



July 12, 2019

Dockets and Management Staff [HFA-305]
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2016-N-3818, Proposed Rule on Content and Format of Substantial Equivalence Reports; Food and Drug Administration Actions on Substantial Equivalence Reports, 84 Fed. Reg. 12740 (April 2, 2019).

Ladies and Gentlemen:

The undersigned public health organizations submit these comments in the above-designated docket.

The Tobacco Control Act defines a “new tobacco product” as any tobacco product that was not commercially marketed on February 15, 2007, including any tobacco product commercially marketed on that date but subsequently modified. Tobacco product manufacturers are prohibited from marketing any new tobacco product unless FDA has (1) granted a new product application pursuant to section 910 of the Act; (2) granted a substantial equivalence application pursuant to sections 910 and 905(j); or (3) determined that a product is entitled to an exemption from the substantial equivalence requirements pursuant to section 905(j)(3). FDA may grant a substantial equivalence application only if the manufacturer demonstrates that the new tobacco product has “the same characteristics” as a product commercially marketed on February 15, 2007 or that the new product does not have the same characteristics as a product commercially marketed on that date but “does not raise a different question of public health.”

The proposed rule is the latest in a long line of FDA policy statements on the requirements for establishing substantial equivalence.¹ In addition to issuing numerous such statements since its first draft guidance, published in 2011, FDA has convened several

¹ Section 905(f) Reports Demonstrating Substantial Equivalence for Tobacco Products (January 2011); Demonstrating the Substantial Equivalence of a New Tobacco Product: Responses to Frequently Asked Questions.” (September 2011); Establishing that a Tobacco Product was Commercially Marketed in the United States as of February 15, 2007 (September 2014); Meetings with Industry and Investigators on the Research and Development of Tobacco Products (July 2016); Demonstrating the Substantial Equivalence of a New Tobacco Product: Responses to Frequently Asked Questions (December 2016);

workshops, including a workshop on October 22-23, 2018, to inform manufacturers about the required content of substantial equivalence reports and to receive comments from industry and the public about the substantial equivalence process. In addition, FDA has now acted on several thousand substantial equivalence applications, granting several hundred.² FDA has published summaries of the applications that have been granted and general summaries of the applications that have been denied, with explanations of the reasons why the applications were denied. Through these processes, FDA has provided manufacturers with a roadmap for the filing of future applications. Not surprisingly, the policies and standards outlined in the above-designated docket largely codify existing standards and practices FDA has adopted since it first started receiving substantial equivalence reports. Nothing significant in the notice should come as a surprise to manufacturers who have been following FDA's practices and policy statements on substantial equivalence. Despite the fact that a number of issues remain open, manufacturers have—and have had for a considerable time—sufficient information about what is required in substantial equivalence reports to understand what must be provided in order to obtain a substantial equivalence determination.

FDA has initiated this rulemaking to establish requirements for the form and content of substantial equivalence reports to ensure that such reports provide the information FDA requires in order to make a substantial equivalence determination. Although FDA states that it intends to “shorten review times for substantial equivalence reports,” the agency must not forget that its principal statutory obligation is to protect the public health—not to facilitate the marketing of deadly and addictive products.

I. Defining Terms.

Congress provided that any modification of an existing tobacco product would make the product a “new tobacco product” and thereby subject it to requirements applicable to new tobacco products. In prior guidance FDA has made clear that any change in the characteristics of a tobacco product is a “modification.” “Modification” therefore includes a change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient” of a tobacco product. 84 Fed. Reg. 12743. The proposed rule properly retains this definition of “modification,” thus requiring any “modified” tobacco product to meet standards applicable to new tobacco products, i.e., either the standards applicable to new products generally or the lesser standards applicable to products demonstrated to be “substantially equivalent” to grandfathered products. It is important for FDA to continue to adhere to this interpretation.

² <https://www.fda.gov/tobacco-products/substantial-equivalence/marketing-orders-se>

The proposed rule defines “accessory” and “component or part” the same way those terms were defined in the final deeming rule. The undersigned support retention of these definitions and reiterate their view, expressed in comments on the proposed deeming rule, that FDA should deem “accessories” to be within its jurisdiction if they have intended or foreseeable effects on public health.

The proposed rule defines “Harmful and Potentially Harmful Constituents.” The list of Harmful and Potentially Harmful Constituents was established in accordance with the advice of an expert subcommittee of the Tobacco Products Scientific Advisory Committee. The definition in the Proposed Rule is consistent with the criteria applied in formulating the list and, importantly, includes not only substances that are inhaled, ingested, or absorbed into the body, but also substances that potentially could be inhaled, ingested or absorbed. It also includes not only substances that cause direct or indirect harm to users or nonusers of tobacco products, but also substances that have the potential to cause harm. The undersigned organizations support this broad definition and urge FDA to retain it in the final rule.

II. Comparison to a single predicate product.

The proposed rule makes clear that in establishing substantial equivalence an applicant must establish that the new tobacco product is substantially equivalent to a single, specified predicate product. 84 Fed. Reg. 12,756, § 1107.18(e)), § 1107.18(f)(1), § 1107.18(f)(2)(iii). It is important for FDA to retain this requirement in any final rule. As urged in numerous prior comments,³ use of a composite or “fictional” predicate product would be inconsistent with the fundamental purposes of the Tobacco Control Act and the requirements it imposed on the establishment of substantial equivalence.

III. Clarifying the requirement that a new tobacco product must be shown to be substantially equivalent to a grandfathered tobacco product.

Although FDA correctly concludes that a finding of substantial equivalence can only be made based on a determination that a new tobacco product is substantially equivalent to a product that was commercially marketed on February 15, 2007 (a “grandfathered product”), 84 Fed. Reg. 12787-88, § 1107.19(g), other statements in the discussion accompanying the proposed rule unnecessarily create confusion by failing to reference this requirement. E.g., 84 Fed. Reg. 12756 (describing “predicate product”), 12748 and 12777 (defining “predicate product”) 12783-4 (discussing information in the summary of an application, § 1107.18(f)). The statutory language of the Tobacco Control Act makes it quite clear that “an Order under subsection (c)(1)(A)(i) [of Section 910 of the Act, 21 U.S.C. 387j] [i.e., the granting of a new product application] is required unless (i) the manufacturer has submitted a report under section 387e(j) of this title, and the Secretary has issued an order that the tobacco product (I) *is*

³ See, e.g., Comments of American Cancer Society Cancer Action Network, et al., March 22, 2011 in Docket No. FDA 20109-D-0635, p. 8.

substantially equivalent to a tobacco product commercially marketed (other than for test marketing) in the United States as of February 15, 2007....” (emphasis added) The statute does not permit FDA to exempt a manufacturer from the requirement of obtaining a new product marketing order simply upon a showing that the new product is substantially equivalent to a product *not* commercially marketed on February 15, 2007, *regardless of whether the predicate product has previously been found substantially equivalent to a grandfathered tobacco product.*

Section 905(j) of the Act (21 U.S.C. 387e(j)(1)(A)(i)) does permit a tobacco product manufacturer to include in a substantial equivalence report “the basis for its determination that the tobacco product is substantially equivalent” both to a grandfathered tobacco product and to “a tobacco product that the Secretary has previously determined, pursuant to subsection (a)(3) of section 387j of this title, is substantially equivalent...” but such a demonstration is insufficient by itself to meet the statutory requirement for establishing substantial equivalence.

FDA recognizes that the successive use of non-grandfathered products as predicate products could result in an application in which a new tobacco product, far removed from the original grandfathered tobacco product, could be “substantially equivalent” to a non-grandfathered predicate product and yet not be “substantially equivalent” to the original grandfathered tobacco product. Quite appropriately, FDA’s discussion accompanying the proposed rule, states:

Although an applicant can support a showing of SE by comparing the new tobacco product to a tobacco product that is grandfathered or that FDA has previously found SE, in order to issue an SE order, FDA must find that the new tobacco product is substantially equivalent to a tobacco product commercially marketed in the United States as of February 15, 2007 (see section 910(a)(2)(A)(i)(I) of the FD&C Act). This statutory provision helps FDA ensure that new tobacco products using the substantial equivalence pathway and relying on predicate tobacco products previously found SE do not vary so much from the original grandfathered tobacco product that the new product would actually raise different questions of public health compared to the originally grandfathered tobacco product. New products with differences that may appear only incremental when a new tobacco product is compared to a predicate product previously found SE may actually have had significant changes when compared to the grandfathered tobacco product. 84 Fed. Reg. at 12765.

The problem of permitting substantial equivalence to be established merely by showing substantial equivalence to a non-grandfathered product is exacerbated by the judicial holding that products with characteristics that are not identical can still have “the same characteristics.”⁴ Thus, Product B, a new tobacco product, may be found substantially equivalent to Product A, a

⁴ *Philip Morris USA, Inc. et al. v. FDA*, 202 F.Supp.3d 31 (D.D.C. 2016).

grandfathered product; but it does not necessarily follow that if Product C is substantially equivalent to Product B it would also be found substantially equivalent to Product A if the two were compared. Successive iterations of substantial equivalence applications, each referencing a predicate product that is not itself a grandfathered tobacco product, could attenuate the relationship between the new tobacco product and the original grandfathered tobacco product and could lead to the introduction of new tobacco products that would not be found substantially equivalent to any product actually commercially marketed on February 15, 2007. Imagine, for example, a chain of eight products, each referencing its immediate predecessor as a predicate product. In such a case, it is not unlikely that Product H might have very different characteristics from the original grandfathered product or raise different questions of public health despite the fact that it could be found substantially equivalent to Product G. A determination of substantial equivalence based on a comparison between Product H and Product G would directly contravene the statute, which, as demonstrated above, requires on a demonstration of substantial equivalence between the new tobacco product and a product actually commercially marketed on February 15, 2007, i.e., a direct comparison between Product H and Product A.

FDA states that to deal with such possibilities “FDA may need to look back to previously submitted SE reports in the SE chain that rely on the original grandfathered product in order to issue an SE order.” *Id.* FDA proposes that, if requested by FDA, the applicant would be required to provide information related to the original grandfathered tobacco product, even if the original grandfathered tobacco product is several tobacco products removed from the predicate product identified by the applicant. *Id.*, § 1107.19(g) Importantly, FDA states that if FDA is unable to look back to data provided to the Agency regarding the grandfathered product and the applicant does not provide the information, FDA would be unable to find the product substantially equivalent. *Id.* FDA “encourages applicants to provide this information with the initial SE report.” *Id.*

At a minimum, the regulation should require applicants relying on a predicate product that is not a grandfathered tobacco product to identify the original grandfathered tobacco product in the SE chain, as well as all other predicate products in the SE chain, and either provide information on such products or explain why they are unable to do so. In no event should FDA issue an SE Order unless the applicant has demonstrated that the new tobacco product is substantially equivalent to a specified grandfathered tobacco product.

FDA should amend its discussion of the requirements for showing substantial equivalence to clarify its intent. In numerous instances in the discussion accompanying the proposed rule FDA states that a manufacturer may use as a predicate product either a grandfathered tobacco product or a new tobacco product previously found substantially equivalent. E.g., 84 Fed. Reg. 12756, 12783-84, § 1107.18(f) Such statements are at best misleading if they do not also refer to the requirement that no new tobacco product can be found substantially equivalent unless it is shown to be substantially equivalent to a grandfathered tobacco product, as FDA clearly states elsewhere in its discussion. In fact, the characterization of

any non-grandfathered tobacco product as a potential “predicate product” is misleading without immediate reference to this important qualification. For example, the proposed rule states that “HPHC information for the new and predicate tobacco product is necessary for FDA to determine whether the new tobacco product raises different questions of public health.” 84 Fed. Reg. at 12748 FDA should make it clear that HPHC information is *always* required concerning both the new product and the grandfathered product to which the new product is being compared and that, without such information, provision of information regarding a non-grandfathered product is *never* sufficient to meet this requirement. It is essential for FDA to make this requirement clear.

IV. Use of surrogates should not be permitted

FDA has asked for comments on the use of information from surrogate tobacco products “where there is inadequate data available for the new or predicate tobacco product.”⁵ There is no statutory basis for the consideration of data concerning surrogate tobacco products and the use of such information should therefore not be permitted in substantial equivalence applications. A manufacturer unable to demonstrate substantial equivalence between a new product and a grandfathered tobacco product has failed to satisfy the statutory requirement. Use of data from “surrogate products” is particularly unjustifiable with regard to new tobacco products, which ought to be available for any necessary testing. FDA has nowhere provided a basis for the use of surrogate data in any context.

V. Defining “same characteristics”

Both prongs of the definition of “substantial equivalence” should be interpreted with the goal of ensuring to the maximum degree possible that new tobacco products should not increase the risk of death, disease and addiction already presented by products that were on the market prior to the grandfather date, February 15, 2007. As long as FDA required a new tobacco product to have characteristics “identical” to a predicate product, it could reasonably conclude that such a product was no more dangerous to the public health than the existing product. In determining that a new product can be found to have “the same characteristics” as an existing product even though its characteristics are not “identical,” in order to act consistently with its statutory responsibility FDA should limit any such findings to instances in which the manufacturer has demonstrated that the differences in characteristics cannot plausibly increase the potential harm to an individual or to the population as a whole. At a minimum, this standard would require the manufacturer to demonstrate both (1) precisely what all the differences in characteristics are and (2) that these differences cannot plausibly increase the potential harm to an individual or to the population as a whole.

⁵ FDA describes a “surrogate product” as “a tobacco product for which the applicant provides data it would like to extrapolate to the new, predicate tobacco product or both new and predicate products. . . where there is inadequate data available for the new or predicate product. . . .” 84 Fed. Reg. 12756-57, n. 8.

- A. FDA should not rely on certification to establish that the characteristics of a new tobacco product are identical to those of a predicate product.

FDA's proposed rule would permit manufacturers to certify that some or all of the characteristics are identical to those of the predicate product. § 1107.18(g), § 1107.18(h), § 1107.18(I)(2) and 84 Fed. Reg. 112757-58. It is essential for FDA to require that any such certification be fully supported by actual test data.

A manufacturer claiming that a new tobacco product has “the same characteristics” as a predicate product should be required both to identify and quantify *all* the characteristics of both products. A general statement that characteristics are identical invites imprecision and falsification and should not be permitted to substitute for a listing of the data establishing that the new product has “the same characteristics” as the grandfathered product. FDA's discussion of its experience with prior applications demonstrates that the summary data provided in applications has sometimes been miscalculated and that there is a need for FDA to examine the actual experimental data to verify that characteristics of the two products are in fact identical. 84 Fed. Reg. at 12757. The provision of the proposed rule permitting manufacturers to certify that some or all of the characteristics are identical to those of the predicate product is inconsistent with the lessons provided by FDA's experience with prior applications.

Comparative testing information should be required for all substantial equivalence reports, including those for which the applicant alleges the product characteristics are “identical” to the predicate product. A conclusory statement that a product's characteristics are “identical” to those of the predicate product should not be considered adequate. The inadequacy of the data submitted by many manufacturers in substantial equivalence applications to date—a fact repeatedly stated by FDA—counsels against the acceptance of conclusory allegations by manufacturers seeking to market new products. The conclusion that a product's characteristics are in fact identical to those of a predicate product should only be made on the basis of comparing actual test data for both products. Provision of such data is not burdensome to the applicant, nor should its review be burdensome to FDA. If test data are in fact identical, the result should be readily apparent. The requirement that actual test data be submitted for all products is more likely to ensure accurate applications. As FDA correctly notes, “Comparative testing supports the SE Report by showing the information contained in the SE Report is meaningful and accurate.” 84 Fed. Reg. at 12757. This statement is as true for products that allegedly have “identical” characteristics as for those that do not. The undersigned organizations oppose reliance on certifications as a substitute for submission of test data.

- B. FDA properly requires detailed information about testing and manufacturing practices.

FDA properly proposes to require the SE Report to include test protocols, quantitative acceptance criteria and test results. It also requires testing to be conducted on a sufficient sample size and on samples that reflect the final tobacco product composition and design, as well as

stating that the testing methods for the new and predicate products are the same. 84 Fed. Reg. 12757, § 1107.18(h)(2), § 1107.18(h)(4). It is important for FDA to retain all these requirements in any final rule.

Moreover, the manufacturer should be required to demonstrate that it employs manufacturing practices that can ensure that products actually produced consistently have the listed characteristics. FDA's discussion of manufacturing practices 84 Fed. Reg. 12755-56 further supports the importance of assessing the effect of manufacturing practices on the product.

- C. FDA should adopt a different criterion for determining whether a new tobacco product has "the same characteristics" as a grandfathered tobacco product.

A manufacturer claiming that a product has "the same characteristics" as a predicate product where the characteristics are not identical should be required to demonstrate that the differences, both individually and collectively, cannot plausibly have an effect on individual health or population-level health.

In discussing this prong of the substantial equivalence standard, FDA states that it is considering whether there is a class of changes as to which "FDA would not need scientific information to determine whether the new product raises different questions of public health." It is unclear what FDA means by "scientific information" in this context but the undersigned believe it would be unwise to adopt such a formulation. The provision of information demonstrating and quantifying the actual characteristics of both the predicate product and subject product is presumably "scientific information" that should *always* be required. Similarly, the explanation of reasons why such differences cannot plausibly have an effect on public health would constitute "scientific information." Although the undersigned organizations agree with FDA that a new product would have "different characteristics" if a product "were dissimilar enough from the predicate product that FDA could not determine without scientific information whether the new product raised different questions of public health," the undersigned do not understand how it is possible to make such a determination "without scientific information." We therefore urge FDA not to adopt this formulation in establishing the parameters of "same characteristics," but rather to restrict "same characteristics" findings to cases where the manufacturer is able to demonstrate that the specific changes, both individually and in the aggregate, cannot plausibly affect individual or population-level health.

FDA lists four examples of changes between the new product and the predicate product that it believes might be appropriate for a "same characteristics" finding. The undersigned organizations believe that "a change in product quantity between the new and predicate tobacco products" is inappropriate for categorization as "same characteristics." All the reasons FDA provided in ruling that a change in product quantity made a tobacco product a "new tobacco product" counsel against defining a product change as qualifying for "same characteristics." As FDA states in this its proposal, "a change in product quantity necessarily entails a change in the

amount of constituent ingredients and additives within the tobacco product, including nicotine.” 84 Fed. Reg. 12744. For this reason alone, changes in product quantity can raise different questions of public health. A manufacturer seeking a substantial equivalence designation for a change in product quantity should have to demonstrate that the particular change in product quantity does not raise different questions of public health in order to qualify. The other three examples FDA provides could plausibly qualify for the “same characteristics” designation.

VI. Demonstrating that a Product Does Not Raise a Different Question of Public Health.

Where a manufacturer is unable to demonstrate that a change in the product cannot plausibly affect individual or population-level health, it must demonstrate that the change does not raise different questions of public health. All the examples provided by FDA in its discussion of this prong of the definition (i.e., change in filter or ventilation of a combusted product, change in container closure for a smokeless tobacco product, or a change in characterizing flavor) clearly constitute changes that plausibly could raise different questions of public health and would require a manufacturer to provide scientific evidence adequate to demonstrate that the change did not do so. FDA enumerates at least six ways in which a new product can raise different questions of public health and all of them clearly do raise such questions. 84 Fed. Reg. 12745. A manufacturer seeking a substantial equivalence order under the second prong would have to demonstrate that, despite having different characteristics, the product would not, compared to the predicate product, increase HPHC yield, increase toxicity, increase initiation, increase abuse liability, increase dependence, or decrease cessation. Any product that had the potential to have any of these effects would raise different questions of public health unless the manufacturer could demonstrate that no such change would occur. Such a standard would, quite properly, be difficult to meet.

In other words, a product could qualify for the “same characteristics” prong if there were no plausible basis to believe that the difference between the predicate product and the new product could increase the risk to individual health or population-level health. A product could qualify for the “no different question of public health” only if the manufacturer could demonstrate that, despite the fact that it failed to meet the standard for “same characteristics,” it nevertheless could demonstrate that it neither increased HPHC yield, nor toxicity, nor initiation, nor abuse liability, nor dependence, and would not decrease cessation. A product that failed to satisfy all these criteria would raise a different question of public health and could not be found substantially equivalent.

VII. Test marketing

FDA properly concludes that unless a product was commercially marketed on February 15, 2007, a marketing order is required for any marketing of the product, whether in “test marketing” or “commercial marketing.”

In addition, FDA correctly concludes that a product that was in test marketing—and not commercial marketing-- on February 15, 2007 is itself a “new tobacco product” requiring a marketing order as a prerequisite for its sale in the United States. Moreover, FDA has consistently and correctly taken the position that a product in test marketing on February 15, 2007 cannot be a predicate product. As the Tobacco Control Act provides, only a product that was commercially marketed on that date can be a predicate product.

FDA has asked for comments on the evidence sufficient to demonstrate that a product was commercially marketed (other than in test markets) as of February 15, 2007. FDA has identified the appropriate documents for providing evidence that the purported grandfathered product was in fact commercially marketed on February 15, 2007. FDA should continue to demand such products and subject them to critical review before concluding that the standard has been met in any particular case.

VIII. Design Parameter Information

The undersigned organizations endorse the content and format of the required design parameter information for various tobacco products. FDA properly requires constituent smoke yields for combusted tobacco products to be measured under two smoking regimens recognized by the International Organization for Standardization and Health Canada. As FDA notes, if constituent yields were only reported from a single smoking regimen, FDA would have limited and potentially misleading information about constituent yields produced by a given product.

IX. Requirement for reporting TSNA and PAH

FDA notes that “based on its experience in reviewing new tobacco products, FDA has found significant increases in TSNAs and PAHs in cigarettes due to changes in types of tobacco compared to a predicate product.” 84 Fed. Reg. 12764. FDA states that “for all new cigarettes that have a substantial increase in other types of tobacco, to support a finding of substantial equivalence the applicant should include a comparison of TSNAs and PAHs in the mainstream smoke of the two products using both intense and non-intense smoking regimes.” *Id.* Such a comparison should be required for all substantial equivalence applications for combusted tobacco products. FDA’s proposed limitation of this requirement to cases in which the increase in other types of tobacco is “substantial” is imprecise and subject to evasion. Moreover, no new tobacco product with TSNA levels in excess of those of the predicate product should be found substantially equivalent. The association of higher levels of TSNA with increased risk of cancer should make it clear that any product with a higher level of TSNA than a predicate product does raise different questions of public health.

X. Categorical approach to substantial equivalence

The undersigned organizations strongly oppose the creation of categories of products eligible for substantial equivalence. The statute clearly contemplates product-by-product review

and requires showings to be made for each product that is the subject of a substantial equivalence application. Moreover, FDA’s experience with substantial equivalence applications—the large majority of which did not result in findings of substantial equivalence—demonstrates that manufacturers, if not required to produce specific evidence in support of substantial equivalence, will make claims of substantial equivalence that cannot be supported.

XI. Definition of Tobacco Product Manufacturer

FDA’s proposed definition of “Tobacco Product Manufacturer” (§ 1107.12, 84 Fed. Reg. at 12778) does not include an entity that contracts with another domestic entity to manufacture a tobacco product. The undersigned organizations understand that many new tobacco products are manufactured by entities who manufacture such products under contract with the entity that actually markets the products. FDA should consider expanding the definition of “tobacco product manufacturer” to include entities that contract with other parties to manufacture tobacco products. Although many such entities may be included in the definition because they “import finished product,” there may be other such entities that contract for the manufacture of such products by domestic manufacturers and thus may assert that they are not Tobacco Product Manufacturers under the proposed rule.

XII. Confidentiality

The level of confidentiality accorded by FDA to substantial equivalence applications has prevented the public from having any significant information about FDA’s review of such applications or the standards FDA is applying. To obtain any information at all, members of the public have had to resort to filing Freedom of Information requests, and FDA’s responses have sometimes been exceedingly slow and uninformative. The standards FDA now proposes make no significant change in these practices and accord far too much deference to the interests of tobacco product manufacturers in concealing information about their products at the expense of the general public’s ability to understand the criteria FDA is applying in its review of substantial equivalence applications. For example, FDA’s continuing refusal to disclose the existence of a substantial equivalence application unless the applicant has publicly disclosed the application prevents the public from knowing about important decisions FDA may be considering and effectively precludes any public participation in the consideration of such applications.

Respectfully submitted,

American Academy of Pediatrics
American Heart Association
American Lung Association
Campaign for Tobacco-Free Kids
Public Health Law Center
Truth Initiative