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February 18, 2014

Division of Dockets Management (HFA-305)
Food and Drug Administration
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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).

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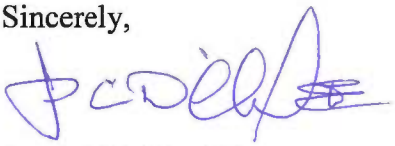
[15] *See* 21 C.F.R. §1107.1(a)(1).
[16] *Id.*

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,



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Attachments

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

Attachment A

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March 22, 2011

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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.

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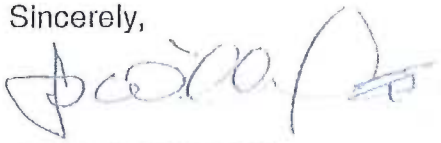
We appreciate the opportunity to submit these comments and urge the Agency to incorporate them in a Revised Guidance. We look forward to further opportunities to provide comments to the Agency as its thinking on substantial equivalence evolves.

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 . . . ."