Guidance for Industry

Demonstrating the Substantial Equivalence of a New Tobacco Product: Responses to Frequently Asked Questions (Edition 3)*

Comments may be submitted at any time for Agency consideration. Electronic comments may be submitted to http://www.regulations.gov. Alternatively, submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD, 20852. All comments should be identified with Docket No. FDA-2011-D-0147. For questions regarding this guidance, contact the Center for Tobacco Products at (Tel) 1-877-CTP-1373 (1-877-287-1373) Monday-Friday, 9 a.m. – 4 p.m. EDT.

Additional copies are available online at http://www.fda.gov/TobaccoProducts/Labeling/RulesRegulationsGuidance/default.htm. You may send an e-mail request to SmallBiz.Tobacco@fda.hhs.gov to receive an electronic copy of this guidance. You may send a request for hard copies to U.S. Food and Drug Administration, Center for Tobacco Products, Document Control Center, Building 71, Room G335, 10903 New Hampshire Avenue, Silver Spring, MD 20993-0002.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Tobacco Products

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*****This is a revision to the second edition of this guidance, which FDA issued September 8, 2015. A summary of the revisions is at the end of the guidance.

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Guidance for Industry[1]

Demonstrating the Substantial Equivalence of a New Tobacco Product: Responses to Frequently Asked Questions

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

This guidance provides information in response to frequently asked questions (FAQs) that the Center for Tobacco Products (CTP) has received from manufacturers and other interested stakeholders (you) on demonstrating the substantial equivalence (SE) of a new tobacco product.[2] Among other things, this guidance includes information on FDA's current thinking on whether a change to the product quantity in the package renders a product "new" and thus subject to premarket review.

FDA is issuing this revised final guidance following a decision by the United States District Court for the District of Columbia.[3] The court found that "a modification to an existing product's label does not result in a 'new tobacco product.'"[4] Accordingly, manufacturers need not receive premarket authorization for existing products that are the

[1] This guidance was prepared by the Office of Science and Office of Regulations in the Center for Tobacco Products at FDA.

[2] FDA first issued guidance regarding SE applications in a guidance entitled, "Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products" (Demonstrating SE Guidance), which is available on the Internet at http://www.fda.gov/downloads/TobaccoProducts/GuidanceComplianceRegulatoryInformation/UCM239021.pdf The notice of availability for this guidance published on January 6, 2011 (76 Federal Register 789).

[3] The previous version of this guidance published September 8, 2015 (80 Federal Register 53810). Please note that in this current version of the guidance, FDA refers to "SE Reports" as "SE applications," but the terms both refer to a premarket submission under section 905(j)(1)(A) of the FD&C Act.

[4] *Philip Morris USA Inc. v. United States Food and Drug Administration*, ___ F. Supp. 3d ___, No. 15-cv1590 (APM), 2016 WL 4378970 (D.D.C. Aug. 16, 2016).

subject of a label change only (e.g., a product that has a new name but is otherwise identical to the predicate) (see also question 17).[5]

This guidance continues to provide recommendations related to SE applications for product quantity changes. This is consistent with the court's finding that a change to an existing product's quantity does result in a "new tobacco product." The guidance explains that a manufacturer may submit a streamlined SE application for certain changes to product quantity as an alternative to the more comprehensive (full) SE applications described in the Demonstrating SE Guidance. The guidance also explains FDA's plans and processes for review of the streamlined SE applications. Finally, this guidance responds to several questions that have been raised about the SE process more generally.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

A. Overview of Premarket Review

The Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act) was enacted on June 22, 2009, and provided FDA with broad authority to regulate tobacco products under the FD&C Act. The FD&C Act generally requires that a tobacco product manufacturer submit a premarket application and obtain a marketing authorization order before the manufacturer may introduce a new tobacco product into interstate commerce (section 910) (21 U.S.C. 387j)). A new tobacco product that does not comply with the premarket requirements of sections 905(j) and 910 of the FD&C Act is both misbranded and adulterated (sections 902(6)(A) and 903(a)(6) of the FD&C Act (21 U.S.C. 387b(6)(A) and 387c(a)(6))).

A premarket application and a marketing authorization order under section 910(c)(1)(A)(i) of the FD&C Act are not required, however, if a manufacturer submits an SE application to FDA under section 905(j) (21 U.S.C. 387e(j)) and obtains an order under section 910(a)(2) finding that the new tobacco product is (1) substantially equivalent to a tobacco product commercially marketed in the United States as of February 15, 2007, and (2) in compliance with the requirements of the FD&C Act.

[5] Please note, however, that certain changes to tobacco products should be submitted to FDA as part of a domestic tobacco product establishment's biannual updates to its product listing under section 905(i)(3) of the FD&C Act. For more information, please see "Registration and Product Listing for Owner and Operators of Domestic Tobacco Product Establishments, Guidance for Industry" (http://www.fda.gov/downloads/TobaccoProducts/Labeling/RulesRegulationsGuidance/UCM191940.pdf).

If a new tobacco product has been modified by adding or deleting a tobacco additive or increasing or decreasing the quantity of an existing tobacco additive, the manufacturer may, instead of a premarket application under section 910(b), submit an exemption request under 21 CFR 1107.1. FDA may grant the exemption request if it determines that (1) the modification is a minor modification of a tobacco product that can be sold under the FD&C Act, (2) an application demonstrating substantial equivalence is not necessary to ensure that permitting the product to be marketed would be appropriate for protection of the public health, and (3) an exemption is otherwise appropriate.

If FDA grants an exemption from the substantial equivalence requirements, manufacturers must also submit a report under section 905(j)(1)(A)(ii), at least 90 days prior to introduction or delivery of the product into interstate commerce, stating (1) the tobacco product is modified within the meaning of the exemptions provision, (2) the modifications are to a product that is commercially marketed and in compliance with the requirements of the FD&C Act, (3) all of the modifications are covered by exemptions granted under section 905(j)(3) of the FD&C Act, and (4) actions taken to ensure that the tobacco product is in compliance with section 907.

In sum, the FD&C Act requires all new tobacco products to have premarket authorization. Section 910(a)(2) of the FD&C Act.

B. Definition of "New Tobacco Product"

A threshold question for determining whether premarket review is required is whether a product is a "new tobacco product." The term new tobacco product means:

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

(Section 910(a)(1) of the FD&C Act (21 U.S.C. 387j(a)(1)).)

The term tobacco product is defined as "any product made or derived from tobacco that is intended for human consumption, including any component, part, or accessory of a tobacco product (except for raw materials other than tobacco used in manufacturing a component, part, or accessory of a tobacco product)" (section 201(rr)(1) of the FD&C Act (21 U.S.C. 321(rr)(1))). This term does not include an article that is a drug, a device, or a combination product as defined in the FD&C Act (see section 201(rr) of the FD&C Act).

C. Submission and Review of an SE Application

The FD&C Act authorizes FDA to issue an order finding substantial equivalence when FDA finds that the new tobacco product, when compared to a predicate tobacco product, either: (1) Has the same characteristics as the predicate tobacco product; or (2) has different characteristics and the information submitted contains information, including clinical data if deemed necessary by FDA, that demonstrates that it is not appropriate to regulate the product under the more extensive premarket requirements because the product does not raise different questions of public health (section 910(a)(3)(A) of the FD&C Act).

The FD&C Act requires that, as part of an SE application, the manufacturer provide an adequate summary of any health information related to the tobacco product or state that such information will be made available upon request (section 910(a)(4)). The FD&C Act otherwise authorizes the agency to determine the form and manner of the SE application (section 905(j)(1)). In the Demonstrating SE Guidance, FDA provided recommendations on the data and information that should be included in a full SE application so that FDA could determine whether the new tobacco product is (1) substantially equivalent, within the meaning of section 910(a)(3) of the Act, to an appropriate predicate product, and (2) in compliance with the requirements of the Act (section 910(a)(2)(A) of the Act). Many of these recommendations applied to *all* SE applications, "whether for a new tobacco product with the *same characteristics* as a predicate product" or "for a new tobacco product with *different characteristics*." (Demonstrating SE Guidance, page 12).

This guidance provides information and clarifies FDA's recommendations with respect to the data and information to be included in a streamlined alternative SE Application for product quantity changes, referred to as "Product Quantity Change SE Applications." As discussed further below, FDA is recommending that manufacturers provide less information in these applications as compared to the recommendations for the full SE applications. Thus, these applications should be easier for industry to prepare and for FDA to review than full SE applications.[6] FDA is also adopting processes and procedures to better enable the agency to review these streamlined applications expeditiously, including placing them in separate queues from full SE applications.

III. RESPONSES TO FREQUENTLY ASKED QUESTIONS

This section provides our responses to questions that you have frequently asked us on the substantial equivalence provisions. The answers provided in this guidance are specific to the premarket requirements of the FD&C Act and are not intended to speak to any other

[6] Information that manufacturers might use to show grandfathered status is discussed in the September 2014 guidance document entitled, "Establishing That a Tobacco Product Was Commercially Marketed in the United States as of February 15, 2007" (http://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/ucm416495.htm). Additional information on preparing environmental assessments is provided at 21 CFR part 25.

requirements of the FD&C Act. Manufacturers are encouraged to review the FD&C Act, the regulations in effect, and any available guidances.

A. Product Quantity Changes

This section of the guidance describes FDA's current thinking on whether a change to a product quantity in the package renders that product a "new tobacco product" subject to premarket review, describes the streamlined submission that may be submitted when a new tobacco product has changes to product quantity but all other product characteristics remain identical (i.e., identical per weight composition, design features, heating source, and other features of the product), and explains FDA's plans for review of such submissions.

Question 1:
Does a change to a product quantity in the package render a product a "new tobacco product" subject to the premarket review provisions of the FD&C Act?

Response:
Yes, the introduction of a product for which the product quantity in the package[7] has changed (e.g., the number of portioned parts per package has changed such that the new product would hold 24 cigarettes per pack instead of 20; the weight of the product has changed such that the new smokeless package would change from 24 grams to 5 grams), even if the per weight composition[8] of additives, ingredients, and other features remains the same, renders it a new product under section 910(a)(1) of the FD&C Act because the characteristics (e.g., amounts of ingredients, materials, other features) have changed. As defined in section 910(a)(1), a new tobacco product is:

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

Changing a product by altering the quantity in the package is a modification of that product (e.g., a change in amounts of ingredients, materials, other features) resulting in a new product under section 910(a)(1), thus requiring premarket authorization. However, we have determined that changes to product quantity (when all other product characteristics remain identical) will require a reduced set of information in order for FDA to determine whether the new product is substantially equivalent within the meaning of section 910(a)(3). Thus, if a product quantity has changed, but the per weight

[7] For example, the pack, box, carton, container, or wrapping (such as cellophane), in which a tobacco product is sold to consumers.
[8] The manner in which the materials (e.g., ingredients, additives, and biological organisms) are arranged and integrated to produce a finished tobacco product.

composition, design features, heating source, and all other features are otherwise identical to the predicate tobacco product, the manufacturer or importer may opt to submit a "Product Quantity Change SE Application"[9] as discussed in more detail in the following questions and answers.

Question 2:
Would a tobacco product be a "new tobacco product," and subject to the substantial equivalence provisions of the FD&C Act, if the tobacco product was commercially marketed as of February 15, 2007, but subsequently the quantity of product sold in a package is changed (e.g., the number of portioned parts per package has changed such that the new product would hold 24 cigarettes per pack instead of 20; the weight of the product has changed such that the new smokeless package would change from 24 grams to 5 grams)?

Response:
Yes. If a tobacco product was commercially marketed as of February 15, 2007, but subsequently the quantity of the tobacco product is changed, the product is a new tobacco product under section 910(a)(1) of the FD&C Act. If the only change to the tobacco product is a change to product quantity and the per weight composition inside the package remains identical, the manufacturer may submit a Product Quantity Change SE Application as an alternative to a full (more detailed) SE application or premarket application under section 910(b) of the FD&C Act (as discussed in the response to question 5).

Question 3:
What purpose is served by the submission of the Product Quantity Change SE Applications?

Response:
As discussed in the response to question 1, the Product Quantity Change SE Application provides FDA with information needed to conduct the premarket review and issue the order required before a new tobacco product may be marketed (section 910 of the FD&C Act). Congress enacted the Tobacco Control Act to provide FDA with broad authority to regulate the introduction, marketing and advertising of tobacco products based in large part on its determination that such regulation would provide significant health and economic benefits to the public. See Tobacco Control Act, Finding 12. Congress also directed FDA to reissue a 1996 final rule that imposed restrictions on breaking apart cigarette and smokeless packages because of concerns about quantity and use by youth (section 102 of the Tobacco Control Act; 21 CFR 1140.14(d)). Product Quantity Change SE Applications involve modifications that result in the new tobacco product having different characteristics from the predicate tobacco product. A change in quantity is a change to the amount of ingredients, materials, and other features within the new tobacco product as compared to the predicate tobacco product. The Product Quantity Change SE

[9] As described in this section, the Product Quantity Change SE Report would be an alternative to submitting a full SE application or a premarket application under section 910(b) of the FD&C Act.

Application is intended to provide manufacturers with a more limited and less burdensome application to support a determination that the new product does not raise different questions of public health.

Changes in product quantity can affect initiation and cessation, such as by affecting consumer harm perceptions, use intentions, and use behavior. The information in these Product Quantity Change SE Applications would allow for FDA to fully evaluate the potential of such changes in product quantity to determine whether the new product raises different questions of public health such that the product should be required to submit a premarket application. Smaller product quantities may allow for increased product uptake due to lower barriers to trying the product, are associated with lower product harm perceptions, and reduce product costs or increase product availability, all of which may affect use intentions and behavior, including initiation among youth.[10] Larger product quantities can potentially reduce cessation behaviors and increase tobacco product use among current users.[11] Additionally, changes in product quantity may make the product appear novel to consumers, increasing appeal and lowering harm perceptions, both of which may lead to increased product use and initiation. Failure to submit such data, or submission of assertions without scientific justification, hinders FDA's ability to fully evaluate the effects of product quantity changes and determine whether the new product raises different questions of public health.

Question 4:
When I have a tobacco product that is to be marketed in a different quantity, but is otherwise identical to one of my products that was commercially marketed as of February 15, 2007 (or one of my products that has been found by FDA to be SE), should I submit a full SE application that contains all of the information FDA recommends including in its Demonstrating SE Guidance?

Response:
No. Section 905(j) authorizes the agency to determine the form and manner of the SE application. FDA has determined that, if you have a tobacco product that is provided in a different quantity, but is otherwise identical (i.e., identical per weight composition, design features, heating source, and other features of the product) to either a tobacco product that was commercially marketed as of February 15, 2007, or a product that has been found by FDA to be substantially equivalent, you may submit a streamlined SE application that contains a brief, specific set of information (Product Quantity Change SE Application). This may occur where the number of portioned parts per package has changed such that the new product would hold, e.g., 24 cigarettes per pack instead of 20, or the weight of smokeless package would change, e.g., from 24 grams to 5 grams.

[10] Rogers, E.M. (2003). Diffusion of innovations (5th ed.). New York: Free Press; Ford, A., Moodie, C., & Hastings, G. (2012). The role of packaging for consumer products: Understanding the move towards 'plain' tobacco packaging. Addiction Research and Theory, 20, 339-347. doi:10.3109/16066359.2011.632700; Chaloupka, F. J., & Warner, K. E. (2000). The economics of smoking. NBER Working Paper no. 7047. Cambridge, MA.: National Bureau of Economic Research.
[11] Wertenbroch, K. (1998). Consumption self-control by rationing purchase quantities of virtue and vice. Marketing Science, 17, 317-337.

The material that should be submitted in a Product Quantity Change SE Application is substantially more limited and less burdensome than for full SE applications. We believe the information included in the Product Quantity Change SE Application should be sufficient for FDA to make its SE determination in this situation. This Product Quantity Change SE Application should be easier for industry to prepare and for FDA to review than would typically be the case for SE applications involving other changes to a tobacco product and, therefore, FDA expects to review these applications more quickly. More information related to the Product Quantity Change SE Application is provided in the following questions and responses.

Question 5:
What information should a Product Quantity Change SE Application contain?

Response:
The following items should be included in your Product Quantity Change SE Application:

- A cover letter that prominently identifies the submission as **"Product Quantity Change SE Application."**
- Full identification of your new tobacco product:[12]
  - manufacturer (We expect the manufacturer of the new product will generally be the same as the manufacturer of the predicate product. If this is not the case, FDA would need adequate assurances that the new product otherwise has identical characteristics to the predicate product because we believe the certification below would not suffice. In such a case, we strongly encourage the applicant to contact FDA about possible ways to provide adequate assurances that the characteristics are otherwise identical.),
  - unique name (i.e., brand name/subbrand or other commercial name used in commercial distribution),
  - product category (e.g., cigarette),
  - product subcategory (e.g., conventional filtered),
  - package size/count (e.g., 7.8 oz. or 20 cigarettes per pack),
  - if portioned, portion size (e.g., 0.5 gram bag of snus),
  - package type (e.g., soft pack, box, plastic can with metal lid, bag),
  - characterizing flavor (e.g., menthol, cherry, none), and
  - any other information needed to uniquely identify the new tobacco product[13] (FDA has received SE applications where the applicant has included some information relating to product identification, such as brand name, but the provided information does not in fact uniquely identify the product. Common instances where such discrepancies have occurred include SE applications where the applicant provided identifying information (such as brand name,

[12] The new tobacco product is the tobacco product that has a different product quantity, but the per weight composition inside the package is unchanged.
[13] If you have questions on information relating to unique identification for your product we encourage you to contact your assigned regulatory health project manager or to review recent order letters posted.

product category, product subcategory, package type, package quantity, and characterizing flavors), which actually covered multiple tobacco products. For example, cigarettes with the same name, package type, package quantity, and characterizing flavors still may contain varying diameters, lengths, and/or ventilation. In these instances, FDA has been unable to determine the identification of the new product. Therefore, an applicant should provide FDA with anything else needed to uniquely identify the product, including, for example, diameter, length, and ventilation, as necessary.)

- Full identification of a predicate tobacco product:[14]
  - manufacturer,
  - unique name (i.e., brand name/subbrand or other commercial name used in commercial distribution),
  - product category (e.g., cigarette),
  - product subcategory (e.g., conventional filtered),
  - package size/count (e.g., 7.8 oz. or 20 cigarettes per pack),
  - if portioned, portion size (e.g., 0.5 gram bag of snus),
  - package type (e.g., soft pack, box, plastic can with metal lid, bag),
  - characterizing flavor (e.g., menthol, cherry, none)
  - any other information needed to uniquely identify the predicate tobacco product[15] (FDA has received SE applications where the applicant has included some information relating to product identification, such as brand name, but the provided information does not in fact uniquely identify the product. Common instances where such discrepancies have occurred include SE applications where the applicant provided identifying information (such as brand name, product category, product subcategory, package type, package quantity, and characterizing flavors), which actually covered multiple tobacco products. For example, cigarettes with the same name, package type, package quantity, and characterizing flavors still may contain varying diameters, lengths, and/or ventilation. In these instances, FDA has been unable to determine the identification of the predicate product. Therefore, an applicant should provide FDA with anything else needed to uniquely identify the product, including, for example, diameter, length, and ventilation, as necessary.)
- Scientific data demonstrating that the change in product quantity is not likely to alter consumer use behavior of the new product compared to the predicate product.
    - Some examples of scientific data include but are not limited to:

[14] The predicate tobacco product for a Product Quantity Change SE Application is a tobacco product commercially marketed (other than for test marketing) as of February 15, 2007, or a tobacco product that has been found substantially equivalent and that is otherwise identical (i.e., the per weight composition of the product inside the package is unchanged) to the new tobacco product, except that the new tobacco product is packaged in a different product quantity.

[15] If you have questions on information relating to unique identification for your product we encourage you to contact your assigned regulatory health project manager or to review recent order letters posted.

  - Studies on purchasing frequency that demonstrate that the amount of product used per day or per week is similar between the predicate and new tobacco products. For example, if you double the count of a portioned tobacco product (e.g., cigarette, pouched snus) or the total amount of an unportioned tobacco product in a single package (e.g., loose moist snuff) offered for purchase, the amount of product per use and per week that users consume is similar.
  - Studies showing that young adults are not more likely to purchase packages that are of lower total quantity compared to older adults.
  - Studies showing that products of lower quantity are not more likely to be purchased as impulse purchases.
  - Peer-reviewed publications supporting that this specific change in product quantity does not substantially alter consumer behavior.
  - Biomarkers of exposure that reflect product use and demonstrate that exposure is similar between use of the predicate and new tobacco products.

- Statement of whether you intend to commercially distribute both the predicate and new tobacco products, or only the new tobacco product, if it is found SE.
- Environmental Assessment (please also see the response to question 22).
- Health Information Summary or a statement that the "information will be made available upon request by any person" (section 910(a)(4) of the FD&C Act).
- Statement of action taken to comply with the requirements under section 907 of the FD&C Act that are applicable to the tobacco product (or a statement that "requirements under section 907 of the FD&C Act are not applicable to the tobacco product").
- Certification statement that is signed by a responsible official who is authorized to act on behalf of the company and that states the following:

  I, [insert name of responsible official], on behalf of [insert name of company], certify that [insert new tobacco product name] is packaged in a different quantity from [insert name of predicate tobacco product] but is otherwise identical to [insert name of predicate tobacco product]. I certify that [insert name of company] understands this means there is <u>no</u> modification, except in product quantity from the predicate tobacco product, and that there has been no change in per weight composition, design features, heating source, or other features. I certify that this information and the accompanying submission are true and correct, and that I am authorized to submit this on the company's behalf. I understand that under Section 1001 of Title 18 of the United States Code, anyone who knowingly and willfully makes a materially false, fictitious, or fraudulent statement to the Government of the United States is subject to criminal penalties.

Question 6:
How will FDA review Product Quantity Change SE Applications?

Response:
There are far fewer materials and information to be submitted in a Product Quantity Change SE Application than a full SE application, and the findings are fairly straight-forward. FDA anticipates that, so long as the appropriate information is included, its review time should be much less than review of a full SE application generally. FDA intends to review Product Quantity Change SE Applications in a queue separate from SE applications involving other changes to a tobacco product.

Due to the far fewer materials, FDA is prepared to commit to a maximum of two review cycles[16] for issuance of a decision to a Product Quantity Change SE Application.

In April 2014 FDA established performance measures that include timeframes for review of regular SE applications. Those performance measures were created for the "full" SE application that included a detailed comparison for each characteristic between the new and predicate product. As the Product Quantity Change SE Applications contain far fewer materials for review, the performance measures have been expanded to reflect timeframes for review specific to Product Quantity Change SE Applications. They can be found at http://www.fda.gov/tobaccoproducts/labeling/TobaccoProductReviewEvaluation/substantialequivalence/ucm475489.htm.

Question 7:
If I currently have an SE application pending with FDA, may I use the Product Quantity Change SE Application instead?

Response:
If your pending application is for a new tobacco product that has only a different product quantity, but is otherwise identical to a predicate tobacco product, you may submit a Product Quantity Change SE Application for the new product, or if this is to a provisional SE Application, you may amend your pending application with all the information to support the product quantity change.

Question 8:
Can I change the quantity of product sold in a package if the product is the subject of a "provisional"[17] SE application that is pending review at FDA?

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[16] A review cycle ends with an action letter, e.g., a preliminary finding letter, advice/information letter, SE order, or not substantially equivalent order. Thus, for example, the issuance of a preliminary finding letter would end the first cycle of review, and the issuance of an SE order would end the second cycle of review.
[17] A "provisional" SE application is one that was submitted prior to March 23, 2011, for a new tobacco product that was first commercially marketed between February 15, 2007, and March 22, 2011. New tobacco products that are the subjects of provisional SE applications may remain on the market unless FDA finds the products not substantially equivalent (NSE) to a predicate product.

Response:
A provisionally marketed tobacco product can never serve as a valid predicate tobacco product. Under section 905(j)(1)(A)(i) of the FD&C Act, SE applications may compare new products only to products that were commercially marketed as of February 15, 2007, or products that FDA has previously determined to be substantially equivalent to a predicate tobacco product. Products that are the subject of "provisional" SE applications, though legally sold or distributed, may not serve as predicate tobacco products under the FD&C Act unless they have been previously found to be SE.

However, FDA intends to exercise enforcement discretion and not take enforcement action against a new tobacco product that is marketed without a required marketing authorization order in the following situation:[18]

- The new tobacco product has been modified to be packaged in a different quantity from, but the per weight composition is identical to, a product that is subject to a "provisional" SE Application for which FDA has not yet issued an order under section 910(a) of the FD&C Act;
- The manufacturer submits a Product Quantity Change SE Application as outlined in the response to question 5 above.[19] The Product Quantity Change SE Application should identify the STN assigned by FDA for the original provisional SE application, and provide information on the provisional product in lieu of the predicate information described in the response to question 5; and
- The manufacturer does not commercially distribute the new tobacco product that is the subject of the Product Quantity Change SE Application until 90 days (see Section 905(j)(1)) after FDA's receipt of the complete Product Quantity Change SE Application.

FDA intends to issue an order on the new tobacco product that is the subject of the Product Quantity Change SE Application only after it has completed its review of the "provisional" SE application because, as explained above, products that are the subject of "provisional" SE applications may not serve as predicate tobacco products under the FD&C Act unless they have been previously found SE. Ultimately, if the product that is the subject of the "provisional" SE application receives an SE order, FDA intends to then issue, if appropriate, an order for the new tobacco product that is the subject of the Product Quantity Change SE Application. If the product that is the subject of the "provisional" SE Application receives a not substantially equivalent (NSE) order, FDA

[18] Products may be subject to enforcement at any time for other violations of the FD&C Act.
[19] If the manufacturer submitted a complete Product Quantity Change SE application by October 8, 2015, for a product already on the market as of September 8, 2015, FDA does not intend to object to the commercial distribution of the new tobacco product while the application is under review (as provided in the second edition of the FAQs guidance, issued September 8, 2015). If the product that is the subject of the "provisional" SE application receives a not substantially equivalent order, or, if after review of the Product Quantity Change SE Application FDA finds that the new product that is the subject of the Product Quantity Change SE Application is NSE to the predicate tobacco product, then such compliance policy will no longer apply.

intends to take appropriate enforcement action if the new tobacco product that is the subject of the Product Quantity Change SE Application continues to be marketed. In sum, if the product that is the subject of the "provisional" SE application is found NSE, then neither it nor the modified new product that is the subject of the Product Quantity Change SE Application, may be introduced or delivered for introduction into interstate commerce for commercial distribution without first obtaining a marketing order (via a different pathway or a new SE application); doing so would render the product adulterated and misbranded (sections 902(6)(A) and 903(a)(6) of the FD&C Act).

Question 9:
What if I have a tobacco product that is legally sold in one quantity because it was commercially marketed as of February 15, 2007, but I have changed the quantity of product sold in a package (e.g., the number of portioned parts per package has changed such that the new product would hold 24 cigarettes per pack instead of 20; the weight of the product has changed such that the new smokeless package would change from 24 grams to 5 grams) and I am now commercially marketing that product with the product quantity change?

Response:
The tobacco product with the product quantity change is a new tobacco product subject to premarket requirements under section 910(a) of the FD&C Act.[20] New tobacco products may not be sold or distributed in interstate commerce without an order from FDA under either section 910(c)(1)(A)(i) or section 910(a)(2)(A) of the FD&C Act. As outlined in the responses to questions 4 and 5, you may submit a Product Quantity Change SE Application, and FDA will determine whether the new tobacco product is substantially equivalent. See also the responses to questions 7 and 8.

Question 10:
If, in addition to changing the product quantity, a manufacturer makes another change to the product, e.g., an addition of an ingredient, can both changes be addressed through a Product Quantity Change SE Application?

Response:
The Product Quantity Change SE Application is a streamlined application intended to address changes to a tobacco product where the only change is a change in quantity of product placed in a package. If you have made other changes to your new product, you should submit a full SE application that addresses all of the changes, not just the product quantity change.

[20] If the manufacturer submitted a complete Product Quantity Change SE application by October 8, 2015, for a product already on the market as of September 8, 2015, FDA does not intend to object to the commercial distribution of the new tobacco product while the application is under review (as provided in the second edition of the FAQs guidance, issued September 8, 2015). If, after review of the Product Quantity Change SE Application, FDA finds that the new product that is the subject of the Product Quantity Change SE Application is NSE to the predicate tobacco product, then such compliance policy will no longer apply.

Question 11:
If I change the product quantity and portion size in a portioned product (e.g., change from 0.5g to 1g sachets of moist snuff or king-size to 100s cigarettes) or just the portion size in a portioned product, can I use the Product Quantity Change SE Application?

Response:
No. The Product Quantity Change SE Application is a streamlined application intended to address changes to a tobacco product where the only change is a change in quantity of product placed in a package where the per weight composition of the new and predicate product are identical. A change in portion is independent from a change in product quantity. If portion size is changed, you should submit a full SE application that addresses all of the changes, not just the product quantity change.

B. Additives/Specifications

This section of the guidance describes FDA's current thinking on whether and when a change to a tobacco product's additives or specifications renders that product a "new tobacco product" subject to premarket review.

Question 12:
Would a tobacco product be a "new tobacco product" subject to the substantial equivalence provisions if the tobacco product was commercially marketed as of February 15, 2007, but subsequently a new supplier was used for an ingredient, additive, component, part, or material?

Response:
It depends. If the tobacco product was commercially marketed in the United States as of February 15, 2007, and subsequently a new supplier is used for the same ingredient, additive, component, part, or material with identical specifications, then this type of change would not render the tobacco product a new tobacco product. For example, if a tobacco product commercially marketed as of February 15, 2007, contained food-grade sodium carbonate from one supplier and a subsequent product was identical in every respect except that it contained food grade sodium carbonate in the same amount from a second supplier, FDA would not consider the second product to be a new product; therefore, submission of a marketing application such as an SE application would not be required.

On the other hand, if a different supplier either uses a different ingredient, additive, component, part, or material, then the product is a new tobacco product and the manufacturer must follow a regulatory pathway to market for the new product (i.e., a premarket tobacco application under 910(b), an SE application under 905(j), or a request for an exemption from the substantial equivalence requirements under 21 CFR 1107.1). For example, the premarket requirements of sections 905(j) and 910(a) would apply if an alternate cigarette paper supplier provided paper that is more porous than the paper used in the product that was commercially marketed as of February 15, 2007. In that

case, if a manufacturer chooses to submit an SE application, it should be the full application listing all characteristics of the new and predicate tobacco products.

Question 13:
Would a tobacco product be a "new tobacco product" and subject to the substantial equivalence provisions if a tobacco blending change is made to address variation in tobacco growing conditions?

Response:
At this time, FDA does not intend to enforce the requirements of sections 910 and 905(j) for tobacco blending changes required to address the natural variation of tobacco (e.g., blending changes due to variation in growing conditions) in order to maintain a consistent product. However, blending changes that are intended to alter the chemical or perception properties of the new product (e.g., nicotine level, pH, smoothness, harshness) compared to the predicate product, should be reported under sections 910 or 905(j). If you have any questions regarding a specific tobacco blending change please contact us.[21]

Question 14:
Would a tobacco product be a "new tobacco product," and subject to the substantial equivalence provisions if the tobacco product was commercially marketed as of February 15, 2007, but subsequently a specification for an additive was tightened (i.e., narrowed) within the range of the original specification or the specification for an additive was changed (for example, from .003 to .005)?

Response:
Any modification made to the level of an additive in a product after February 15, 2007, renders the product a new tobacco product subject to one of the regulatory pathways to market (i.e., a premarket tobacco application under section 910(b), an SE Application under section 905(j), or a request for an exemption from the substantial equivalence requirements under 21 CFR 1107.1). Changes in controls on production (such as improved quality control) that would not affect the actual level of an additive in a product would not make that product a "new tobacco product" under the FD&C Act.

Question 15:
Would a cigarette be a "new tobacco product," and subject to the substantial equivalence provisions, if the cigarette was commercially marketed as of February 15, 2007, but subsequently the paper was changed to fire standard compliant (FSC) paper?

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[21] For additional information on meetings, please refer to the CTP guidance, "Meetings with Industry and Investigators on the Research and Development of Tobacco Products" (CTP Meetings Guidance) (July 2016) available on the Internet at http://www.fda.gov/downloads/TobaccoProducts/GuidanceComplianceRegulatoryInformation/UCM305282.pdf. This guidance provides information on how to request a meeting, along with recommendations about what to include in a request, etc.

Response:
Yes. A modification made to the cigarette paper to change it to FSC paper after February 15, 2007, renders the product a new tobacco product and subject to one of the regulatory pathways to market (such as a premarket tobacco application under section 910(b) or an SE application under section 905(j)). This is because the change to FSC paper leads to a difference in design parameters, ingredients, and/or materials, and is therefore a modification as defined under section 910(a)(1)(B) of the FD&C Act. If a manufacturer chooses to submit an SE application, it should be the full application listing all characteristics of the new and predicate tobacco products.

Question 16:
Would a tobacco product be a "new tobacco product" and subject to the substantial equivalence provisions if the tobacco product was commercially marketed as of February 15, 2007, but subsequently a supplier of a component (e.g., the filter) began using a new processing aid (e.g., an antimicrobial agent) for a subcomponent (e.g., paper used for the filter's plug wrap) and the change is so minor that it is not even capable of being quantified in the finished product?

Response:
Yes. Any change in a tobacco product's composition fits the definition of a modification under section 910(a)(1)(B) of the FD&C Act and renders the product a new tobacco product. The new tobacco product would be subject to one of the regulatory pathways to market (e.g., a premarket tobacco application under section 910(b), an SE application under section 905(j), or a request for an exemption from the substantial equivalence requirements under 21 CFR 1107.1).

C. Other Questions About Section 905(j)/SE Applications

This section of the guidance responds to other questions related to the submission and review of SE applications.

Question 17:
Does a change in a product label render an existing tobacco product a "new tobacco product" subject to the premarket review provisions of the FD&C Act?

Response: No, a modification to an existing tobacco product's label, standing alone, does not result in a new tobacco product subject to the premarket review provisions of the FD&C Act. This position is consistent with a decision of the U.S. District Court for the District of Columbia (see *Philip Morris USA Inc. v. United States Food and Drug Administration*, ___ F. Supp. 3d ___, No. 15-cv1590 (APM), 2016 WL 4378970 (D.D.C. Aug. 16, 2016)).

Question 18:
May companies contact the Agency to determine if certain modifications convert an existing product into a "new tobacco product" and require a substantial equivalence filing?

Response:
Yes. If you have questions regarding whether a particular change would require submission of an SE application, please contact CTP to request a meeting.[22]

Question 19:
How do I know whether a characteristic should be reported as a material or ingredient?

Response:
The statute defines "substantial equivalence" in terms of characteristics (section 910(a)(3)(A) of the FD&C Act). The statute also defines "characteristics" as the materials, ingredients, design, composition, heating source, or other features of a tobacco product (section 910(a)(3)(B) of the FD&C Act). However, the statute does not further define each of the terms used in the definition of "characteristics." The Demonstrating SE Guidance provides recommendations related to characteristics (http://www.fda.gov/downloads/TobaccoProducts/GuidanceComplianceRegulatoryInformation/UCM239021.pdf). In general, in preparing your SE application, it is important that your comparison to a predicate include all characteristics. FDA recognizes that you may be uncertain of the category (e.g., material or ingredient) in which a particular characteristic best fits. For purposes of comparison, it is important that characteristics be reported in the same category for both the new tobacco product and the predicate. FDA will review your submission as a whole and consider the totality of the data presented when making FDA's determination of substantial equivalence. You may also consider requesting a meeting with CTP.[23]

Question 20:
Glue is not listed as an example of a component, part, or accessory of a tobacco product in the Demonstrating SE Guidance. Is glue considered a component, part or accessory such that a change in the glue might render a product a new tobacco product subject to the substantial equivalence provisions?

Response:
It depends. For purposes of substantial equivalence, the characteristics of the new tobacco product should be compared to the characteristics of a predicate. Characteristics means the materials, ingredients, design, composition, heating source, or other features of the tobacco product. If the glue is modified in a tobacco product after February 15, 2007, the product is a new tobacco product and is subject to premarket review (e.g., a premarket tobacco application under section 910(b) or SE Application under section 905(j)). As discussed in more detail in the Demonstrating SE Guidance, for unfinished products

[22] For additional information on meetings, please refer to the CTP Meetings Guidance.
[23] As noted, please refer to the CTP Meetings Guidance.

(including products where glue is a component, part or accessory), FDA intends to limit its enforcement of the requirements of sections 910 and 905(j) of the FD&C Act to finished, regulated products. To avoid the submission of duplicative information, FDA does not at this time intend to enforce the requirements of 910 and 905(j) for components, parts or accessories of regulated tobacco products that are sold or distributed solely for further manufacturing into finished tobacco products. We anticipate receiving all relevant information regarding such new tobacco products in the 905(j) applications of the finished regulated tobacco products. It is therefore the finished product manufacturer's responsibility to ensure it has accurate information regarding the components, parts and accessories included in its product. The manufacturer must obtain appropriate market authorization for any changes to a tobacco product, including modifications to components, parts, or accessories.

Question 21:
How should harmful and potentially harmful constituents (HPHCs) be reported in my SE application?

Response:
It is an applicant's responsibility to provide appropriate scientific evidence and data if FDA is to make a finding that the predicate and new products are substantially equivalent. Reporting quantities of HPHCs in predicate and new products is a useful mechanism for manufacturers to demonstrate that the differences in characteristics between the predicate and new products do not cause the new products to raise different questions of public health within the meaning of 910(a)(3)(A)(ii) of the FD&C Act. When providing HPHCs in an SE application, they should be appropriate for the type of tobacco product (e.g., cigarette, smokeless) and predicate product used for comparison. For example, when submitting an SE application for a change to FSC paper in a cigarette after February 15, 2007, many manufacturers have provided information for TNCO (tar, nicotine, and carbon monoxide) as this type of modification may change TNCO. However, for this FSC example you may not need to include information about aflatoxin B1 in your SE application as it is not expected to change due to this modification.

If you have additional questions regarding reporting of HPHCs in your SE application and would like to discuss your questions with the Agency, please contact CTP to request a meeting.[24]

Question 22:
Do I need to submit an environmental assessment as part of my section 905(j) SE application?

Response:
Yes. FDA's regulations implementing the National Environmental Policy Act (NEPA) of 1969 require that "[a]ll applications or petitions requesting agency action require the submission of an [environmental assessment] or a claim of categorical exclusion" (21

[24] For additional information on meetings, please refer to the CTP Meetings Guidance.

CFR 25.15(a)). Manufacturers submitting applications or reports for any of the three regulatory pathways (including reports under section 905(j)) must include environmental assessments or a valid claim of categorical exclusion, if applicable, as part of their submissions.[25] You should refer to 21 CFR part 25 for additional information. If you have questions regarding what you should include in your environmental assessment, and would like to discuss your questions with the Agency, please contact CTP to request a meeting.[26]

[25] On September 24, 2015, FDA issued a final rule providing categorical exclusions for certain actions, including actions related to substantial equivalence (SE) applications (80 Federal Register 57531) (codified at 21 CFR 25.35).

[26] Please refer to the CTP Meetings Guidance.

Document History.

March 2015. Original final guidance is published (the notice of availability published on March 5, 2015; 80 Federal Register 12011).

May 2015. FDA added an interim enforcement policy note to the guidance while the Agency considered new comments.

September 2015. The second edition of the guidance is published (the notice of availability published on September 8, 2015; 80 Federal Register 53810). Revisions included:

- Removal of the interim enforcement policy note;
- The addition of background information to the introduction section, including a section on the submission and review of an SE Report;
- The insertion of new questions/responses and the addition of information in responses throughout section II (Responses to Frequently Asked Questions) on FDA's current thinking on label changes and product quantity changes;
- The addition of information on the additional properties needed to identify a product;
- The addition of two appendices.

December 2016. The third edition of the guidance is published. Revisions include:

- The addition of information on the U.S. District Court for the District of Columbia's decision in *Philip Morris USA Inc. v. United States Food and Drug Administration*, ___ F. Supp. 3d ___, No. 15-cv1590 (APM), 2016 WL 4378970 (D.D.C. Aug. 16, 2016)).
- The deletion of questions/responses related to SE Applications for label/name changes; the addition of one clarifying question on whether a label change to an existing product results in a new tobacco product; the renumbering of remaining questions; and, as needed, related edits and clarifications in the responses to other questions;
- Deletion of an expired enforcement discretion policy (the policy had provided a 30-day period to submit certain SE applications for new tobacco products that had proceeded to market without first obtaining marketing authorization);
- An update to reflect the final rule status of the categorical exclusions rulemaking (related to NEPA);
- The deletion of two appendices.