error of the Agency's reliance on the word "part." For example, the definition of "new tobacco product," includes "part" in a list of terms that refer

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[11] 21 U.S.C. §§ 321(f), 321(g)(1), 321(h), 321(i), 321(w), 321(ff)(3), 321(rr).

[12] *Id.* § 321(k) (emphasis added).

[13] *Id.* § 387(13) (emphasis added).

[14] "Package" is also defined under the Federal Cigarette Labeling and Advertising Act using almost identical wording but with reference to the sale of "cigarettes." 15 U.S.C. § 1332(4). Cigarettes are defined as the "roll of tobacco" itself and not the packaging. *Id.* § 1332(1). Congress, by using the same definition of package under the FSPTCA, is presumed to have intended for the provisions to be interpreted in parallel. *See, e.g.*, *Sullivan v. Stroop*, 496 U.S. 478 (1990).

[15] 21 U.S.C. § 321(rr)(1).

[16] Draft FAQ § II(A).

[17] *See* http://www.merriam-webster.com/dictionary/part (defining "part" as "a constituent member of a machine or other apparatus"); Webster's Third New International Dictionary (Unabridged) (1993) (defining "part" as "one of the equal or unequal portions into which something is or is regarded as divided").

to specific physical changes to the tobacco product,[18] and Section 904(a)(1) includes the phrase "other part" at the end of a list including tobacco, papers, and filters.[19] Under well-settled canons of statutory construction, the word "part" must draw its meaning from the terms around it and thus should be read to refer to a physical element of the tobacco product, such as tobacco, papers, or filters.[20] Similarly, the definition of "characteristics" demonstrates that Congress did not intend to make labels or packaging part of substantial equivalence review. "Characteristics" is defined to include "the materials, ingredients, design, composition, heating source, or other features of a tobacco product."[21] Labels and packaging cannot fit comfortably within that definition.[22]

Finally, at numerous other places in the statute, Congress indicated that a tobacco product's label and packaging are different from, rather than a "part" of, the product. For example, Section 902 contains separate provisions deeming a tobacco product adulterated based on the presence of any "poisonous or deleterious substance" in the product itself *or in its packaging*; and Section 301(qq) prohibits the creation of counterfeit tobacco products by placing an identification device such as a "label ... upon any tobacco product or container *or labeling thereof*."

2. The Draft FAQ Conflicts with the Basic Structure of the Statute.

The Draft FAQ conflicts with the basic structure of the statute, which provides FDA authority to regulate labels and packaging that is wholly separate from the regulation of new tobacco products. Under FDCA provisions applicable to other product categories, labels and packaging are regulated directly, not by implication. For example, FDA regulation of labels and packaging for drug products is based on the statute's general misbranding and new drug approval provisions.[23] The FSPTCA applies that same framework to tobacco products,[24] and absent contrary legislative intent, labels and packaging under the FSPTCA should be treated consistently.

For example, Section 905 requires every manufacturer to register its establishments with FDA and submit a listing of each tobacco product in commercial distribution. This submission

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[18] *See id.* § 387j(a)(1) ("change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient").

[19] 21 U.S.C. § 387d(a)(1) (a manufacturer must list all ingredients "added by the manufacturer to the *tobacco, paper, filter, or other part* of each tobacco product" (emphasis added)).

[20] *See, e.g., Wash. State Dep't of Soc. & Health Servs. v. Guardianship Estate of Keffeler*, 537 U.S. 371, 384 (2003) (canons of *ejusdem generis* and *noscitur a sociis* require that "general words are construed to embrace only objects similar to those enumerated by the specific words" enumerated in the same list) (internal quotation marks omitted); *see also United States v. Tinklenberg*, 131 S. Ct. 2007, 2019 (2011) (absent indication to the contrary, "[i]dentical words used in different parts of a statute are presumed to have the same meaning").

[21] 21 U.S.C. § 387j(a)(3)(B).

[22] Indeed, FDA itself implicitly recognized this difficulty when it provided guidance that the requirement to provide an ingredient list does not apply to "packaging differences that do not affect the characteristics of the product." FDA Guidance, *Guidance for Industry: Listing of Ingredients in Tobacco Products* § III(C) (Nov. 2009), *available at* http://1.usa.gov/pCVt43 (hereinafter "Listing Guidance").

[23] *See, e.g.*, 21 U.S.C. § 355(d)(7); 21 C.F.R. § 201.10.

[24] *See* 21 U.S.C. § 387c.

includes "a copy of all consumer information and other labeling for such tobacco product."[25] Section 911 authorizes FDA to review data and information relating to tobacco products "the label, labeling, or advertising of which represents" that the product presents a reduced risk or lower exposure to a substance.[26] And Section 903, the statute's misbranding provision, provides the Agency with ample tools to combat any potentially "false or misleading" statements, including names.[27] In light of these and other provisions, premarket review is simply unnecessary for changes to product labels or packaging.[28]

If the Agency's interpretation of "tobacco product" is designed to guard against the possibility that a change to a label or packaging could modify the product itself, that interpretation is unnecessary. The Agency's response to FAQ3 notes, for example, the possibility that a switch from a hard pack to a soft pack might lead to "a change in moisture content, shelf life, ingredient composition, [or] nicotine delivery." To the extent FDA has authority to require premarket review in such a case, it is not because the packaging has changed, but because there has been a change to the tobacco product. For example, "ingredients" are among the "modifications" expressly included in Section 910(a)(1)(B) and the characteristics intended to be included in substantial equivalence review.[29] There is no need for FDA to contort the definition of tobacco product to reach those situations.

Perhaps most tellingly, in Section 903(b), Congress expressly provided that FDA may "require prior approval of statements made on the label of a tobacco product"[30] only "by regulation"[31] issued "in accordance with chapter 5 of title 5, United States Code."[32] The Draft FAQ seeks effectively to "require prior approval of statements made on the label" – that is, to require prior FDA authorization of product names – without satisfying the clear and unambiguous requirement

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[25] *See* 21 U.S.C. § 321(m)(1) (the statutory term "labeling" includes "all labels and other written, printed or graphic matter … upon any article or any of its containers or wrappers"). FDA guidance states that "labeling is to be submitted as an exact, legible, full color copy." *See* FDA Guidance, *Guidance for Industry: Registration and Product Listing for Owners and Operators of Domestic Tobacco Product Establishments* (Nov. 2009), *available at* http://1.usa.gov/nDD9mU (hereinafter "Listing Guidance").

[26] *See* 21 U.S.C. § 387k(b).

[27] 21 U.S.C. § 387c(a); *cf.* 21 C.F.R. § 201.10 (regulating drug names in labeling).

[28] Significantly, Section 905(i)(3)(D) reflects a scheme in which FDA receives notification of labeling changes *after* they occur. 21 U.S.C. § 387e(i)(3)(D) (requiring the manufacturer to notify FDA of "[a]ny material change" in biannual updates). This mirrors the Agency's approach in other contexts. For example, FDA guidance regarding the labeling for OTC topical acne drug products states that "[l]abeling that is revised to meet the requirements of this rule should be submitted to FDA through the drug listing process." FDA Guidance, *Guidance for Industry: Topical Acne Drug Products for Over-the-Counter Human Use—Revision of Labeling and Classification of Benzoyl Peroxide as Safe and Effective; Small Entity Compliance Guide* (June 2011), *available at* http://1.usa.gov/pKrtrm.

[29] 21 U.S.C. §§ 387(j)(a)(1)(B), 387(a)(3)(B).

[30] *Id.* § 387c(b).

[31] *Id.*

[32] *Id.* § 387a(d).

that the Agency proceed through notice-and-comment rulemaking.[33] The Agency's use of Draft FAQ in this instance is contrary to law and invalid for this additional and independent reason.[34]

3. Treating Labels and Packaging as "Part" of the Tobacco Product Leads to Unintended Results.

The Agency's interpretation of "tobacco product" is flawed because it leads to unintended results.[35] For instance, Section 904(a)(1) requires a manufacturer to provide FDA a listing of all ingredients "added by the manufacturer to the tobacco, paper, filter, or other part of each tobacco product by brand and by quantity in each brand and subbrand." If the label and packaging were parts of the tobacco product, then a manufacturer would be required to submit a listing, by quantity, of all the ingredients added by the manufacturer to the label of its tobacco products. But it is clear that a "label" (a term that refers to "a display of written, printed, or graphic matter upon the immediate container of any article")[36] could never have "ingredients" to be listed.

The Draft FAQ itself recognizes that results not intended by Congress would follow if labels and packaging were part of the tobacco product. For example, label changes required by Section 911 (to remove descriptors) and Section 201 (to add graphic warnings) would trigger the need for premarket review.[37] To avoid this result, the Agency says it will exercise "enforcement discretion" to allow manufacturers to comply. The Agency also recognizes that its interpretation leads to the conclusion that modifications to font, ink, or color used on a tobacco product's label or packaging might transform it into a new tobacco product,[38] and it likewise relies upon enforcement discretion to the extent those changes do not raise "different questions of public health." As a legal matter, FDA cannot cure an incorrect statutory interpretation by invoking enforcement discretion. Doing so is also bad policy because it blurs the line between lawful and prohibited conduct.

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[33] Even if FDA had proceeded by regulation as described in Section 903(b), it could not have required premarket review of product names under Sections 905(j) and 910(b) because, as shown above, that interpretation is unambiguously foreclosed by other statutory provisions and the statutory context and purpose.

[34] The notion that label and packaging changes trigger premarket review under Sections 905(j) and 910(b) also cannot be reconciled with Title II of the FSPTCA, which includes specific amendments addressing many aspects of product labels. Title II delimits the scope of FDA's ability to regulate the content of product labels and also reflects Congress's intention not to empower FDA to regulate the content of labels indiscriminately. *See, e.g.*, 15 U.S.C. § 1333 (specifying warning content and format for cigarettes).

[35] *Cf. Nixon v. Missouri Mun. League*, 541 U.S. 125, 138 (2004) (explaining canon against "'construe[ing] a statute in a manner that leads to absurd or futile results'").

[36] 21 U.S.C. § 321(k).

[37] Draft FAQ § II(A), FAQ1 and FAQ2.

[38] *Id.* § II(A), FAQ4

II. FDA Should Confirm That A Product's Name Is Not "Part" Of A Tobacco Product, And That Name Changes Do Not Require Substantial Equivalence Reports or Section 910(b) Submissions.

In the Draft FAQ the Agency incorrectly asserts that any change to the name of a product after February 15, 2007 makes that product a "new tobacco product" subject to the requirements of Sections 905(j) and 910(b).[39] Nothing in the FSPTCA supports that construction. As discussed above, the word "part" must be understood to refer to a *physical* element within the tobacco product;[40] a name does not qualify. Moreover, the structure of the statute precludes construing labels and packaging (and thus, the names printed on them) to be parts of the tobacco product.[41] Likewise, there is no need to depart from the unambiguous text with respect to names.

Congress knew how to refer to product names when that was its intention. For example, Section 904 contains multiple reporting requirements—such as reporting of ingredient, nicotine, and constituent information—that require submissions to be made on a brand and subbrand basis.[42] Section 915 likewise requires the testing and reporting of constituents, ingredients, and additives for each brand and subbrand.[43] Section 301(qq) prohibits the sale of a tobacco product that misrepresents its name as that of another.[44] In addition, the relevant provisions specifically use "brand name" and related terms when Congress intended for FDA to regulate these commercial designations. There is no comparable reference to names in the definition of "tobacco product" or "new tobacco product."[45] Had Congress intended to regulate product names through these definitions, it would have said so explicitly.[46]

In addition, including a product's name in the definitions of tobacco product and new tobacco product would violate the First Amendment's Free Speech Clause. Brand names are protected as commercial speech.[47] An interpretation of the FSPTCA that would require manufacturers to obtain FDA authorization before changing the names of their products would impose a

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[39] In particular the Draft FAQ states that (1) a cigarette would be a new tobacco product "if the cigarette was marketed on February 15, 2007, but subsequently the name of the product was modified or changed," and (2) if a manufacturer markets a cigarette as "Brand X" on February 15, 2007, and, after that date, continues to market Brand X but also begins to market the identical cigarette under the additional name "Brand Y," then Brand Y "is a new tobacco product subject to the premarket review requirements."

[40] *Supra* § 1.

[41] *Supra* § 2.

[42] *See, e.g.*, 21 U.S.C. § 387d(a)(1). FDA guidance for Section 904 states that "[e]ach product for which an ingredient list is submitted is to be clearly and uniquely identified by its brand and subbrand, [as well as additional information] as needed to uniquely identify the brand and subbrand of the product." Listing Guidance § III(C)(2).

[43] 21 U.S.C. § 387o(b)(1).

[44] 21 U.S.C. § 331(qq).

[45] *E.g.*, 21 U.S.C. §§ 387(2), 387(6), 387o(b); 21 C.F.R. Part 1140.

[46] *See Whitman v. Am. Trucking Assns., Inc.*, 531 U.S. 457, 468 (2001) ("Congress . . . does not, one might say, hide elephants in mouseholes").

[47] *See, e.g., San Francisco Arts & Athletics v. United States Olympic Comm.*, 483 U.S. 522, 535 & 537 n.16 (1987) (the "Olympic" mark receives First Amendment protection as commercial speech); *Friedman v. Rogers*, 440 U.S. 1, 11 (1979) ("The use of trade names . . . is a form of commercial speech . . . .").

constitutionally suspect prior restraint.[48] Such restraints are impermissible absent procedural safeguards sufficient to protect against the "danger of suppressing constitutionally protected speech."[49]

The Draft FAQ, however, provides no information regarding the standards or procedures FDA would employ when evaluating name changes or additional names. Neither the Draft FAQ nor any other FDA pronouncement regarding Section 905(j) indicates how the Agency would intend to judge names or determine whether a "new" name is substantially equivalent. Such standardless discretion to allow or disallow otherwise lawful speech violates traditional principles of prior restraint under the First Amendment.[50]

A blanket prohibition on all new names that have not obtained FDA authorization—a process that could prevent a manufacturer from engaging in speech for a period of months or years (if the speech is allowed at all)—would also clearly violate the *Central Hudson* test for assessing the constitutionality of restrictions on commercial speech.[51] Such a prohibition would bar speech regarding lawful products and applies to all names without regard to whether they are misleading or not. Moreover, it is unnecessary to advance any governmental interest in ensuring that names comply with the provisions of the FSPTCA because, as explained above, other provisions of the statute provide FDA with the tools it needs to advance this interest in a less restrictive way.[52]

At the very least, the Agency's interpretation raises sufficiently grave constitutional questions that a reviewing court would construe the statute to exclude names from the definitions of "tobacco product" and "new tobacco product."[53] Because the interpretation proposed in the

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[48] *See, e.g., Southeastern Promotions, Ltd. v. Conrad*, 420 U.S. 546, 558 (1975) ("Any system of prior restraint . . . comes to this Court bearing a heavy presumption against its constitutional validity.") (internal quotation marks omitted); *New York Magazine v. MTA*, 136 F.3d 123, 131-32 (2d Cir. 1998) (affirming injunction of prior restraint on commercial speech).

[49] *Freedman v. Maryland*, 380 U.S. 51, 58 (1965) (A system of prior restraint "avoids constitutional infirmity only if it takes place under procedural safeguards designed to obviate the dangers of a censorship system."). Congress's sensitivity to this issue is reflected in the requirement in Section 903(b) that any requirement for prior approval of label statements be established by regulation only after notice-and-comment procedures.

[50] *Shuttlesworth v. Birmingham*, 394 U.S. 147, 150-51 (1969) ("[A] law subjecting the exercise of First Amendment freedoms to the prior restraint of a license, without narrow, objective, and definite standards to guide the licensing authority, is unconstitutional."). In addition, the absence of a fixed deadline by which FDA must make a substantial equivalence determination weighs heavily against the constitutionality of the proposed interpretation. *Cf. Nutritional Health Alliance v. Shalala*, 144 F.3d 220, 228 (2d Cir. 1998) (upholding FDA review of dietary supplement labels on the basis of a statutory deadline for completion of such review).

[51] *Central Hudson Gas & Electric Corp. v. Public Service Commission*, 447 U.S. 557 (1980).

[52] For example, manufacturers could notify FDA of name changes by updating their ingredient submissions under Section 904, or through regular product listing submissions. *See supra* notes 28 and 42.

[53] As noted, the text, context, and structure of the statute unambiguously foreclose the interpretation in the Draft FAQ under which FDA could require a Section 905(j) or a Section 910(b) submission for a change to the label or packaging of a tobacco product. Even if the statute were ambiguous, however, the ambiguity would have to be resolved against the speech-restrictive interpretation under the avoidance canon. *Edward J. DeBartolo Corp. v. Fla. Gulf Coast Bldg. & Constr. Trades Council*, 485 U.S. 568, 575 (1988) ("[W]here an otherwise acceptable construction of a statute would raise serious constitutional problems, the Court will construe the statute to avoid such problems unless such construction is plainly contrary to the intent of Congress.").

Draft FAQ is plainly not required by the statute, (and, indeed is contrary to it), these constitutional infirmities must be avoided in the Final Guidance.

III. FDA Should Confirm That Actions That Do Not Change The Finished Tobacco Product Are Not Modifications Within The Meaning of 910(a)(1)(B) And Do Not Require A Substantial Equivalence Report Or A 910(b) Submission.

In a number of instances, the Draft FAQ indicates that manufacturer actions that do not change the finished tobacco product may nonetheless constitute "modifications" that require a substantial equivalence report or a 910(b) submission. As explained below, these statements are inconsistent with the statute, which imposes premarket review obligations only upon modifications "of a tobacco product."[54] These aspects of the Draft FAQ should therefore be removed from the Final Guidance.

A. FDA Should Affirm That Tightening The Range For A Tobacco Product Additive Is Not A Modification Within The Meaning of 910(a)(1)(B).

FDA should affirm that a manufacturer's decision to make the specification range for a product additive more precise, but still within the previously reported range, does not constitute a modification that would trigger premarket review. The Draft FAQ currently takes the opposite view. FDA's response to FAQ9 states that "[a]ny modification made to the level of an additive" would require premarket clearance. This interpretation is overbroad.

We agree that a change to a static specification (*e.g.*, from 0.003 to 0.005) or expanding a range specification for tobacco product additive (*e.g.*, from 0.003-0.005 to 0.003-0.007) will likely result in a modification to the finished product triggering the need for premarket review. Tightening the range for an additive (*e.g.*, from 0.003-0.005 to 0.003-0.004), however, is different. In such cases, the "new" product by definition will fall within the permissible range of the "old" product. FDA should clarify that, in such situations, the finished product is not modified such that it requires premarket clearance.

Otherwise, the Agency will use valuable resources reviewing substantial equivalence reports for products that have not actually been modified. Assuming the only change between two products is a narrowed range for an additive, the new and predicate products would necessarily share the same characteristics and thus be substantially equivalent.[55] In addition, requiring premarket review in these circumstances would discourage manufacturers from continuing to refine and improve their manufacturing processes and controls. FDA should avoid these problems by making clear in the Final Guidance that increasing the precision of an additive specification within a preexisting range does not constitute a modification of a tobacco product.[56]

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[54] 21 U.S.C. § 387j(a)(1)(B).

[55] 21 U.S.C. § 387j(a)(3)(A)(i).

[56] As we previously noted, FDA's support for the concept of "design space" in the pharmaceutical industry counsels against the view that increasing the precision of a specification range constitutes a product modification. *See* 905(j) Comments at n.11 ("'Working within the design space is not considered as a change. Movement out of the design space is considered to be a change and would normally initiate a regulatory postapproval change process.'" (quoting

B. A Change In A Processing Aid That Does Not Have An Identifiable Effect On The Tobacco Product Is Not A Modification Within The Meaning of 910(a)(1)(B).

The statutory definition of new tobacco product is only triggered by an actual "modification" of "a tobacco product."[57] The statute refers to "any modification (including a change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient)."[58] This statutory language clearly does not reach changes in manufacturing processes unless they result in an identifiable change to the product (or the components, parts, or constituents thereof).

Nevertheless, in response to Question 11, the Agency states that premarket review would be required if a supplier begins using a new processing aid for a subcomponent of a tobacco product even if any resulting change "is so minor that it is not even capable of being quantified in the finished product." The Agency's apparent reasoning is that even if no quantifiable change has been made to the finished product, the switch in a subcomponent processing aid "may" nevertheless "have an impact on other characteristics within the tobacco product."

The Agency's response reflects a flawed analysis that is inconsistent with the statute. If Congress had intended to require premarket review solely on the basis of a change in manufacturing process, it would have said so.[59] In the final guidance, FDA should clarify that, absent an identifiable change to the resulting product, there is no modification within the meaning of Section 910(a)(1)(B).[60]

FDA Guidance For Industry: Q8 Pharmaceutical Development, at 2 (May 2006), available at http://1.usa.gov/pJpK2N)).

[57] 21 U.S.C. § 387(a)(1)(B).

[58] *Id.*

[59] Other provisions of the FSPTCA support this conclusion. "[R]aw materials used in manufacturing a component, part, or accessory of a tobacco product" are excluded from the statutory definition of "tobacco product." *See* 21 U.S.C. § 321(rr)(1). A change in raw material therefore cannot amount to a modification of a tobacco product unless the change results in identifiable alteration of the finished product. The same logic should apply to manufacturing processes, which are not mentioned in the tobacco product definition and are regulated under different provisions of the FSPTCA that direct FDA to establish manufacturing controls through regulations. *See* 21 U.S.C. § 387f(e)(1)(A). Moreover, in light of the explicit statutory requirement to include information about the manufacturing process in a Section 910 application, *see id.* § 387j(b)(1)(C), the absence of any specific requirement to include that information in a substantial equivalence report indicates that Congress did not view a change in the manufacturing process alone as triggering premarket review.

[60] At a minimum, FDA should clarify that the *possibility* of an unquantifiable change is not a modification. The response to FAQ11 justifies its conclusion by noting that a change in processing aid "*may* have an impact on other characteristics within the tobacco product (e.g., *may* alter chemical reactions and create a new ingredient, additive, or constituent)." (Emphases added). Such speculation is inconsistent with the premise of the question (that there was no quantifiable change to the finished product) and, in all events, is no basis for expanding the scope of the FSPTCA's premarket review requirements.

C. Adjustments Made To Ensure Product Consistency Are Not Modifications Within The Meaning Of 910(a)(1)(B).

We previously asked the Agency to confirm that the frequent adjustments a manufacturer must make to maintain consistent product characteristics are not "modifications" within the meaning of Section 910(a)(1)(B).[61] FAQ8 provides a partial response by stating that FDA will use its "enforcement discretion" to allow "tobacco blending changes required to address the natural variation of tobacco." While we agree that consistency-maintaining changes are permissible, we do not agree that such changes implicate FDA's enforcement discretion. Rather, adjustments made by a manufacturer to maintain consistent product characteristics are not modifications within the meaning of Section 910(a)(1)(B). In the final guidance, FDA should acknowledge that Section 910 does not apply in this scenario.

IV. FDA Should Provide Guidance Regarding The Level Of Specificity Needed In Substantial Equivalence Reports Regarding Tobacco Product Additives.

In response to requests that FDA identify the level of specificity required for 905(j) reports when reporting the amounts and levels of additives in products, FAQ 13 says that it is the manufacturer's responsibility to "present the data in a form that will provide the basis for" substantial equivalence review. It is unrealistic to expect stakeholders to predict in advance the level of the specificity that the Agency will require. Moreover, the Agency's failure to provide more specificity could lead to inconsistent applications from manufacturers and to inconsistent reviews within the Center for Tobacco Products. FDA should, therefore, provide a substantive response to FAQ13 and reopen public comment to provide an opportunity for meaningful public participation.

V. New Requirements For Substantial Equivalence Reporting Should Not Be Added in This FAQ Document.

A. Substantial Equivalence Reports Should Not Require Reporting On Harmful Or Potentially Harmful Constituents.

We urge the Agency to reconsider its response to FAQ17 that manufacturers "provide information regarding harmful or potentially harmful constituents ("HPHC") as appropriate to demonstrate that the new tobacco product is substantially equivalent to the predicate product."[62] In its Final Guidance the Agency should state that HPHC data will not be required in Section 905(j) reports.

Any requirement that substantial equivalence reports contain HPHC data would be contrary to the FSPTCA. Substantial equivalence review is based on a comparison of the "characteristics"

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[61] 905(j) Comments at 3.

[62] ALCS previously provided comments on the 905(j) Guidance stating that substantial equivalence review should not require HPHC reporting. *See* 905(j) Comments at 7-8; *cf.* 905(j) Guidance at 11 ("For all products, you should report levels of all HPHC in tabular format, with a side-by-side comparison with the predicate tobacco product and, where applicable, to a grandfathered tobacco product.").

of the new and predicate products.[63] The statute defines the term "characteristics" to mean "the materials, ingredients, design, composition, heating source, or other features of a tobacco product."[64] Constituents are thus not included in the list of characteristics that are part of substantial equivalence review. Nor can the trailing phrase "other features of a tobacco product" be read to include constituents. The FSPTCA specifically defines the term "smoke constituent,"[65] and constituents are expressly regulated throughout the statute.[66] Moreover, the different schedules for reporting ingredients and constituents make clear that the statutory term "ingredient" does not include constituents.[67] Had Congress meant to include constituents as part of substantial equivalence review, it would have done so expressly.

The Agency's position that substantial equivalence reports must contain HPHC data also raise practical difficulties that further indicate that Congress did not intend this requirement. Manufacturers were required to file initial 905(j) reports by March 2011, well before the Agency's April 2012 deadline to publish a list of HPHCs and the April 2013 deadline to promulgate regulations for testing and reporting.[68] Obviously, manufacturers cannot test against a list that does not exist. Moreover, the current pending 905(j) reports generally rely on tobacco products that were on the market as of February 15, 2007 as predicates for the substantial equivalence comparison. Given the passage of time, it is unlikely that cigarettes and smokeless tobacco products that were on the market as of February 15, 2007 still exist in quantities sufficient to enable the testing necessary to generate HPHC data for most, if not all, predicate products.[69]

Thus, a requirement that HPHC reporting be included in 905(j) reports is contrary to law and creates substantial practical difficulties. The Agency's Final Guidance should make clear that reporting on HPHCs is not required as part of substantial equivalence review.

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[63] *See* 21 U.S.C. § 387j(a)(3)(A).

[64] 21 U.S.C. § 387j(a)(3)(B).

[65] 21 U.S.C. § 387(22).

[66] *See, e.g.*, 21 U.S.C. §§ 387g(a)(4)(A)(ii), 387g(a)(4)(B)(i) (FDA has authority to promulgate tobacco product standards addressing constituents); *id.* § 387o(b)(1) (directing FDA to promulgate regulations for the "testing and reporting of tobacco product constituents, ingredients, and additives"). *See also* Altria Client Services, Inc., R.J. Reynolds Tobacco Co., and Lorillard Tobacco Company, Comments dated October 11, 2011, Docket ID No. FDA-2011-N-0271, at 1 & n.5 (hereinafter, "2011 HPHC Comments").

[67] *See* 21 U.S.C. §§ 387d(a)(1), 387d(a)(3); *see also id.* §§ 387g(a)(1)(A), 387g(a)(3)(B)(ii) (indicating that "constituents" and "additives" are conceptually distinct categories under the FSPTCA).

[68] *See* 21 U.S.C. §§ 387d(d)(1), 387d(e), 387(o)(b)(1).

[69] For a fuller discussion related to HPHCs, we refer the Agency to previous submissions in which we discuss our experience with tobacco constituent testing and evaluation of such data as part of our ingredient testing program. *See* Altria Client Services, Inc., Comments dated August 23, 2010, Docket ID No. FDA-2010-D-0281-0003.1, *available at* http://1.usa.gov/oLwObl; *see also* 2011 HPHC Comments.

B. FDA Should Exempt Substantial Equivalence Reports From The Environmental Assessment Requirement.

In response to Question 18, FDA states that all Section 905(j) reports must include environmental assessments under 21 C.F.R. § 25.15(a). This requirement is new and was not stated or implied in the final 905(j) Guidance FDA published in January 2011.[70] In fact, this new requirement was not announced until almost six months *after* manufacturers submitted their initial 905(j) reports in March 2011. This new requirement is thus procedurally improper with respect to reports previously submitted by manufacturers and, at a minimum, the Agency should clarify that this newly stated requirement does not apply to them. It would make no sense to apply the requirement to these reports because they pertained to products that were on the market in March 2011. The intent of these reports is to obtain an agency determination that such products are substantially equivalent to one or more predicate products that were on the market on or before February 15, 2007. In other words, the only requested agency action is to maintain the status quo—not the type of agency action that requires an environmental review.

More fundamentally, substantial equivalence reports for tobacco products are not included among the agency actions for which an environmental assessment is necessary under 21 C.F.R. § 25.20. To the extent the Agency wishes to amend Part 25 to include tobacco products, it must do so through formal notice and comment rulemaking.[71]

Requiring environmental assessments for substantial equivalence is also substantively unjustified, and FDA should establish a categorical exemption from the environmental assessment for all 905(j) reports. Essentially every other FDA-regulated industry benefits from a categorical exemption for agency actions similar to substantial equivalence determinations. In each of these industries, FDA has taken the position that environmental assessments are not necessary if the requested agency action does not increase overall use of the product type.[72] Section 905(j) reports seek only an agency determination that a given product is equivalent to, and thus likely to compete with or replace, products that already are or have been on the market. Therefore, 905(j) reports should be categorically exempt from the environmental assessment requirement.

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[70] The Preface of the 905(j) Guidance states that the Agency's intent in promulgating the guidance was to clarify "FDA's expectations regarding 905(j) reports" in "sufficient time" for stakeholders to prepare submissions prior to March 2011. The guidance specifically represented that it included a list of "the information [FDA] believes a typical 905(j) report may need to include." 905(j) Guidance at 7.

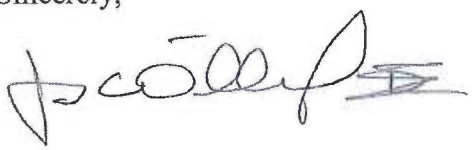
[71] When the Agency has expanded the scope of other preexisting regulations to include tobacco products, it has done so by amendment to the regulation. *See, e.g.*, 76 Fed. Reg. 20,901 (Apr. 14, 2011). From both a consistency and an administrative law perspective, *see supra* note 5. FDA should take the same approach here and undertake notice-and-comment rulemaking before substantively amending Part 25.

[72] *See, e.g.*, 21 C.F.R. §§ 25.15(c) (agency actions that "do not significantly affect the quality of the human environment" are ordinarily excluded), 25.30(k) (labeling changes that do not affect levels of use); 25.31(a) (new drug approval applications that will not "increase the use of the active moiety"), 25.31(g) (bioequivalence determinations for human drugs and comparability determinations for biologics), 25.32(f) (determinations that food is GRAS if it is already marketed for the proposed use), 25.33(a) (new animal drug approval applications that will not increase use), 25.34(b) (device classification determinations that will not increase or expand the use of the device), 25.34(d) (class III medical device approvals if the device is of the same type and use of a previously approved device), 25.34(f) (restricted device regulations that will not expand or increase the use of the product).

* * * * *

We appreciate the opportunity to submit these comments and urge the Agency to revise the Draft FAQ as described above. We look forward to further opportunities to provide comments to the Agency as its thinking on substantial equivalence continues to evolve.

Sincerely,



James E. Dillard III

Altria
Altria Client Services

James E. Dillard III
Senior Vice President
Regulatory Affairs

April 8, 2014

Via Electronic Submission

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. FDA-2013-N-1282 (79 Fed. Reg. 3742 (Jan. 23, 2014)) — Comments on "Proposed Rule: National Environmental Policy Act; Environmental Assessments for Tobacco Products; Categorical Exclusions" ("Proposed Rule")

Altria Client Services Inc. ("ALCS"), on behalf of Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC"),[1] submits these comments to the U.S. Food and Drug Administration ("FDA" or "the Agency") in response to the above-captioned *Federal Register* notice ("Notice").

We support the Agency's proposal to amend 21 C.F.R. Part 25 to provide a categorical exclusion ("CE") for FDA's actions related to substantial equivalence ("SE") reports for "provisional" tobacco products ("Provisional SE Reports") under Section 910(a)(2)(B) of the Federal Food, Drug and Cosmetic Act ("FDCA"). We agree with FDA that the best available information demonstrates that those actions will not significantly affect the quality of the human environment individually or cumulatively. In fact, we believe that the same information also supports CEs for FDA's other actions relating to SE reports – namely, FDA's actions on SE reports under Section 910(a)(2)(A) of the FDCA for non-"provisional" tobacco products ("Non-Provisional SE Reports"), and on FDA actions on requests for an exemption from demonstrating substantial equivalence under Section 905(j)(3) of the FDCA ("SE Exemption Requests").

[1] PM USA and USSTC are wholly-owned subsidiaries of Altria Group, Inc. ALCS provides certain services, including regulatory affairs, to the Altria family of companies. "We" and "our" are used throughout these comments to refer collectively to PM USA and USSTC.

Altria Client Services Inc.
2325 Bells Road
Richmond, Virginia 23234
(804) 335-2679
James.E.Dillard@altria.com

Accordingly, we propose that the Agency revise the proposed rule to provide CEs for all classes of actions involving an affirmative SE determination or the granting of an SE exemption under the FDCA. In addition, we urge the Agency to revise its descriptions of the extraordinary circumstances applicable to the new CEs so that the descriptions more closely follow the language of the regulations codifying them.[2]

I. Introduction.

Categorical exclusions apply to categories of agency actions that have been determined not to have a significant effect on the quality of the human environment either individually or cumulatively. Because actions qualifying for a CE should not meet the "significance" threshold triggering National Environmental Policy Act ("NEPA") review, those actions generally do not need an environmental assessment ("EA") or an environmental impact statement ("EIS") under the statute.[3]

Federal courts often address the propriety of categorically excluding agency actions from NEPA's EIS requirement in terms of those actions' effects on the status quo. Courts have explained that where an agency action would not change the status quo, an EIS is not necessary.[4] Courts, therefore, recognize that CEs are appropriate in situations where the agency action does not result in a change to the status quo.[5] FDA's proposed CE for actions on Provisional SE Reports reflects the rationale of those courts.

II. FDA's Proposed Categorical Exclusion of Actions on Provisional SE Reports is Appropriate.

As described in the Notice, FDA proposes to issue a CE for Agency actions related to making SE determinations for "provisional" tobacco products. "Provisional" tobacco products are those that first entered the marketplace or were modified between February 15, 2007, and March 22, 2011, and for which an SE report was submitted to FDA by March 22, 2011.[6] These products may remain on the market unless FDA issues an order that they are not substantially equivalent to a tobacco product or products marketed in the United States as of February 15, 2007.[7] We agree that the Agency's SE determinations on Provisional SE Reports should be covered by a categorical exclusion.

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[2] Compare 79 Fed. Reg. 3742, 3746 (descriptions) to 21 C.F.R. § 25.21(a) and (b) (regulations).
[3] 40 C.F.R. § 1508.4.
[4] See e.g., San Louis & Delta Mendota Water Authority v. Jewell, 2014 U.S. App. LEXIS 4781, 173-74 (9th Cir., March 13, 2014); Upper Snake River Chapter of Trout Unlimited v. Hodel, 921 F.2d 232, 235 (9th Cir. 1990); Pacific Coast Fed'n of Fishermen's Ass'ns v. DOI, 2014 U.S. Dist. LEXIS 015072, 79-80 (E.D. Cal., Feb. 6, 2014) ("an action that does not change the status quo cannot cause any change in the environment and therefore cannot cause effects that require [NEPA] analysis").
[5] See Sierra Club v. Hassell, 636 F.2d 1095, 1099 (5th Cir. 1981); see also Nat Res. Def. Council v. Vaughn, 566 F. Supp. 1472, 1475-1476 (D.D.C. 1983).
[6] 21 U.S.C. § 387j(a)(2)(B).
[7] *Id.*

FDA correctly recognizes in the Notice that its actions related to Provisional SE Reports will not significantly affect the quality of the human environment individually or cumulatively. Determining that a "provisional" tobacco product is substantially equivalent for purposes of Section 910(a)(2)(B) simply allows that product to remain on the market.[8] By their nature, "provisional" tobacco products are the products currently being manufactured, used and ultimately disposed. They are part of the environmental baseline – indeed, some of these products could have been on the market for over seven years.

An FDA determination allowing a product that already is on the market to remain there will neither increase overall consumption of tobacco products in the United States, nor alter consumption trends.[9] As a result, FDA's actions on Provisional SE Reports will not alter the environmental impacts currently associated with the manufacture, use, or disposal of tobacco products. In other words, FDA's actions on Provisional SE Reports will not significantly affect the quality of the human environment because they do not alter the status quo.

III. FDA Also Should Issue CEs for the Other Classes of Agency Actions Involving "Substantially Equivalent" Tobacco Products.

In addition to providing a CE for Agency actions related to Provisional SE Reports, FDA should provide CEs for two other types of FDA actions: (1) Agency actions on Non-Provisional SE Reports under Section 910(a)(2)(A) of the FDCA; and (2) Agency actions on SE Exemption Requests under Section 905(j)(3) of the FDCA.

FDA's assessment of reasonably foreseeable environmental effects associated with manufacturing and use of products covered by the proposed CE for Provisional SE Reports applies equally to Agency actions on Non-Provisional SE Reports and on SE Exemption Requests. For reasonably foreseeable impacts associated with product manufacturing, FDA considered the 2011 Toxics Release Inventory ("TRI") National Analysis and concluded that "the amount of waste released, recycled, and treated due to the manufacture of ***all tobacco products*** on the market is a fraction of the total toxic waste released from and managed in industrial facilities in the United States."[10] For possible impacts from product use, the Agency considered tobacco product consumption rates, secondhand smoke from cigarettes, and environmental impacts resulting from the use of smokeless tobacco products and concluded "that ***any new tobacco products*** that receive marketing authorization through the ***available pathways***" would have less or no more environmental impact than that of tobacco products currently on the market."[11] Because FDA's analysis of reasonably foreseeable impacts from product manufacturing and use accounted for the entire tobacco product market as well as any new tobacco products entering the market following FDA actions on Non-Provisional SE Reports and SE Exemption Requests, that analysis and the

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[8] *Id.*

[9] The FDA correctly observes that tobacco product consumption in the United States is steadily decreasing. *See* 79 FR 3742, 3745 (Jan. 23, 2014). Agency determinations allowing "provisional" SE products to remain on the market would not affect this trend.

[10] 79 Fed. Reg. at 3744 (emphasis added).

[11] *Id.* at 3745 (emphasis added).

proposed CE should apply to those types of FDA actions the same as it applies to FDA actions on Provisional SE Reports.

Other aspects of the rationale underlying FDA's proposed CE for Provisional SE Reports also support CEs for Non-Provisional SE Reports and SE Exemption Requests because FDA's actions on Non-Provisional SE Reports and on SE Exemption Requests are virtually identical to its actions on Provisional SE Reports. Non-Provisional SE Reports differ from Provisional SE Reports in that Non-Provisional SE Reports concern products not currently on the market. For several reasons, however, that difference should not cause the Agency's actions on Non-Provisional SE Reports to significantly affect the quality of the human environment.

First, when FDA makes an SE determination for a non-"provisional" tobacco product, that determination is unlikely to result in a larger overall tobacco product market. As with "provisional" SE products, the only reasonably foreseeable effect of FDA finding a non-"provisional" product substantially equivalent to a predicate product or products would be a potential change in the market share held by the manufacturer, but otherwise would not change the status quo. FDA's actions on Non-Provisional SE Reports, therefore, should not result in significant impacts on the quality of the human environment, either individually or cumulatively.

Second, FDA's SE determination for Non-Provisional SE products is based on the same standard as its determinations for Provisional SE products. That standard, set forth in the FDCA's definition of SE, will help ensure that agency actions on Non-Provisional SE Reports will not exceed NEPA's significance threshold.[12] The SE standard limits FDA's SE determinations to only those products that: (a) have the same characteristics (*i.e.*, materials, ingredients, design, composition, heating source or other features); or (b) do not raise different questions of public health compared to the predicate product or products.[13] As a result, the SE standard itself will help prevent FDA's actions on Non-Provisional SE Reports from significantly affecting the quality of the human environment. FDA's extraordinary circumstances review, requiring NEPA review in the rare case where the Agency's action on a "substantially equivalent" product may have significant environmental impacts, will further ensure protection of the quality of the human environment.

Finally, our experience providing environmental assessments for all of our Non-Provisional SE Reports supports the conclusion that "substantially equivalent" tobacco products are unlikely to result in significant environmental effects. Our consultant, ERM, has prepared all of the EAs for our SE Reports that include both Non-Provisional and Provisional SE Reports for both cigarettes and smokeless tobacco products. ERM's April 1, 2014, memorandum summarizes its approach and conservative assumptions for conducting our EAs.[14] ERM concluded that, even under worst-case scenarios, no significant environmental impacts were associated with the requested Agency action on our Provisional and Non-Provisional SE Reports.

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[12] 21 U.S.C. § 387j(a)(3)(A)-(B).
[13] *See id.*
[14] Attached as Appendix A.

For SE Exemption Requests, the reasonably foreseeable environmental effects would be even less significant. As with FDA's actions on Provisional and Non-Provisional SE Reports, the environmental effects of the Agency's actions associated with SE Exemption Requests would be limited by the decreasing total tobacco product consumption, the definition of "substantial equivalence" under the FDCA, and the operation of FDA's extraordinary circumstances review. And, those effects would be limited further by the circumstances appropriate for granting SE Exemption Requests.

FDA may exempt a proposed tobacco product from the substantial equivalence requirements of Section 910(a)(3) of the FDCA only if it represents a "minor modification" of a tobacco additive in an existing tobacco product and an SE report "is not necessary to ensure that permitting the tobacco product to be marketed would be appropriate for protection of the public health."[15] Because SE exemptions are appropriate only in limited circumstances, FDA's actions granting SE exemptions do not alter the status quo and cannot significantly affect the quality of the human environment for purposes of NEPA.

Finally, authorizing CEs for Agency actions associated with Non-Provisional SE Reports and SE Exemption Requests, in addition to issuing a CE for Provisional SE Reports, would be consistent with FDA's regulatory approach to premarket clearances and approvals for other product categories regulated by the Agency. Nearly every other category of FDA-regulated products benefits from CEs that cover all classes of similar agency actions as long as each similar class of actions independently meets the criteria for a CE. For each of those categories of products, FDA has taken the reasonable position that NEPA analysis is not necessary if the agency actions for a product type are not expected to increase overall use of the product.[16]

Limiting CEs to only some FDA SE actions is not necessary given that none of FDA's three possible affirmative SE actions is expected to increase overall use of the product types in question or expand tobacco product consumption, and none is expected to significantly affect the quality of the human environment individually or cumulatively. The three FDA SE actions all should receive the same treatment that FDA accords similar actions for products in other industries with coverage under a CE.

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[15] 21 U.S.C. § 387e(j)(3).

[16] *See, e.g.,* 21 C.F.R. §§ 25.15(c) (agency actions that "do not significantly affect the quality of the human environment" are ordinarily excluded), 25.30(k) (labeling changes that do not affect levels of use are categorically excluded); 25.31(a) (new drug approval applications that will not "increase the use of the active moiety" are categorically excluded), 25.31(g) (bioequivalence determinations for human drugs and comparability determinations for biologics are categorically excluded), 25.32(f) (determinations that food is GRAS are categorically excluded if it is already marketed for the proposed use), 25.33(a) (new animal drug approval applications that will not increase use are categorically excluded), 25.34(b) (device classification determinations that will not increase or expand the use of the device are categorically excluded), 25.34(d) (class III medical device approvals are categorically excluded if the device is of the same type and use of a previously approved device), 25.34(f) (restricted device regulations that will not expand or increase the use of the product are categorically excluded).

The Agency should amend its Proposed Rule to include CEs in 21 C.F.R. Part 25 for all SE actions, including Non-Provisional SE Reports and SE Exemption Requests.[17] Such CEs would reduce paperwork and delay, and benefit the public interest by eliminating unnecessary NEPA analyses, thereby allowing the Agency to focus its resources on actions that are expected to significantly affect the quality of the human environment.[18] Finally, as a safeguard, FDA would retain the authority to require NEPA analysis based on extraordinary circumstances for all actions that are subject to a CE.

IV. FDA's Descriptions of Applicable Extraordinary Circumstances Should More Closely Track the Language in its Regulations.

The Notice explains that FDA has identified in its regulations several examples of extraordinary circumstances in which a particular action would be ineligible for a CE. It then discusses two examples in particular that FDA states are applicable to tobacco products, and describes how those extraordinary circumstances would apply in the context of the proposed tobacco product CEs. Unfortunately, those descriptions are far broader than the promulgated extraordinary circumstances they attempt to describe, which could cause the exceptions to swallow the rules.

FDA's regulations define the first extraordinary circumstance as "[a]ctions for which available data establish that, at the expected level of exposure, there is the potential for serious harm to the environment."[19] The Agency significantly expands on this in the Notice, however. It states that this extraordinary circumstance would preclude use of a CE "[i]f any tobacco product submission indicates that the action could result in **the *exposure of substances harmful to some biological mechanisms or systems in the environment***."[20]

FDA's regulations define the second extraordinary circumstance as

> [a]ctions that adversely affect a species or the critical habitat of a species determined under the Endangered Species Act or the Convention on International Trade in Endangered Species of Wild Flora and Fauna to be endangered or threatened or wild flora or fauna that are entitled to special protection under some other Federal law.[21]

But in its proposal, the Agency paraphrases the rule and significantly expands upon its scope by stating that this extraordinary circumstance would preclude the use of a CE "[i]f any tobacco product submission indicates that the action . . . may cause harm to a protected or endangered species . . . ."[22]

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[17] Correspondingly, the Agency would need to remove the requirement to perform an environmental assessment for SE Exemption Requests in 21 C.F.R. § 1107.1(b)(9).

[18] In its justification of its proposed CE for Provisional SE Reports, FDA states that "this rule would benefit the public health by allowing both FDA and industry to better focus their resources on other matters that could have a direct impact on public health." 79 Fed. Reg. at 3747.

[19] 21 C.F.R. § 25.21(a) (quoted in the Notice at 79 Fed. Reg. 3746).

[20] 79 Fed. Reg. at 3746 (emphasis added).

[21] 21 C.F.R. § 25.21(b).

[22] 79 FR at 3746.

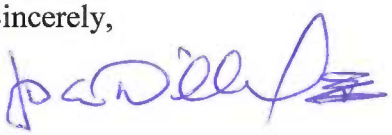
In each case, FDA's description of the extraordinary circumstance and its applicability in the context of tobacco product regulation goes far beyond the actual language of that extraordinary circumstance in the Agency's regulations. That regulatory language is important because it provides express standards and criteria. The descriptions of the extraordinary circumstances in the Proposed Rule, though, would inject ambiguities and broad generalizations into the NEPA process. To correct these problems, FDA should replace the descriptions of 21 C.F.R. §§25.21(a)-(b) found in the Notice with descriptions that more closely follow the language of the Agency's regulations.

Finally, in evaluating the use of extraordinary circumstances, the Agency should not engage in a "worst case" analysis of low probability events.[23] An effect is "reasonably foreseeable" only if it is "sufficiently likely to occur that a person of ordinary prudence would take it into account in reaching a decision."[24] Revising the descriptions of the two extraordinary circumstances discussed above will better enable FDA to comply with these standards as part of its analysis.

Conclusion

We appreciate the opportunity to submit these comments. We look forward to further opportunities to work with the FDA as it revises its NEPA implementing regulations to categorically exclude certain actions related to tobacco products.

Sincerely,



James E. Dillard III

Attachment

[23] Robertson v. Methow Valley Citizens Council, 490 U.S. 332, 355-56 (1989) (NEPA "does not mandate that uncertainty in predicting environmental harms be addressed" through conjectural "worst case" analysis). Rather, the correct level of review is based on the long-standing principle that an agency must only evaluate impacts determined to be "reasonably foreseeable." Village of Bensenville v. FAA, 457 F.3d 52 (D.C. Cir. 2006); Airport Impact Relief, Inc. v. Wykle, 192 F.3d 197 (1st Cir. 1999).

[24] Gulf Restoration Network v. Dep't of Transp., 452 F.3d 362, 368 (5th Cir. 2006).

Memorandum

Environmental Resources Management

1011 E. Main Street
Suite 227
Richmond, VA 23219-3537
(804) 420-3665
(804) 253-1091 (fax)

To: Altria Client Services on behalf of Philip Morris USA and US Smokeless Tobacco Company (USSTMC)

From: Donna D. Morrall, Ph.D.
Salvatore T. Giolando, Ph.D.

Date: 1 April 2014

Subject: Federal Register Vol. 79, No. 15/Thursday, January 23, 2014/Proposed Rules, National Environmental Policy Act; Environmental Assessments for Tobacco Products; Categorical Exclusions, 21 CFR Part 25 [Docket No. FDA-2013-N-1282]

At the request of Altria Client Services (ALCS), Environmental Resources Management, Inc., (ERM) is summarizing below the findings of the numerous environmental assessments we prepared in support of cigarette and smokeless tobacco product substantial equivalence reports. After compiling and analyzing the best available science for the products addressed in each of those reports, we concluded in each instance that the requested FDA action would pose no significant environmental effects, even when applying extremely conservative assumptions.

Tobacco Product Environmental Assessments

ERM has developed environmental assessments, at the request of ALCS, for Altria Group Inc. (Altria) on behalf of Philip Morris USA (PM USA) and US Smokeless Tobacco Company (USSTC) to comply with 21 CFR Part 25 when submitting Substantial Equivalence Reports for both "provisional" tobacco products and non-"provisional" tobacco products under Section 910(a) (2) (A) and (B) of the Federal Food, Drug and Cosmetic Act ("FDCA"). Using a very conservative set of assumptions, all EAs developed for the cigarette and smokeless products resulted in a conclusion in each assessment that a "Finding of No Significant Impact" was warranted due to the absence of significant environmental effects associated with manufacture, use and disposal of the products.

ERM conducted the environmental assessments in accordance with 21 CFR §§ 25.20 and 25.40 and relevant aspects of the FDA's technical guidance document(s) including the *Guidance for Industry: Environmental Assessment of Drug and Biologics Applications, Section III.A.2 (July, 1998)*. ERM used an extremely conservative set of assumptions for all EAs to help assure that any uncertainties were outweighed by double and triple counting of product volumes and by assuming that each product would be

introduced into environmental matrices where it would be unlikely to be introduced. For example, ERM assumed that the entire production volume of each product would be introduced into commerce and enter the environment. ERM further assumed that there would be no metabolism or significant environmental depletion of each product's ingredients that would mitigate toxicity once they entered the environment. Then ERM identified the individual ingredients (by CAS number) in each product and analyzed each ingredient for any potential impact on the atmospheric, aquatic, and terrestrial environments.

ERM's assessments also considered potential impacts from product use, disposal and misuse by applying similarly conservative assumptions. For example ERM assumed that the entire production volume of each product would enter the aquatic environment through misuse even though only a small proportion of some ingredients likely will enter the aquatic environment through human excretion or environmental transport. For the terrestrial assessment, the non-burned constituents of each product should all be disposed of to landfill. However, some improper use does occur. Therefore, ERM assessed the impact of non-burned constituents to land by assuming that the entire production volume for each product would be improperly disposed of on land and by assessing the potential impact if individual units of the improperly disposed of product would be dropped, unused, onto the ground. In addition, burned constituents of each product are considered to go to air, land, and landfill as either gases or ash. When properly used, the majority of ash should be disposed of to landfill. However, some ash does go into the air, and some ash is improperly disposed of to the ground. Thus, ERM's assessments conservatively assumed that air and land would be exposed to ash from the entire production volume of each product. Further, land exposure to burned constituents is unlikely except for ash. However, during smoking, burned constituents do enter the filter. Because filters are in some instances improperly disposed of, we also have calculated the concentration of the total production volume of burned constituents that could potentially go to land due to improper disposal of filters. Finally, we considered the potential for the entire unused product to be disposed of as another assumption in the environmental assessments.

Finally, ERM's assessments for cigarette products also considered the reasonably foreseeable impacts to air resulting from the combustion of tobacco product constituents, including banded paper, the ingredient package, adhesives, and monogram ink. Again, we used an extremely conservative set of assumptions in estimating the chemical composition of the combustion by-product (which is similar to burning wood) and the levels of ash and carbon monoxide released into the air. The assessments each found that, even with these conservative estimates, exposure levels to carbon monoxide were several orders of magnitude lower than the Recommended Exposure Limits set by the National Institute of Occupational Safety and Health and that ash exposure was negligible. The extremely low

concentration in the air of by-products produced from the burned constituents of tobacco products, combined with the expectation that there would be minimal and temporary exposure to smoke in the environment, provides the basis for the conclusion that the burning of tobacco products would not have a significant environmental effect.

Even with these very conservative assumptions, ERM concluded in each assessment (for both provisional and non-provisional Substantial Equivalence Reports) that the requested action would not pose the risk of significant environmental effects and that a Finding of No Significant Impact was warranted.

Donna Morrall, Ph.D.
Senior Project Manager,
ERM Global Product Stewardship

Salvatore T. Giolando, Ph.D.
Partner in Charge,
ERM Inc.

Attachments:
CV of Dr. Donna Morrall
CV of Dr. Salvatore Giolando

Donna D. Morrall, Ph.D.

Dr. Donna Morrall is a Senior Project Manager within ERM based in Cincinnati, Ohio. She has more than 20 years of experience in environmental monitoring, risk assessment, environmental toxicology, and insilico modeling.

Donna brings diverse industry experience in global product stewardship (15 of those years at Procter & Gamble Co.), with a focus on environmental risk assessment and the development of computational models to predict performance and safety. Donna has extensive experience in the development of aquatic monitoring programs to support chemical safety. She also has designed, managed and helped implement global modeling and training programs focused on integrating the process of chemical design, product performance, safety and consumer acceptance.

Donna is well versed in the use of QSAR/SAR and weight of evidence modeling related to international regulatory compliance issues and is familiar with USEPA TSCA and FIFRA ; EU REACH, CLP, Dangerous Substances, Dangerous Preparations, and Safety Data Sheets. She has extensive experience working with international multistakeholder teams.

Professional Affiliations & Registrations

- The Society of Toxicology and Chemistry (SETAC)

Fields of Competence

- Stream Ecology
- Data analysis and experimental design
- Environmental and Human Risk Assessment
- Computational modeling (QSAR/SAR/Similarity analysis/Domain analysis/Systems Modeling)
- Global Regulatory Compliance (e.g., EU REACH and CLP, TSCA, FIFRA, etc.)
- Technical External Relations and Communications

Key Industry Sectors

- Consumer Products
- Chemicals

Education

- B.A. Wittenberg University U.S.A., 1984
- M.S. Michigan Technological Univ. U.S.A., 1986
- Ph.D. Virginia Technological Univ. U.S.A., 1990

Languages

- English, native speaker
- Italian, conversational
- Spanish, minimal

Key Projects:

- **Modelling and development of environmental monitoring plans to support chemical safety**
- **Read across and QSAR strategies**
- **Preparation for 2013 Reach Registrations**
- **Preparation of technical dossiers and CSRs**
- **Technical and toxicological support for key global customers**

Industry Experience:

Environmental Impact

Environmental impact projects included local and global efforts. Impacts such as fishing, land use, and sewage treatment plant effluents were evaluated. Effects were evaluated in relation to populations, geomorphology, aquatic structure, material transport and processing, and toxicity. Selected studies include:

- Completing a field study of triclosan loss rates in river water.
- Conducting monitoring studies to determine removal rates of chemicals by sewage treatment plants and release rates to the environment.
- Using changes in biota to determine of zones of impact for risk assessment.
- Understanding physical and biological linkages within stream geomorphic hierarchies to predict the distribution of solutes and aquatic organisms;
- Identifying factors affecting ammonium uptake in streams – an inter-biome perspective.
- Identifying factors contributing to the collapse of lake herring populations in Lake Superior; and
- Determining effects of forest disturbance on particulate organic matter budgets of small streams.

Data Analysis and Experimental Design

Data mining and analysis efforts are critical precursors to environmental risk assessment and modeling. They allow efficient use of available data prior to spending effort developing new information. Data Q/A is imperative for the development of quality models. Laboratory and field projects utilized classic experimental design procedures as well as SAS JMP Design of Experiments (DOE) techniques. Data development projects included:

- Design of a database to house a large body of environemental toxicity data and transfer from a text based system;
- Mining of datasets for similarity analysis and "readover" opportunities, and training and test sets for models;
- Design of a data collection program to support an integrated series of models designed to develop new chemistries and optimize consumer product performance; and
- Comparison of similarity and substructure analysis procedures and development of guidance on when and how each procedure should be used.

Risk Assessment and Hazard Communication

Risk assessment and hazard communication projects ranged across consumer product chemistries such as surfactants, metals, chelants, polymers, dyes, amines, nutrients, etc. Risk assessments were conducted for individual companies as well as part of trade and industry associations. Much of this work is confidential but efforts of note include:

- Evaluatoin of methods for calculating surfactant log P values and their use in risk assessments and models.
- Running experimental stream studies on high volume surfactants and selected polymers. These studies were supported with stable isotope (^{13}C and ^{15}N) research to track chemical fate and integrated with stable isotope studies used to demonstrate comparability between natural and experimental streams for environmental risk assessment.
- Development of concepts and methods for assessing solute dynamics (Solute work group).
- Using stable isotopes tracers to predict the fate and effects of natural and man-made materials on stream biota.

Computational Modeling

Modeling projects ranged from the evaluation of regulatory models, use of available models to predict the properties or toxicity of a single ingredient to the development of complex integrated sets of environmental and product performance models. Modelling efforts included developing modeling programs and implementation plans for a consumer products division to guide their efforts to optimize chemical performance and minimize toxicity. Examples of projects include:

- Development of models based on surfactant properties and data to optimize consumer product formulations;
- Predicting the effects of copper toxicity to algae in lake ecosystems;
- Developing a genetic algorithm to predict the toxicity of surfactants to algae;
- Identifying Acute and Chronic Aquatic Toxicity Structure Activity Relationships for Alcohol Ethoxylate Surfactants;
- Development of a coordinated suite of approaches (similarity analysis, substructure search, domain analysis, nearest neighbor evaluation) to predict aromatic amine mutagenicity and carcinogenicity;
- Evaluation of EPI Suite™ for use with specific classes of compounds;
- Using QSAR for the design and optimization of laundry brighteners;
- Developing guidance on techniques for the use of domain analysis;
- Development of a new weight of evidence approach to building chemically-intuitive predictive models building techniques to determine effective variable selection and reduction approaches;
- Development of fish population models (Lake Superior Coregonus artedii) and stream ecosystem models;
- Identification of ecological applications of genetic progamming: predicting organism distributions in complex physical habitats;
- Fusing of genetic algorithms and genetic programming techniques for symbolic regression;
- Development of state of the art ecological modeling by Genetic Algorithms; and
- Applying the results from a variety of Genetic Algorithm applications to show the robustness of the approach.

Salvatore T. Giolando, Ph.D.

Associate Partner

Dr. Giolando is based in our Cincinnati, Ohio office.

Dr. Giolando brings over 25 years of global industry and consulting experience, currently as an ERM Partner focusing on Global Product Stewardship and integrated product support across the ERM business lines. He holds a BS in Chemistry and a Ph.D. in Environmental Health. His career is highlighted by 10+ years in industry working for the Procter & Gamble Company managing global product safety and regulatory compliance for numerous brands and innovative technologies during tenures in both Cincinnati and Brussels, Belgium.

Since 2002 Sal has been developing domestic and international product stewardship programs with several multi-national clients, especially in the area of EU REACH regulation. He will be focused on developing a North American Center of Excellence in global product stewardship, product safety and global regulatory compliance programs as he integrates his Cincinnati/North American team with the existing Global ERM team collaborating in this area.

Dr. Giolando is an internationally recognized and respected GPS expert and a proven leader with vision and key insights into GPS emerging markets. In addition to GPS professional services, Sal's specific areas of technical expertise include: Strategic GPS planning and program implementation; EU REACH and related international chemical product regulatory schemes; TSCA, the Globally Harmonized System for Hazard Classificzation and Labelling(GHS); Sustainability; Risk Assessment; Industrial Hygiene, Exposure Assessment; Government Relations; Bioavailability; and Environmental Fate/Modeling.

Professional Affiliations & Registrations

- Member, Society for Environmental Toxicology and Chemistry
- Member, American Chemical Society

Fields of Competence

- Product Stewardship
- Peformance Assurance
- Strategic Planning
- Industrial Hygiene
- REACH CLP & Chemical Control
- Environmental Fate/Modeling
- Bioavailability
- Risk Assessment/Management

Education

- Ph.D., Environmental Health, University of Cincinnati, College of Medicine, 1991
- Appointed Graduate Scholar in Biotechnology, 1989
- B.S., Chemistry, Canisius College, 1986

Languages

- English, native speaker
- Conversational French

Key Industry Sectors

- Consumer Products, Industrial Chemicals, Pesticide/Biocide, Oil & Gas, Aviation, Automotive, Pharmaceutical, Food Contact, Batteries and Electronics

Certification and Training

- Certified Hazardous Materials Manager, CHMM #2204 - 1990 and 1991
- Certified OSHA Competent Person - Asbestos Abatement Contractor/Supervisor, 1990
- Industrial Hygienist in Training 1990

James E. Dillard III
Senior Vice President
Regulatory Affairs

April 28, 2014

Via Electronic Submission

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. FDA-2013-D-1600 (79 Fed. Reg. 10534 (February 25, 2014)) Comments on "Draft Guidance for Industry and Tobacco Retailers; Enforcement Policy for Certain (Provisional) Tobacco Products that the FDA Finds Not Substantially Equivalent"

Altria Client Services Inc. ("ALCS"), on behalf of Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC"),[1] submits these comments in response to the above-referenced docket and February 25, 2014, Federal Register notice.[2]

FDA seeks comments on a draft guidance ("Draft Guidance") concerning "its enforcement policy to retailers regarding so-called 'provisional' tobacco products that become subject to not substantially equivalent (NSE) orders" issued under the Family Smoking Prevention and Tobacco Control Act (the "Act"). Under the Draft Guidance, when provisional tobacco products receive an NSE order and therefore must be removed from the market, "FDA does not intend to take enforcement action for at least 30 calendar days from the date the NSE order issues for those products that are in the retailer's current inventory at a specific retail location on the date FDA issues the NSE order."[3] The Draft Guidance further states: "This policy extends only to tobacco products that are already in a retail store that offers the products for sale directly to consumers."[4]

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[1] PM USA and USSTC are wholly-owned subsidiaries of Altria Group, Inc. ALCS provides certain services, including regulatory affairs, to the Altria family of companies. "We" and "our" are used throughout these comments to refer collectively to PM USA and USSTC.

[2] 79 Fed. Reg. 10534.

[3] Enforcement Policy for Certain (Provisional) Tobacco Products That FDA Finds Not Substantially Equivalent ("Draft Guidance") at 1-2.

[4] Id. at 2.

Altria Client Services Inc.
2325 Bells Road
Richmond, Virginia 23234
(804) 335-2679
James.E.Dillard@altria.com

Our comments on the Draft Guidance will address the following three points:

1) The Draft Guidance should treat all participants in the distribution chain consistently with a grace period for removal of provisional products.
2) The Draft Guidance should conform to Congress's and FDA's past approach to the removal of tobacco products from the marketplace with a grace period for all participants in the distribution chain.
3) The Draft Guidance should not provide for abrupt and immediate removal of provisional products because there are no urgent circumstances.

As explained below, FDA should modify its Draft Guidance to provide that, upon issuance of an NSE order for a provisional product:

- Manufacturers shall immediately cease the manufacture of the product and may sell existing inventory for 30 days from the NSE order.
- Wholesalers and retailers may sell-through their existing inventories until exhausted.

This approach would immediately bar manufacturers from making additional product, but would allow those companies, their customers, and their customers' customers a reasonable time to sell products already on hand and in the stream of commerce.

I. FDA's Policy Should Treat All Participants in the Distribution Chain Consistently.

The Draft Guidance limits the 30-day grace period to "products that are in ***the retailer's*** current inventory at a specific retail location on the date FDA issues the NSE order."[5] The focus on only retailers arbitrarily excludes many similarly-situated businesses in the distribution chain, causing unnecessary disruption and imposing unnecessary hardships on these other participants in the market.

For example, many companies participate in a complex distribution process for cigarettes. Manufacturers transport newly produced cigarettes to bonded warehouses where they pay the federal excise tax before shipping the product to public warehouses. From there, the products are sold to independent wholesalers nationwide.[6] Under state tax laws, wholesalers typically pay state excise taxes and stamp the products. The wholesalers, in turn, sell the products to retailers across the country passing on the excise tax. Along the way, the products are often in transit nationwide.

Under the Draft Guidance, the instant FDA issues an NSE order, manufacturers, as well as wholesalers and everyone else in the distribution chain (except retailers), must immediately stop the distribution and sale of the affected tobacco products. Without advance notice, a wind-down period, and time to develop an orderly plan for compliance, existing inventory will remain embargoed in warehouses. Trucks will have to turn around mid-transit. And manufacturers will

[5] Id. (emphasis added).
[6] These wholesalers may sell to other wholesalers or distributors who are not direct customers of manufacturers, before the cigarettes eventually are sold to retailers.

have paid federal excise taxes on product that has been shipped to wholesalers, but that never makes it to the marketplace.

Moreover, the hundreds of wholesalers who own the product (many of whom will already have paid the state excise taxes on it) will confront tax refund, distribution, and legal issues concerning the product. For instance, wholesalers and retailers will be required to navigate an array of differing state laws and regulations governing the excise tax refund process. Under New York laws, for example, when cigarettes "have become unfit for use and consumption or unsalable," then "a dealer who is a licensed agent shall, upon timely application, be entitled to . . . a refund" of excise taxes paid on the products.[7] Wholesalers and retailers may be required to demonstrate (a) which packages bear the excise tax stamps, (b) evidence that the manufacturer has not reimbursed the business for payment of the tax, and (c) evidence of destruction of the tax stamps.[8] While awaiting confirmation that these requirements have been satisfied, the wholesaler or retailer could be required to store the tobacco products that are subject to the NSE order, yet ensure that these products are not sold. California laws, by contrast, require collection of cigarette excise taxes but make no express provision for the refund of stamped products.[9] Distributors must work with the State Board of Equalization on an individual basis prior to returning product to the manufacturer or destroying the stamped cigarettes.[10] Further, while manufacturers and retailers work through these state laws, federal and state governments will have to process numerous requests for refunds of excise taxes paid on products that can no longer be sold.

The Draft Guidance, though, affords only retailers – and not manufacturers, wholesalers and others in the distribution chain – additional time to avoid these practical dilemmas and sell their existing inventories of provisional products subject to a new NSE order. And even then, the 30 days provided to retailers is an insufficient amount of time for retailers to sell products in their inventories and avoid these issues. An NSE order would impose burdens on all participants in the chain of distribution, and all of them should have the same opportunity to develop a plan for compliance, including a reasonable sell-through period for existing inventory.

II. Congress's and FDA's Past Approach to the Removal of Tobacco Products from the Marketplace Should Apply to Provisional Products Subject to an NSE Order.

The Draft Guidance also is contrary to Congress's and FDA's past approach to removing tobacco products from the market under Section 911 of the Act.

Section 911 of the Act prohibits descriptors such as "light" or "low" in tobacco product labeling. Congress determined that prohibiting such descriptors "was necessary to protect the public health . . . ."[11] This prohibition took effect on June 22, 2010. Recognizing that these products had been

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[7] N.Y. Comp. Codes R. & Regs. Tit. 20, § 77.1(a)(1)(iii).
[8] *Id.* § (b).
[9] *See* Cal. Rev. & T. Code § 30101 *et seq.*
[10] *See* Cal. State Bd. of Equal. Pub. 93 LDA (Aug. 2013).
[11] FDA, *Guidance for Industry and FDA Staff, Use of "Light," "Mild," "Low," or Similar Descriptors* (June 2010) at 4 ("Descriptor Guidance").

on the market for years and that participants in the distribution chain held substantial inventories, Congress gave manufacturers 30 days to sell their existing inventories. Act § 911(b)(3).

In a Guidance document, FDA also allowed manufacturers to continue distributing or selling tobacco products with prohibited descriptors in their existing inventories, "if the products were manufactured before June 22, 2010, and introduced into domestic commerce by the manufacturer . . . before July 22, 2010."[12] Notably, even after the July 22, 2010, deadline for manufacturers to cease manufacturing products with descriptors, wholesalers and retailers could sell such products in the ordinary course of business.[13]

Congress and FDA recognized that (1) although manufacturers should immediately stop *manufacturing* prohibited tobacco products, they should have a reasonable period after the prohibition to *sell* their existing inventories; and (2) wholesalers, retailers, and others in the distribution chain should be allowed to sell their existing inventories of the product without a 30-day or other deadline.

That approach is consistent with FDA's approach to the removal of non-tobacco products it finds unsafe. In 2011, when FDA ordered the removal of certain unapproved prescription drugs from the market because they "cannot be legally marketed in the United States" and posed "an unnecessary risk," the Agency advised that manufacturers should "stop *manufacturing* them within *90 days* and stop *shipping* the products within *180 days*."[14] FDA should not depart from that approach for provisional tobacco products.

First, like products with prohibited descriptors, provisional products subject to an NSE order have been on the market for years, and there is no cause for an urgent and immediate removal. Further, unlike the removal of products with prohibited descriptors, tobacco manufacturers, wholesalers, and retailers will not have advance notice of the date a particular provisional product will be taken off the market. The industry had a year's notice that products with prohibited descriptors would have to stop being manufactured, but Congress still gave manufacturers an additional 30 days to introduce already manufactured products into the market.[15] By contrast, under FDA's Draft Guidance for provisional products, only retailers will be able to sell their existing inventories and then only for 30 days following FDA's issuance of the NSE order. The Draft Guidance approach is arbitrary and unfair.

Second, as with the removal of products bearing descriptors, all participants in the distribution chain should be provided a period in which to comply with an NSE order and sell their existing inventories. In banning products with prohibited descriptors, FDA afforded all participants in the distribution chain a reasonable chance to exhaust their existing inventories and to comply with the prohibition, avoiding the disruption and unfairness attendant to an abrupt and immediate removal of products from the market.

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[12] Id. at 5.
[13] Id.
[14] FDA, News Release, FDA Prompts Removal of Unapproved Drugs from Market (Mar. 2, 2011) (emphases added).
[15] Descriptor Guidance at 4.

Third, the Draft Guidance should not impose an arbitrary and unfair time limit on retailers and wholesalers with existing inventories. Thirty days' notice is not sufficient. It does not account for tobacco products in transit. Nor does it account for products unsold during the 30-day period. The Draft Guidance seeks to address some of these issues by "encourag[ing] retailers to contact their supplier or manufacturer to discuss possible options for the misbranded and adulterated product that they may have in their current inventory."[16] That outreach, however, will only compound the legal and practical complexity at every level in the distribution chain. FDA avoided such problems with regard to the descriptor prohibition by allowing wholesalers, retailers, and others in the distribution chain to exhaust their existing inventories of the products in the ordinary course of business, rather than imposing an arbitrary and unfair deadline.

Finally, making the Draft Guidance effective "immediately" threatens many in the distribution chain who may not learn of an NSE order on the day it is issued. While the affected manufacturer will receive the NSE order directly, and while FDA will announce the order publicly, thousands of businesses and links in the chain of distribution, many of which are not direct customers of manufacturers, may not learn about the NSE immediately. For those businesses with inventory of the product at that time, immediate enforcement of a prohibition on any distribution or sale is unreasonably burdensome and fundamentally unfair.

III. Abrupt and Immediate Removal of Provisional Products is Unnecessary.

As the Draft Guidance recognizes, "[b]ecause the FD&C Act permitted [provisional] products to remain on the market pending FDA's review . . . there will very likely be products at retail locations within the United States when FDA issues an order finding a tobacco product NSE."[17] Provisional products have been available to consumers for anywhere from three to seven *years* because they were first introduced into interstate commerce between February 15, 2007, and March 22, 2011.

Although FDA may find some of these provisional products to be not substantially equivalent to a predicate product, these provisional products have remained on the market for years pending the Agency's review of substantial equivalence reports. In fact, FDA determined that its review of provisional product reports – the reports covering products currently being sold to consumers – warranted a lower priority than reports for products that are not currently marketed.[18] FDA issued its first substantial equivalence order in June 2013 and to date, the Agency has issued only 34 such orders (17 finding SE, 17 NSE,) out of more than 4,000 applications (more than 3,100 of which were for provisional products). Only 4 of those NSE orders – all issued in February 2014 – involved provisional products. [19] The Agency has not even established performance measures for review of provisional products, although it has established such measures for most other key aspects of substantial equivalence review.[20] Absent an immediate and urgent problem, which a

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[16] Draft Guidance at 2.
[17] Id.at 1.
[18] *See* GAO, *FDA Needs to Set Time Frames for Its Review Process*, GAO-13-723 (Sept. 2013).
[19] *See* FDA News Release, *FDA Announces First Decisions on New Tobacco Products Through the Substantial Equivalence Pathway* at 15 (June 25, 2013).
[20] *See* FDA, Establishing Four CTP Performance Measures (Apr. 18, 2014).

finding of NSE will rarely, if ever, signal there is no basis for the precipitous action the Draft Guidance recommends.

If a particular provisional product presented a need for immediate withdrawal, then FDA could likely justify exigent measures. But here, the time FDA has allowed provisional products to stay on the market, the lower priority it has assigned to their review, and the 30-day grace period it affords retailers to sell their current inventory preclude any claim of urgency across the board. Lacking such a foundation, FDA's Draft Guidance is arbitrary and unfair.

Conclusion

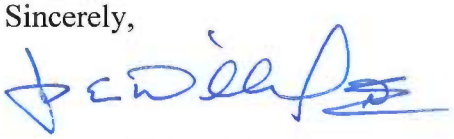
We appreciate the opportunity to submit these comments and urge FDA to modify its Draft Guidance to provide that:

- Manufacturers shall immediately cease the manufacture of the product and may sell existing inventory for 30 days from the NSE order.
- Wholesalers and retailers may sell-through their existing inventories until exhausted.

Such a policy would immediately bar manufacturers from making additional product, but would allow those companies, their customers, and their customers' customers a reasonable time to sell products already on hand and in the stream of commerce.

We look forward to opportunities to work with FDA as it further develops and refines the substantial equivalence process.

Sincerely,



James E. Dillard III

James E. Dillard III
Senior Vice President
Regulatory Affairs

September 15, 2014

Via Electronic Submission

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. FDA-2014-D-0800 (79 Fed. Reg. 41292 (July 15, 2014)) – Comments on "Draft Guidance for Industry on Substantial Equivalence Reports: Manufacturer Requests for Extensions or to Change the Predicate Tobacco Product"

Altria Client Services Inc. ("ALCS"), on behalf of Philip Morris USA Inc. ("PM USA") and U.S. Smokeless Tobacco Company LLC ("USSTC"),[1] submits these comments in response to the Draft Guidance identified above.

Our comments will address three issues raised by FDA's Draft Guidance:

1) FDA should proceed with rulemaking to avoid creating arbitrary and capricious outcomes and uncertainties that complicate the SE process.
2) FDA's proposed approach to extension requests is inflexible and will produce unfair results.
3) FDA's proposed approach to changing predicate products is similarly inflexible and unfair.

Because the Draft Guidance is an application of regulatory authority that is not an appropriate subject for FDA guidance only, FDA should initiate a rulemaking process to address the SE report process, including requests for extensions of time for manufacturers to respond to deficiency letters and amendments to change the predicate tobacco products. In the interim, FDA should revise and reissue the Draft Guidance to incorporate a more reasonable approach to these issues pending rulemaking.

[1] PM USA and USSTC are wholly-owned subsidiaries of Altria Group, Inc. ALCS provides certain services, including regulatory affairs, to the Altria family of companies. "We" and "our" are used throughout these comments to refer to PM USA and USSTC.

Altria Client Services Inc.
2325 Bells Road
Richmond, Virginia 23234
(804) 335-2679
James.E.Dillard@altria.com

1. **FDA's failure to promulgate regulations setting forth the standards for SE determinations creates arbitrary and capricious outcomes and uncertainties that complicate the SE process, and FDA should proceed with rulemaking.**

The Administrative Procedure Act (APA) requires notice-and-comment rulemaking when agencies impose binding norms having the force of law.[2] Courts will invalidate rules that agencies adopt without following that process.[3] A key rationale for the notice-and-comment rulemaking process is to help develop clear rules - practical, workable regulatory requirements that inform regulated companies of the applicable standards and that assist agencies in regulating with consistency and predictability.

FDA's Good Guidance Practices regulation[4] defines guidance documents as documents that describe the "agency's interpretation of or policy on a regulatory issue."[5] By FDA's own definition, guidance documents are to be used only when interpreting statutory and regulatory requirements, not for the purpose of creating the requirements themselves. The creation of regulatory requirements and binding policies is reserved for notice-and-comment rulemaking. FDA's proposal to create a regulatory standard of denying all extensions of time to respond to deficiency letters for non-provisional tobacco products, regardless of underlying need or assessment of need, and prohibiting any change to the identified predicate tobacco product during an ongoing substantial equivalence review, operates as *de facto* rules inappropriate for promulgation solely through the guidance development process.

In January 2011, FDA recognized that "interested parties need clarity as to FDA's expectations regarding [SE] reports."[6] FDA accordingly stated it would "initiate a rulemaking that would establish requirements and standards for substantial equivalence . . . ."[7] Yet three-and-a-half years later and five years after Congress adopted the FSPTCA, FDA still has not promulgated regulations regarding the SE process and has established no time frame for FDA's review of SE reports.[8] Instead, FDA has issued informal guidance documents and other *ad hoc* communications that, as explained below, do not adequately clarify FDA's requirements or expectations. Even members of Congress have expressed "significant concern" regarding FDA's extensive "use of draft guidances to make substantive policy changes."[9] While we appreciate FDA's efforts to streamline the SE review process, FDA's promulgation of valid, enforceable regulations through notice-and-comment rulemaking would minimize the need for extensions in the SE process and changes to predicate products, and would enable both FDA and manufacturers to more fully achieve efficiency in the SE process.

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[2] 5 U.S.C. § 553; *Appalachian Power Co. v. EPA*, 208 F.3d 1015, 1024 (D.C. Cir. 2000); *American Mining Congress v. Mine Safety & Health Admin.*, 995 F.2d 1106, 1109 (D.C. Cir. 1993).

[3] *NLRB v. Bell Aerospace Co.*, 416 U.S. 267, 294 (1974).

[4] 21 C.F.R. 10.115.

[5] *Id.*

[6] FDA, *Guidance for Industry and Staff, Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products* [hereinafter "SE Guidance"], 76 Fed. Reg. 789 (Jan. 6, 2011) at 2.

[7] SE Guidance at 1.

[8] We note that any such time frame for FDA review should be "tolled" for the periods of time spent by manufacturers to respond to deficiency letters.

[9] Letter from Sen. Lamar Alexander, Ranking Member, et al. to Margaret Hamburg, Commissioner, FDA (May 6, 2014) at 1, *available at* http://www.hpm.com/pdf/blog/AlexanderFDAGuidanceLetter.pdf.

2. FDA's Proposed Approach to Extension Requests is Inflexible and Will Produce Unfair and Counterproductive Results.

The Draft Guidance states that extensions of time to respond to FDA deficiency letters are, as a general matter, no longer warranted because FDA has fully educated the industry about the SE process "through guidance documents, webinars, meetings, issuance of scientific advice/information requests, and preliminary finding letters."[10] FDA asserts that "manufacturers should now have enough information to prepare SE reports and amend pending SE reports to address any deficiencies in their SE reports within the time period specified in the deficiency letter."[11] FDA's premise is incorrect for several reasons.

a. FDA's guidance documents and webinars on substantial equivalence have been unclear and contradictory.

Apart from disclaiming any binding effect, FDA's informal "guidance documents" and "webinars" have provided vague and often contradictory advice. For example, FDA stated in the SE Guidance that manufacturers should choose a single predicate product, rather than asserting that a new product is substantially equivalent to multiple products.[12] Fifteen months later, in an April 2012 webinar, FDA reversed that view.[13] FDA reiterated this revised position in an August 13, 2014, webinar.[14]

FDA also has failed to clarify its interpretation of essential provisions of the FSPTCA. For example, beyond repeating the statutory language, FDA has not publicly explained what "same characteristics" means. In some places, FDA has suggested that any change in a product, no matter how trivial, means that the new product does not have the "same characteristics" as its predicate. Given that an SE report is required only when the manufacturer changes the product, this approach inappropriately reads the "same characteristics" assessment of Section 905(j) out of the statute.[15]

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[10] *Id.*

[11] *Id.*

[12] SE Guidance at 4.

[13] FDA, Webinar: Reports on Substantial Equivalence (905(j)(1)(A)(i) Reports): One Year Later (Apr. 24, 2012), http://fda.yorkcast.com/webcast/Play/9b7db16f6bf24869a938b15fd61943c11d.

[14] FDA, Webinar: Compliance Training for Small Businesses, "Draft Guidance – Substantial Equivalence Reports: Manufacturer Requests for Extensions or to Change the Predicate Tobacco Product" (Aug. 12, 2014).

[15] As we have previously commented, a product that is *identical* to its predicate products is, by definition, neither new nor modified, and therefore is not a "new tobacco product" that must undergo premarket review by the FDA to be lawfully marketed. Interpreting the term "same characteristics" in Section 905(j) to mean "identical characteristics" would render the "same characteristics" assessment of Section 905(j) meaningless because *any* product that is new or modified automatically would be evaluated under the "different questions of public health" assessment. *See* 21 U.S.C. § 387j; Docket FDA-2013-N-1558, Altria Client Services Inc., Comments on "Agency Information Collection Activities; Proposed Collection; Comment Request; Guidance for Industry and Food and Drug Administration Staff; Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products" (Feb. 25, 2014) at 2-4; Docket No. FDA-2010-D-0635, Altria Client Services Inc., Comments on "Guidance for Industry and FDA Staff, Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products" (Feb. 8, 2011) at 5-6.

Nor has FDA indicated the standard it will apply to determine whether a change implicates "different questions of public health."[16] The Agency has not clarified, for example, how small a change in a harmful or potentially harmful constituent the Agency will consider as important in evaluating whether the new tobacco product presents a different question of public health.

To the extent FDA has addressed these and other gaps at all, its informal and *ad hoc* communications have again increased the uncertainty. The Agency itself has acknowledged the inconsistencies in its pronouncements, explaining that its changing requirements for SE reports reflect the "learning experience" of reviewing submissions.[17]

The specific SE determinations that FDA has made public do not alleviate the confusion. FDA has released only 71 determinations out of 3,800 submissions, not a robust pool from which to deduce the standards FDA is applying. In addition, many of these determinations involve atypical products or unique changes, reducing the informational value for most manufacturers.[18] FDA also has appropriately redacted the determinations to prevent disclosure of confidential and proprietary material without providing specific direction that doesn't involve proprietary information of a manufacturer. Finally, many of the determinations do not even discuss what FDA considered when determining whether the new product and predicate product possess the same characteristics.

FDA's publicly-released NSE determinations have been less informative. Rather than describing its NSE orders in detail, or specifying the standards being applied, the Agency has primarily communicated its conclusions through a high-level "Brief Summary of 'Not Substantially Equivalent' Determinations."[19] In the small number of NSE orders FDA has made available, the Agency likewise has not identified the relevant standards.[20]

Manufacturers' efforts to satisfy FDA's shifting requests and requirements regarding SE reports have been marked by confusion, misunderstanding, and duplication. These conditions persist, and they both generate delay and necessitate modifications in manufacturers' SE reports.

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[16] 21 U.S.C. § 387j(a)(3).

[17] FDA, Webinar: Update on Review of Substantial Equivalence Reports (SE Reports), *available at* http://fda.yorkcast.com/webcast/Viewer/?peid=056c3ad31d934f1eb93caeb925f1f80c1d.

[18] For instance, several of the SE determinations concerned cigarette paper and filter tubes for roll-your own-tobacco. And forty-four of the determinations involved products marketed by one manufacturer and pertained to a single product change: the change from non-fire-safe paper to fire-safe paper. *See* FDA, 2013 Substantial Equivalence Marketing Orders, http://www.fda.gov/TobaccoProducts/Labeling/MarketingandAdvertising/ucm403542.htm; FDA, 2014 Substantial Equivalence Marketing Orders, http://www.fda.gov/TobaccoProducts/Labeling/MarketingandAdvertising/ucm403549.htm

[19] FDA, Brief Summary of "Not Substantially Equivalent" Determinations (June 25, 2013), *available at* http://www.fda.gov/tobaccoproducts/labeling/marketingandadvertising/ucm339928.htm.

[20] *See* FDA, CTP FOIA Electronic Reading Room, NSE Letters, http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/AbouttheCenterforTobaccoProducts/ucm221165.htm; FDA, Tobacco Product Marketing Orders, Provisional Not Substantially Equivalent Orders, http://www.fda.gov/tobaccoproducts/labeling/marketingandadvertising/ucm339928.htm.

b. The other communications to which the Draft Guidance refers generally are not public and do not provide guidance to all companies that have submitted SE reports.

The Draft Guidance also points to various types of private communications between FDA and individual manufacturers, such as "meetings, issuance of scientific advice/information requests, and preliminary finding letters."[21] But FDA's private communications with one company do nothing to inform *other* companies about the Agency's interpretation and application of SE standards. In addition, given the array of tobacco products a manufacturer may market, as well as the differences among those products, and the number of SE reports still awaiting scientific review by FDA, manufacturers can have no assurance that their own communications with FDA on some products identify the range of issues for others. As a result, FDA is incorrect in concluding that "manufacturers should now have enough information to prepare SE reports and amend pending SE reports."[22]

c. FDA continues to dramatically underestimate the time burden the SE process places on manufacturers.

FDA has dramatically underestimated the time required to prepare an SE report and to respond to the Agency's deficiency letters. This misjudgment undermines the foundation of FDA's proposed new approach to extension requests.

As we have previously commented,[23] Congress intended the SE process for tobacco products to be a streamlined pathway to market, modeled on the 510(k) process for medical devices. FDA, however, has inflated the SE process beyond what Congress intended, undertaking intensive and burdensome scientific review of every report. In some instances, the Agency's inquiries have necessitated responses running hundreds of pages. Beyond the problem of volume, FDA has directed manufacturers to collect and analyze data regarding predicate products, which were never collected when those products were on the market many years ago. FDA's guidance documents further direct that SE reports include packaging and labeling data, analysis of tobacco use behavior, shelf life data, and environmental assessments, all of which exceed the SE requirements specified in the FSPTCA.

We previously have described in detail the burdens imposed by these extra-statutory requirements.[24] Nonetheless, FDA has not simplified the SE process or even acknowledged the burdens that this inflation of the process has imposed on manufacturers.

In its estimates required under the Paperwork Reduction Act of 1995, FDA previously predicted that completing an SE report and responding to scientific inquiries would take a manufacturer

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[21] Draft Guidance at 2.

[22] *Id.* at 2.

[23] *See* Docket FDA-2013-N-1558, Altria Client Services Inc., Comments on "Agency Information Collection Activities; Proposed Collection; Comment Request; Guidance for Industry and Food and Drug Administration Staff; Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products" (Feb. 25, 2014).

[24] *See, e.g., id.*; Docket FDA-2011-D-0147, Altria Client Services Inc., Comments on "Draft Guidance for Industry and Staff, Demonstrating Substantial Equivalence of a New Tobacco Product: Responses to Frequently Asked Questions" (Nov. 8, 2011).

360 hours.[25] In its recently announced "deeming" proposed rule, FDA decreased the estimated time burden for SE reports for cigars and pipe tobacco even further, to only 180 hours per report.[26] In reality, the time required to complete SE submissions for cigarettes and smokeless tobacco products has been *many* multiples of 360 hours, as numerous industry reports confirm.[27] These reports match our experience.

From review of publicly available deficiency letters, it appears that FDA typically demands a response from the manufacturer within 30 or 60 days regardless of whether FDA seeks scientific information on one or multiple products. Typically, FDA sends multiple requests for scientific information for multiple products at one time. For instance, FDA may send a manufacturer one scientific information request that contains 20 products with 30 questions and the time for response is the same as if they had sent it for only one product with one question. And, it may take more than 500 hours just to respond to a *single* scientific information request from FDA.

Because FDA has significantly underestimated the burdens that the Agency has imposed on manufacturers in the SE process and the amount of time it takes to comply, implementing a new blanket policy against extensions would be arbitrary and capricious.

3. FDA's Proposed Approach to Changing Predicate Products is Inflexible and Unfair.

Under the Draft Guidance, a manufacturer that wishes to change the predicate product after scientific review of the SE report has begun should "withdraw the SE report and submit a new report comparing the new tobacco product to that predicate."[28] For provisional products, the manufacturer must remove the product from the market pending FDA's review of the new SE report. That approach is arbitrary and unfair, particularly given FDA's contradictory guidance regarding predicate products.

As described above, FDA changed its policy regarding the use of multiple predicate products after the deadline for manufacturers to submit provisional SE reports.[29] As a result, we - and no

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[25] FDA, *Agency Information Collection Activities; Proposed Collection; Comment Request; Guidance for Industry and Food and Drug Administration Staff; Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products*, 79 Fed. Reg. 78,974, 78,975 (Dec. 27, 2013).

[26] FDA, *Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; Regulations on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products*, 79 Fed. Reg. 23,142, 23,189 (Apr. 25, 2014).

[27] *See* U.S. Gov't Accountability Office, Report to the Ranking member, Subcomm. on Primary Health and Aging Comm. On Health, Education, Labor, and Pensions, U.S. Senate, NEW TOBACCO PRODUCTS - FDA Needs to Set Time Frames for its Review Process 25-26, GAO-13-723 (Sept. 2013); Docket FDA-2013-N-1558, Cigar Association of America, Comments on "Agency Information Collection Activities; Proposed Collection; Comment Request; Guidance for Industry and Food and Drug Administration Staff; Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products" (Feb. 24, 2014) at 2; Docket FDA-2013-N-1558, SMARTT Coalition, Comments on "Agency Information Collection Activities; Proposed Collection; Comment Request; Guidance for Industry and Food and Drug Administration Staff; Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products" (Feb. 25, 2014) at 4.

[28] Draft Guidance at 2.

[29] The SE Guidance stated that manufacturers should identify only a single predicate product. SE Guidance at 4. Thus, in the provisional SE reports filed in 2011, we submitted SE reports that compared each new product with only one predicate product. Over the following years, FDA's position on predicate products changed. FDA said in webinars that manufacturers could in fact use multiple predicate products. FDA, Webinar: Reports on Substantial

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doubt, other companies as well - amended various SE reports to include additional predicate products. Given the uncertainty it has engendered, FDA cannot and should not penalize manufacturers for changes with regard to predicate products.

Moreover, FDA's recommendation that a manufacturer withdraw its SE report and remove the affected provisional product from the market if the company changes the predicate products is unexplained. Presumably, FDA believes that changing the predicate products renders the SE submission a "new report," submitted after the March 2011 deadline for provisional products.[30] This approach, however, improperly converts provisional products into non-provisional products, with no statutory basis for the transformation.

Additionally, FDA's categorical approach inappropriately treats all changes in the predicate product as if they were the same in scope, importance, and legal effect: change of a predicate product is assumed to be so extensive as to render the entire report new. Many such changes, however do not modify the original provisional SE report in any way that could raise new issues regarding the effects on public health.

Rather than pronouncing a blanket rule predicated on the assumption that any change of a predicate product is significant, FDA should adopt a flexible policy on the issue. By analogy, within FDA's Center for Devices and Radiological Health (CDRH) it is permissible for premarket notification (510(k))[31] submitters to amend their submissions during CDRH's substantive substantial equivalence review process. In the 510(k) review process it is common for FDA to find a new medical device substantially equivalent to a predicate device that was (1) only identified by the submitter after questions were raised by the Agency, or (2) unilaterally identified by CDRH as a more appropriate predicate than the one originally provided by the submitter. In the device context, allowing for the amendment of identified predicates has allowed submitters and FDA to address previously unresolved scientific questions and regulatory requirements without creating unnecessary hurdles such as withdrawing and re-filing a submission. Likewise, here, FDA should allow amendments to SE reports, including a change in predicate products, unless those amendments are so significant that they fundamentally change the nature of the submission as a whole.

Such a commonsense, flexible standard would benefit FDA. Updates to SE reports, including those relating to the predicate product, can provide FDA with more and better data on a new product. These modifications can help the Agency confirm, based on the best available

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Equivalence: An Update (Aug. 21, 2012),
http://fda.yorkcast.com/webcast/Viewer/?peid=df74168e0fb148289c4146184a278da31d; FDA, Webinar: Compliance Training for Small Businesses - "Draft Guidance – Substantial Equivalence Reports: Manufacturer Requests for Extensions or to Change the Predicate Tobacco Product" (Aug. 12, 2014).

[30] 21 U.S.C. § 387j(a).

[31] CDRH's premarket notification program requires manufacturers to submit a 510(k) to FDA at least 90 days before introducing, or delivering for introduction, a device into interstate commerce for commercial distribution so the Agency can determine whether or not the device meets the criteria for market clearance (Sections 510(k) and (n) of the Federal Food, Drug and Cosmetic Act (FFDCA) (21 U.S.C. §§ 360(k) & (n))). FDA bases its decision on whether the device is substantially equivalent to a legally marketed (predicate) device (Section 513(i) of the FFDCA (21 U.S.C. § 360c(i))). The device cannot be commercialized until FDA issues an order stating that the device has been determined to be substantially equivalent (Section 513(f)(1) of the FD&C Act (21 U.S.C. § 60c(f)(1))).

information, that the new product will not present more harm to public health. FDA should encourage, not inhibit, such changes.

By retaining the flexibility to evaluate the significance of the proposed change, FDA also could better ensure fairness to regulated parties as they seek to follow the Agency's evolving requirements.

Conclusion

We appreciate the opportunity to submit these comments and to share our perspective on the need for a flexible approach to extensions of time and changes to the predicate product in the context of SE reports. As always, we would be happy to discuss these comments.

Sincerely,

James E. Dillard III