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

Re: Guidance for Industry and FDA Staff: Section 905(j) Report: Demonstrating
Substantial Equivalence for Tobacco Products (Docket No. FDA-2010-D-0635)

Dear Sir or Madam:

Lorillard Tobacco Company (Lorillard) submits these comments in response to FDA's Guidance for Industry and FDA Staff: Section 905(j) Report: Demonstrating Substantial Equivalence for Tobacco Products (the Guidance) issued on January 5, 2011.

While Lorillard appreciates that the Food and Drug Administration (FDA) issued guidance regarding section 905(j) of the Federal Food, Drug, and Cosmetic Act (FDCA), the Guidance does not provide meaningful assistance to Lorillard and other tobacco product manufacturers as these companies prepare to comply with the requirements of section 905(j) of the FDCA. Several provisions of the Guidance are unclear and others are inconsistent with the text and intent of the Tobacco Act. Moreover, FDA takes, in many respects, an extremely strict interpretation of the Family Smoking Prevention and Tobacco Control Act (FSPTCA or Tobacco Act).¹ This interpretation does not account for the practical realities of tobacco product manufacturing and creates an unnecessarily burdensome regulatory regime. FDA's failure to propose any exempt categories in the proposed minor modification rule² makes even more imperative that the Guidance provide reasonable flexibility for section 905(j) submissions and create a streamlined alternative to the new tobacco product approval process. FDA should revise the Guidance to provide greater clarity, to eliminate unnecessary burdens on FDA and tobacco product manufacturers, and to conform to the intent of Congress.

¹ Pub. L. No. 111-31, 123 Stat. 1776 (2009).

² Tobacco Products, Exemptions From Substantial Equivalence Requirements, Proposed Rule, 76 Fed. Reg. 737 (Jan. 6, 2011). Lorillard intends to submit comments on this proposed rule.

Lorillard respectfully offers the following comments on the Guidance.

I. FDA must interpret the FSPTCA in a way that gives meaning to all provisions of the law.

A. With respect to the definition of “substantial equivalence,” FDA should not interpret “same” to mean “identical.”

The Tobacco Act defines a new tobacco product as “substantially equivalent” to a predicate product if the new product has (1) “the same characteristics” as the predicate tobacco product or (2) different characteristics that do not raise different questions of public health.³ The Guidance suggests that FDA interprets “same” to mean “identical.”⁴ Under the Guidance, then, any new product that is not identical to a predicate product would be regarded as having “different characteristics” and thus subject to the requirements of the second half of the substantial equivalence definition. This interpretation renders the first half of the substantial equivalence definition without meaning as it is extremely unlikely that a new tobacco product will be identical to a predicate product with respect to each and every characteristic (including ingredients and materials). FDA’s interpretation violates a basic principle of statutory interpretation that “every clause and word of a statute” must be given meaning and treated as having an effect.⁵

This interpretation is also inconsistent with FDA’s regulatory schemes for medical devices and generic drugs. Most medical devices are marketed after submission of a premarket notification under section 510(k) of the FDCA, often referred to as a “510(k) notification.” A device may be marketed under a 510(k) notification only if it is “substantially equivalent” to a “predicate device.” The FDCA defines “substantial equivalence” to mean that the device has the same intended use as the predicate device and (1) has the same technological characteristics as the predicate device, or (2) if it has different technological characteristics, must be demonstrated to be as safe and effective as the predicate device and must not raise different questions of safety and effectiveness than the predicate device raises.⁶ In its interpretation of the device substantial equivalence definition, FDA has not interpreted the term “same” to mean “identical.” Rather, the agency has allowed for some differences between the products but still concluded that they were the “same” for purposes of the substantial equivalence determination. This interpretation is consistent with the legislative history, which stated, “the term ‘substantially equivalent’ is not intended to be so narrow as to refer only to devices that are identical to

³ 21 U.S.C. § 387j(a)(3)(A).

⁴ See Guidance at 13 (“Where you believe that all the characteristics of the new tobacco product are identical to those of the predicate tobacco product . . .”).

⁵ *Montclair v. Ramsdell*, 107 U.S. 147, 152 (1883). See also *Astoria Federal Savings & Loan Ass’n v. Solimino*, 501 U.S. 104, 112 (1991) (stating that statutes should be construed ‘so as to avoid rendering superfluous’ any statutory language).

⁶ 21 U.S.C. § 360c(i)(1)(A).

marketed devices nor so broad as to refer to devices which are intended to be used for the same purposes as marketed products.”⁷

FDA follows a similar approach in its regulation of generic drugs. Under section 505(j) of the FDCA, in order for an abbreviated new drug application (ANDA) for a generic product to be approved, the applicant must show, among other things, that the generic product is the “same as” an innovator reference listed drug (RLD).⁸ FDA implementing regulations define “same as” to mean identical in regard to active ingredient, dosage form, strength, route of administration, and conditions of use.⁹ Despite the seemingly rigorous requirements imposed by FDA regulations, the agency has in practice approved generic products as the “same as” the reference listed drug even though the products are not identical. For example, the FDCA requires a generic drug approved through an ANDA to have the same route of administration, strength, and dosage form as its RLD, but allows for differences if approved by FDA through a suitability petition.¹⁰ In addition, there have been several instances in which FDA has permitted approval of generic drugs without use of the petition process notwithstanding certain differences in the formulation of the generic product.¹¹ As another example, the FDCA requires a generic drug to have the “same” labeling as its reference drug, with only limited exceptions.¹² Despite the apparent narrow statutory exceptions to the requirement that generics have the same labeling as a reference drug, FDA has promulgated regulations that permit generic drug manufacturers to use labeling with different information on expiration dates, formulation, bioavailability, and pharmacokinetics, to make labeling revisions to comply with current FDA labeling guidance, and to omit any labeling material that is protected by patents or exclusivity (unless the omission raises a safety or effectiveness issue).¹³ These generic products are still considered the “same as” the innovator products for purposes of the statutory requirement.

Consistent with the approach taken by FDA for medical devices and generic drugs, the agency should interpret the Tobacco Act to not require that constituents be identical to fit within “same characteristics” of the substantial equivalence definition.

⁷ H.R. Rep. No. 94-853 (1976), at 36-37.

⁸ 21 U.S.C. §§ 355(j)(2)(A)(ii).

⁹ 21 C.F.R. § 314.92.

¹⁰ See 21 U.S.C. § 355(j); 21 C.F.R. § 314.92.

¹¹ For example, FDA approved a generic version of Dilantin[®] (phenytoin) as a capsule, even though the generic drug was in fact a tablet inserted into a capsule shell, rather than powder in a capsule as is the case for the innovator version. See *Warner-Lambert Co. v. Shalala*, 202 F.3d 326, 327-28 (D.C. Cir. 2000).

¹² 21 U.S.C. § 355(j)(2)(A)(v).

¹³ See 21 C.F.R. § 314.94(a)(8)(iv).

B. Limiting substantial equivalence comparisons to a single predicate product is inconsistent with the structure and intent of the FSPTCA.

The Guidance provides that for purposes of 905(j) reports, FDA interprets “predicate tobacco product” to mean “that a single predicate tobacco product should be used for comparison purposes.”¹⁴ This interpretation is inconsistent with the language and structure of the Tobacco Act as well as with FDA’s interpretation of similar requirements in the device context.

As explained above, under the Tobacco Act, “substantially equivalent” is defined to mean that a new tobacco product has been found to have (1) “the same characteristics” as the predicate tobacco product or (2) different characteristics that do not raise different questions of public health.¹⁵ Under the Guidance, any new tobacco product that is not identical to a single predicate product would be regarded as having “different characteristics” and thus subject to the requirements of the second half of the substantial equivalence definition. This interpretation again renders the first half of the substantial equivalence definition meaningless. In contrast, an interpretation of the Tobacco Act that permits multiple predicate products gives meaning to the first half of the substantial equivalence definition and accords with the intent of the law to create a streamlined regulatory pathway for new products that have the same characteristics as preexisting products.

Moreover, an interpretation of the Tobacco Act that permits multiple predicate products is consistent with FDA’s historical approach to the concept of substantial equivalence for medical devices. The statutory definition of “substantial equivalence” for devices is similar to the definition used for tobacco products in that both definitions contemplate the comparison of the new product to a “predicate product.”¹⁶ As opposed to FDA’s interpretation of a single predicate product for tobacco products, however, in the device context, the agency has typically permitted the use of multiple predicates as the basis for comparison in a 510(k) notification. For example, a 510(k) submitter may seek to compare its device to more than one predicate and demonstrate that each functional component of the new device is substantially equivalent to its corresponding predicate.¹⁷ A recent report from FDA indicates that the agency intends to continue to “strongly support” the use of multiple predicates to demonstrate substantial equivalence.¹⁸

Consistent with the approach taken by FDA for medical devices, the agency should interpret the Tobacco Act to permit multiple predicate products.

¹⁴ Guidance at 4.

¹⁵ 21 U.S.C. § 387j(a)(3)(A).

¹⁶ Compare 21 U.S.C. § 360c(i)(1)(A) and 21 U.S.C. § 387j(a)(3)(A).

¹⁷ See CDRH Preliminary Internal Evaluation, Vol. 1, 510(k) Working Group Preliminary Report and Recommendations at 58 (Aug. 2010).

¹⁸ See 510(k) and Science Report Recommendations: Summary and Overview of Comments and Next Steps at 3, 14-15 (Jan. 2011).

C. 905(j) reports should be treated as premarket notifications rather than as new product applications requiring FDA approval.

The Guidance inappropriately converts the statutory scheme for premarket notification under section 905(j) of the FDCA into a premarket approval requirement. The Guidance provides that for new tobacco products introduced into interstate commerce after March 22, 2011, a new tobacco product application under section 910 of the FDCA is not required if the tobacco product manufacturer submits a report under section 905(j) and FDA has issued an order finding the tobacco product to be substantially equivalent to an appropriate predicate product and in compliance with the requirements of the Tobacco Act.¹⁹ According to FDA, there is no time limit on its review and approval of a 905(j) report.²⁰

This interpretation is inconsistent with the structure and intent of the Tobacco Act. Indeed, the language and structure of the Tobacco Act demonstrate that Congress intended 905(j) reports, as compared to new product applications, to be premarket notifications and that the submitter could proceed to market after 90 days absent FDA objection.²¹ FDA's interpretation renders meaningless the requirement in section 905(j) that a substantial equivalence report must be filed with the agency at least 90 days prior to the introduction of the relevant product into interstate commerce.²² If a manufacturer must wait until FDA approves its 905(j) report before introducing the product into interstate commerce, and there is no time limit on FDA's review and approval of that report, there is no process by which the manufacturer can calculate the date which will be 90 days prior to the introduction of the product. Moreover, FDA's interpretation that there is no time limit on its review and approval of a 905(j) report would give the agency greater discretion in reviewing a 905(j) report than it has for reviewing a new product application, which must be approved or denied within 180 days.²³ This is inconsistent with the clear Congressional intent for the substantial equivalence review process to offer an accelerated, less intensive, and less burdensome alternative to the new product approval process.

Moreover, FDA's interpretation fails to give meaning to the entire statutory scheme created by Congress. For example, FDA's interpretation renders meaningless the reporting scheme contained in section 904(c) of the FDCA.²⁴ Under section 904(c)(2), a

¹⁹ Guidance at 5, 6.

²⁰ See Substantial Equivalence Webinar: Tobacco Industry, Small and Large Business Professionals (Jan. 12, 2011), available at <http://www.fda.gov/TobaccoProducts/ResourcesforYou/ForIndustry/ucm239639.htm>.

²¹ See H. Rep. No. 111-058, Part 1 (2009), at 19 (stating that the Tobacco Act would require "manufacturers of certain products that are 'substantially equivalent' to ones already on the market before a particular date to *notify* FDA by submitting a report with specified information before entering the market.") (emphasis added).

²² 21 U.S.C. § 387e(j)(1).

²³ 21 U.S.C. § 387j(c)(1)(A).

²⁴ 21 U.S.C. § 387d(c).

manufacturer must report to FDA new or increased quantities of tobacco additives at least 90 days before introduction into commerce.²⁵ In addition, section 904(c)(3) provides that, if at any time a tobacco product manufacturer eliminates or decreases an existing additive, the manufacturer shall within 60 days of such action so advise FDA of the change.²⁶ This provision seems to clearly contemplate that tobacco product manufacturers can take such action without FDA premarket approval. Under FDA's interpretation in the Guidance, however, any product change, including the reduction or elimination of an additive, would trigger the requirement for a full 905(j) report and FDA approval before it could be marketed. This interpretation simply ignores the fact that Congress, by including section 904(c), intended to allow manufacturers to make certain changes to a tobacco product without triggering the requirement for a substantial equivalence report. FDA must interpret the FSPTCA in a way that gives meaning to all provisions of the Tobacco Act.

II. FDA should take an integrated approach to implementing the FSPTCA.

A. FDA should not require 905(j) reports to include levels of harmful and potentially harmful constituents in the absence of an established list of such constituents.

The Guidance provides that each 905(j) submission should report the presence of all harmful and potentially harmful constituents (HPHC) in the new tobacco product and predicate tobacco product, including quantitative levels of each HPHC in cigarette smoke using both International Organization for Standardization (ISO) and Canadian Intense (CI) smoking regimes.²⁷

In the Tobacco Act, Congress explicitly limited FDA's authority to require harmful constituent information by providing a specific process and timetable for identifying and submitting such information. Under section 904(e) of the FDCA, FDA is required to establish a list of HPHCs by April 2012.²⁸ Only after FDA generates this list are tobacco product manufacturers and importers required under section 904(a)(3) to submit to FDA information relating to HPHCs.²⁹ Until FDA fulfills its duty under 904(e) to establish a list of HPHCs, and before manufacturers and importers are required to submit information relating to HPHCs under section 904(a)(3), FDA cannot require tobacco product manufacturers, as part of a section 905(j) report, to submit information regarding harmful constituents. This interpretation makes sense from a practical perspective. Until FDA establishes the list required under section 904(e), tobacco product manufacturers have no reliable guidance on which constituents may be regarded as harmful. Without an FDA list, different manufacturers may report different constituents,

²⁵ 21 U.S.C. § 387d(c)(2).

²⁶ 21 U.S.C. § 387d(c)(3).

²⁷ Guidance at 11.

²⁸ 21 U.S.C. § 387d(e).

²⁹ 21 U.S.C. § 387d(a)(3).

causing confusion, precluding meaningful product comparisons, and imposing inconsistent compliance burdens. Moreover, in order to require certain smoking regimes (such as ISO or CI), the agency must issue regulations as required by section 915 and allow for meaningful comment by all stakeholders.

Although FDA has established the Tobacco Products Constituents Subcommittee of the Tobacco Products Scientific Advisory Committee and tasked the Subcommittee with recommending a list of such substances, the Subcommittee's draft list of HPHCs is only a draft recommendation issued by an advisory committee to FDA. As such, it cannot be used to require information on HPHCs in section 905(j) submissions.³⁰ TPSAC's list, moreover, is unwieldy; it comprises over 100 constituents. Analysis of all of the proposed constituents would impose an enormous scientific burden on both the regulated industry as well as FDA. There may not be sufficient world laboratory capacity to analyze such an extensive list of constituents for all of the hundreds of tobacco brands on the U.S. market. Moreover, this sort of analysis would be limited in its scientific value. Many of the proposed constituents lack well-established validated, and sensitive methods of analysis to permit meaningful comparisons among different tobacco products. In addition, methods for the measurement of human exposure biomarkers and the correlation of those levels to reliable indices do not exist for the majority of the proposed candidates.

FDA's recently issued a final guidance that discusses the meaning of "harmful and potentially harmful constituent" in the context of implementing the HPHC list requirement³¹ similarly should not be used, at this point, to require information on HPHCs in section 905(j) submissions. The final guidance defines HPHCs to include substances that have the potential to cause direct or indirect harm. Substances that have the potential to cause direct harm include "toxicants, carcinogens and addictive chemicals".³² This definition is broad and imprecise and provides no meaningful assistance to tobacco product manufacturers in determining listable substances. Indeed, all chemicals are toxic at some level, and various authoritative bodies have developed different definitions and lists of carcinogens.

B. FDA should implement the reporting requirements of section 904 and section 905(j) in a consistent manner.

Both section 904 and section 905(j) require that tobacco product manufacturers submit certain information regarding the ingredients in their products. In addition to the section 904(c) reporting requirements described above, section 904(a) of the FDCA requires that tobacco product manufacturers submit "a listing of all ingredients, including tobacco, substances,

³⁰ See

<http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM219548.pdf>.

³¹ 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 (Jan. 2011).

³² *Id.* at 5.

compounds, and additives that are . . . 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.”³³ This requirement became effective in December 2009, and manufacturers, including Lorillard, have submitted the relevant ingredient information according to FDA guidance interpreting this requirement.³⁴ As part of the substantial equivalence report under section 905(j), a manufacturer must include, among other things, a comparison of the ingredients and materials in the new tobacco product and the predicate tobacco product.³⁵

There appear to be differences between what FDA requires for ingredient submissions under section 904 and what ingredient information the agency requires to be included in section 905(j) reports. For example, FDA’s guidance on the section 904 requirements provides that a manufacturer does not “need to list any substance contained in a complex purchased ingredient where the ingredient is not made to [the manufacturer’s] specifications.”³⁶ The substantial equivalence guidance does not, however, contain this same provision and could be read to require that all ingredients, including all substances in a complex ingredient not made to the manufacturer’s specifications, must be included in the section 905(j) report. Requiring a manufacturer to submit different information about the same ingredients for the two reporting requirements imposes an administrative burden on the manufacturers and their suppliers as well as on the agency. In addition, as a practical matter, it may be quite difficult, if not impossible, for manufacturers to obtain such detailed information from their suppliers about proprietary blend ingredients. Instead, FDA should interpret section 904 and section 905(j) to require reporting of information in the same manner. FDA should follow the same approach as required by section 904 for information to be submitted as part of the 905(j) reports.

As another example, the Guidance recommends that 905(j) reports should include a listing of, among other things, ingredients and materials in the new tobacco product and in the predicate tobacco product.³⁷ Substantial overlap exists between the features used to describe what information should be reported in each section; for example, both the “Ingredients” and “Material” sections list “the component of the tobacco product” and “the subcomponent” as examples of the features to include in the section 905(j) report. FDA’s guidance on section 904 requirements suggests, however, that materials and ingredients are one category.³⁸ FDA should follow this same approach for 905(j) reports, that is, the agency should clarify that manufacturers may report materials and ingredients together in section 905(j) reports, as manufacturers already do for section 904 ingredient reports.

³³ 21 U.S.C. § 387d(a)(1).

³⁴ See Guidance for Industry: Listing of Ingredients in Tobacco Products (Nov. 2009).

³⁵ 21 U.S.C. § 387j(a)(3)(B).

³⁶ Guidance for Industry: Listing of Ingredients in Tobacco Products (Nov. 2009) at 8.

³⁷ Guidance at 9-10.

³⁸ Guidance for Industry: Listing of Ingredients in Tobacco Products (Nov. 2009) at 5 (“Each listed ingredients is to be uniquely identified so as to distinguish it from similar or related materials.”).

III. FDA must clarify and provide meaningful explanations of several provisions of its Guidance.

A. FDA should clarify that packaging and labeling changes that do not alter the composition of the product do not by themselves trigger the requirement for a 905(j) report.

A tobacco product manufacturer, throughout the lifecycle of a particular tobacco product brand, may make changes to the packaging or labeling of a tobacco product. These changes may be made voluntarily by the manufacturer or may be made pursuant to a statutory obligation. For example, section 911(b) of the FDCA prohibits the use of the descriptors "light," "mild," "low," or similar descriptors for a tobacco product unless FDA has approved the product as a modified risk tobacco product. Upon this prohibition becoming effective, tobacco product manufacturers were required to modify the labeling on their packages in order to comply with the new statutory obligation. This packaging and labeling change did not effect the composition of the product.

FDA should clarify that packaging or labeling changes that do not alter the composition of the product do not trigger the requirement to submit a section 905(j) report. This approach is practical. It makes little sense to require a manufacturer to submit and FDA to review and approve a 905(j) report when the only change is to the packaging or labeling of a tobacco product and that change has in no way affected the characteristics of the product. Moreover, this approach is consistent with the Tobacco Act's definition of "characteristics," which suggests that the analysis of substantial equivalence should focus on the constituents that comprise the tobacco product (for example, the materials, ingredients, design, composition, and heating source) rather than on any external features of a particular product (for example, packaging or labeling).³⁹ This approach is also consistent with FDA's approach to the regulation of food additives. For a substance that is a "food additive," as defined by the FDCA, section 409 of the FDCA requires that the substance must be formally approved by FDA and codified in FDA's regulations prior to its use in food.⁴⁰ The term "food additive" encompasses all substances that become part of food or affect the characteristics of any food.⁴¹ Thus, to the extent that a change to food packaging or labeling does not affect the characteristics of a food, FDA does not require prior approval of the change.

B. FDA should clarify the reporting obligations triggered by a change in ingredient supplier.

The Guidance suggests that a change in ingredient supplier of the same ingredient or material triggers the requirement to submit a section 905(j) report.⁴² This approach is

³⁹ See 21 U.S.C. § 387j(a)(3)(B).

⁴⁰ See 21 U.S.C. § 348.

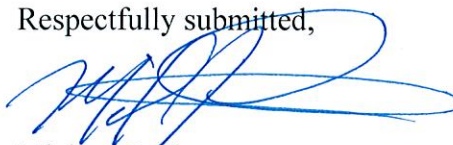
⁴¹ 21 U.S.C. § 321(s).

⁴² Guidance at 13.

impractical in light of how tobacco product manufacturers generally procure ingredients for their products. Tobacco product manufacturers use many ingredients in their products, ingredients that are often complex ingredients (for example, flavor extracts) bought “off-the-shelf,” that is ingredients that are not made to a manufacturer’s specification and are commercially made available for sale to others by the supplier. In the normal course of business, some ingredient suppliers may cease selling a specific ingredient or there may be other commercial reasons for a manufacturer to switch to a different source of the same complex ingredient. Requiring a manufacturer to submit a 905(j) report and wait for FDA approval each and every time the manufacturer needs to switch the supplier of the same ingredient or material imposes an enormous administrative burden on both the regulated industry and FDA. Moreover, this approach is inconsistent with the approach FDA has taken to implement the ingredient reporting requirements of section 904 of the FDCA. There, the agency has recognized that tobacco product manufacturers often use multiple sources interchangeably to supply an ingredient. In its guidance on tobacco product ingredient submissions, the agency stated that manufacturers who “use a complex ingredient provided by multiple sources interchangeably in a single tobacco product” should “report all alternative sources in [their] ingredient listing.”⁴³ To the extent that a manufacturer reports alternative sources of the same ingredient or material in its ingredient listing submission, FDA should not require that a manufacturer submit a section 905(j) report if it switches to one of the listed alternative sources.

Lorillard looks forward to a continued dialogue with FDA about the important issues raised in the Guidance. Please do not hesitate to contact us if you would like to discuss any of Lorillard’s comments further.

Respectfully submitted,



Michael J. Shannon

⁴³ Guidance for Industry: Listing of Ingredients in Tobacco Products (Nov. 2009) at 10.