

Guidance for Industry and Investigators

Meetings with Industry and Investigators on the Research and Development of Tobacco Products

Written comments may be submitted at any time for Agency consideration to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD, 20852. Alternatively, electronic comments may be submitted to <http://www.regulations.gov>. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this guidance, contact the Center for Tobacco Products at (Tel) 1-877-CTP-1373 (1-877-287-1373) Monday-Friday, 9:00 a.m. – 4:00 p.m. EDT.

Additional copies are available online at <http://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/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, Attn: Office of Small Business Assistance, 9200 Corporate Blvd., Rockville, MD 20850.

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

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This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

This guidance is intended to assist tobacco manufacturers, importers, researchers, and/or investigators who seek meetings with staff of FDA's Center for Tobacco Products (CTP), relating to their plans to conduct research to inform the regulation of tobacco products or support the development or marketing of tobacco products. This guidance document discusses, among other things:

- What information FDA recommends you include in a meeting request,
- How and when to submit a request, and
- What information FDA recommends you submit prior to the meeting.

This guidance does not pertain to other types of meetings or meeting requests other than those described throughout this document. 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.

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

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II. BACKGROUND

You must generally obtain an order from FDA authorizing the commercial marketing of a *new tobacco product*, including when you modify a tobacco product, before the product may be introduced or delivered for introduction into interstate commerce (section 910(a)(2) of the Federal Food, Drug, & Cosmetic Act (FD&C Act) (21 U.S.C. 387j(a)(2))). *Modification* 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” (section 910(a)(1)(B)).

To introduce or deliver for introduction a new tobacco product into interstate commerce, there must be:

- A marketing authorization order issued by FDA for the tobacco product under section 910(c)(1)(A)(i) of the FD&C Act;
- An order issued by FDA and in effect for the tobacco product, finding it to be substantially equivalent under section 910(a)(2)(A)(i) of the FD&C Act; or
- A written finding from FDA that the tobacco product is exempt from the requirement to obtain a substantial equivalence order granted under 21 CFR 1107.1.

For information on how to submit a substantial equivalence report under section 905(j) of the FD&C Act (21 U.S.C. 387e(j)), see FDA’s guidance for industry *Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Product*.² For information on how to request an exemption from the substantial equivalence requirements, see FDA’s final rule “Exemptions from Substantial Equivalence Requirements for Tobacco Products” (76 FR 38961; July 5, 2011).³

Furthermore, modified risk tobacco products (MRTPs) are tobacco products that are sold or distributed for use to reduce harm or the risk of tobacco-related disease associated with commercially marketed tobacco products. Before an MRTP can be introduced or delivered for introduction into interstate commerce, an order from FDA under section 911(g) of the FD&C Act must be in effect with respect to the tobacco product.

FDA staff intends to participate in many meetings with industry and investigators who seek assistance relating to the research and development of particular tobacco products. Because these meetings often represent important opportunities in the regulatory process, it is important that there are efficient, consistent procedures for the timely and effective conduct of such meetings. This guidance is intended to provide consistent principles and procedures to promote well-managed meetings pertaining to tobacco product research and development.

² Available on the Internet at

<http://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/default.htm>

³ Available on the Internet at <http://www.gpo.gov/fdsys/pkg/FR-2011-07-05/pdf/2011-16766.pdf>.

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III. DEFINITIONS

This section provides definitions of certain terms used in this guidance.

A. Tobacco Product

Tobacco product means “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))). Thus, the term is not limited to products containing tobacco, but also includes components, parts, or accessories of tobacco products, whether they are sold for further manufacturing or for consumer use. For example, cigarettes, rolling papers and filters are tobacco products, whether they are sold to consumers for use with roll-your-own tobacco or are sold for further manufacturing into a product sold to a consumer, such as a cigarette. This term does not include an article that is a drug, a device, or a combination product as defined in the FD&C Act (section 201(rr)(2) of the FD&C Act (21 U.S.C. 321(rr)(2))).

B. New Tobacco Product

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).

C. Substantially Equivalent or Substantial Equivalence

The terms *substantially equivalent* and *substantial equivalence* are defined at section 910(a)(3)(A) of the FD&C Act as follows:

In this section and section 905(j), the term “substantially equivalent” or “substantial equivalence” means, with respect to the tobacco product being compared to the predicate tobacco product, that the Secretary by order has found that the tobacco product—

- (i) has the same characteristics as the predicate tobacco product; or
- (ii) has different characteristics and the information submitted contains information, including clinical data if deemed necessary by the Secretary, that demonstrates that it is not appropriate to regulate the product under [section 910 of the FD&C Act] because the product does not raise different questions of public health.

A tobacco product may not be found to be substantially equivalent to a predicate tobacco product that has been removed from the market at the initiative of the FDA or that has been determined by a judicial order to be misbranded or adulterated (section 910(a)(3)(C) of the FD&C Act).

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IV. DISCUSSION

A. What is the scope of this guidance?

This guidance is intended to assist tobacco manufacturers, importers, researchers, and/or investigators who seek meetings with CTP regarding their research and development plans related to tobacco products.

B. Which FDA staff would likely attend this meeting?

Staff from FDA's CTP would attend this meeting. Staff from other parts of FDA may also participate as appropriate.

C. How do I request a meeting?

Any tobacco product manufacturer, researcher, importer, or investigator involved in the development or marketing of a tobacco product, or their representatives, should submit a written meeting request to the Director, Office of Science, CTP, at FDA. The request should be prominently identified as "OS Meeting Request" and can be sent by mail, courier, or securely transmitted electronically via the FDA Electronic Submissions Gateway (ESG) and the eSubmitter tool. Please refer to section IV.L in this document for the mailing address.⁴

D. When should I submit my meeting request?

A meeting request usually should be submitted prior to filing a tobacco product submission. Occasionally, a meeting request is submitted during the review of a submission. For example, an applicant can request a meeting to discuss the appropriate design of postmarketing studies during the review of a pending modified risk tobacco product application (MRTPA).

E. What should I include in my meeting request?

A meeting request should include adequate information for FDA to determine the potential utility of the meeting and to identify appropriate FDA staff to discuss the proposed agenda items. A meeting request should include the following information:

1. Product name and FDA-assigned Submission Tracking Number (if applicable)
2. Product category (e.g., cigarettes, smokeless tobacco) (if applicable)
3. Product use (indicate for consumer use or for further manufacturing)
4. Contact information for individual or company requesting the meeting
5. The type of meeting being requested (e.g., tobacco product application, such as a premarket tobacco application or MRTPA, or research regarding the development of a tobacco product)

⁴ Please refer to the ESG website instructions for setting up a WebTrader account at: <http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway/ucm114831.htm>. Information about the eSubmitter tool can be found at: <http://www.fda.gov/ForIndustry/FDAeSubmitter/ucm189469.htm>.

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6. A brief statement of the purpose of the meeting, which could include a discussion of the types of studies or data to be discussed at the meeting, the general nature of the primary questions to be asked, and where the meeting fits in the overall product development plans
7. A draft list of the specific objectives/outcomes expected from the meeting
8. A preliminary proposed agenda, including estimated amounts of time needed for each agenda item and designated speaker(s)
9. A draft list of specific questions, grouped by discipline
10. A list of all individuals (including titles and responsibilities) who will attend meeting on your behalf
11. The approximate date on which supporting documentation (i.e., the information package described in section IV.K of this document) likely will be received by FDA
12. Suggested format of the meeting (e.g., conference call, in person at FDA offices, video conference) and suggested dates and times for the meeting (note that generally a meeting will be scheduled for approximately 1 – 1.5 hours)

F. When should I expect FDA to respond to my request?

FDA generally intends to respond in writing *within 21 calendar days* of receipt of the meeting request. If FDA agrees to the meeting, the written response should include:

- the date, time, and place of the meeting,
- the expected FDA participants, and
- instructions for submitting the meeting information package.

If a meeting request is denied, the response should include a clear explanation of the reason(s) for the denial (e.g., the meeting request did not provide enough information for FDA to determine the utility of the meeting).

G. If FDA denies my initial meeting request, can I resubmit my request?

If FDA denies your initial request, FDA intends to consider a subsequent meeting request to be a new request.

H. Could FDA decide that a meeting is unnecessary?

FDA may determine that a meeting is unnecessary and, instead, submit written responses to questions contained in the meeting request. If you believe that the responses are insufficient, you can submit a subsequent request for a meeting.

I. Who will be my point of contact for the meeting?

FDA's response to your meeting request should list the name and contact information for an employee of CTP's Office of Science, which will likely be a Regulatory Health Project Manager. This employee will be your point of contact for additional questions regarding the meeting.

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J. Is there any additional information that I should submit prior to the scheduled meeting?

If FDA schedules the meeting, we recommend that you submit a “meeting information package” at least 45 days prior to the scheduled meeting. You can also submit this package with the meeting request. However, if this information changes prior to the scheduled meeting, you should update the information accordingly. If these changes are voluminous and/or complex, FDA may choose to reevaluate whether a meeting or a written response is appropriate and/or postpone the meeting to give staff appropriate time to review the new materials.

K. What should I include in my meeting information package?

Your meeting information package should include summary information relevant to your product(s) and the proposed agenda. Full study reports or detailed data generally are not appropriate for meeting packages; the summarized material should describe the design, conduct, analysis, and results of relevant studies and clinical trials with some degree of quantification. The pre-specified study endpoints should be stated, as should whether endpoints were altered or analyses changed. Also, merely describing a result as *significant* does not provide enough information for FDA to give good advice or identify important problems the requestor may have missed.

To facilitate FDA’s review of your meeting information package, we suggest you organize the contents according to the proposed agenda. The meeting package should be a sequentially paginated document (individual sections can be numbered separately) with a table of contents, appropriate indices, appendices, cross references or hyperlinking, and tabs differentiating sections.

The meeting information package should support the intended meeting objectives. Although the contents of the meeting information package will vary depending on the product, the phase of the tobacco product development, and issues to be discussed, the meeting information package generally should include the following (as applicable):

1. Product name and FDA-assigned Submission Tracking Number
2. Product category
3. Product use (indicate for consumer use or further manufacturing)
4. Product type (e.g., finished tobacco product or component, part, accessory)
5. A brief statement of the purpose of the meeting, which could include a discussion of the types of studies or data that you intend to discuss at the meeting, the general nature of your critical questions, and where the meeting fits in overall development plans
6. A list of the specific objectives/outcomes expected from the meeting
7. An agenda, including estimated amounts of time needed for each agenda item and designated speaker(s)
8. A list of specific questions grouped by discipline

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9. Chemistry, manufacturing, and control data summary
10. Preclinical data summary
11. Clinical data summary
12. Behavioral and product use data summary
13. User and non-user perception data summary
14. Investigational plans for studies and surveillance of the tobacco product, including a summary of proposed study protocols containing the following information:
 - a. Study objective(s),
 - b. Study hypotheses,
 - c. Study design,
 - d. Study population (inclusion/exclusion criteria, comparison group(s)),
 - e. Human subject protection information, including Institutional Review Board (IRB) information,
 - f. Primary and secondary endpoints (definition and success criteria),
 - g. Sample size calculation,
 - h. Data collection procedures,
 - i. Duration of follow-up and baseline and follow-up assessments, and
 - j. Data analysis plan(s).

The content of your meeting information package should include the information necessary to support your meeting purpose and objectives. Although the request for a meeting should include items 1 through 8 above (as applicable), these items should be updated in the information package if necessary to reflect the most current and accurate information available to you. For specific guidance regarding the contents of the information package, you should contact your CTP point of contact.

L. Where do I send my meeting requests and meeting information packages?

You should send your request for a meeting and meeting information package to FDA's Center for Tobacco Products at the following address:

Center for Tobacco Products
Attn: Document Control Center, Room 020J
9200 Corporate Boulevard
Rockville, MD 20850

If you have a WebTrader account, you can send your request and meeting information package via the FDA ESG (www.fda.gov/esg). We encourage you to submit the meeting information package electronically. To facilitate the meeting process, we strongly suggest that copies of meeting information packages provided in electronic format also be provided in paper format. Your CTP point of contact will advise you on the number of paper copies you should submit for the planned FDA meeting attendees.

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M. What if I am unable to provide adequate supporting documentation in my meeting information package within 45 days prior to the scheduled meeting?

FDA may decide to postpone or cancel a meeting if we have not received adequate supporting documentation for a productive meeting within this timeframe. You should get in touch with your point of contact as soon as possible if you will not be able to meet this deadline.

N. If my initial meeting request is postponed or canceled, can I resubmit my request?

FDA intends to take reasonable steps to avoid postponing or canceling a scheduled meeting. If you cancel a previously scheduled meeting, FDA will consider a subsequent meeting request to be a new request.

O. What, if anything, should I bring to the meeting?

At least two business days prior to the scheduled meeting, you should provide your point of contact with an electronic copy of your presentation. Alternatively, you can bring to the meeting paper copies for all attendees. Your CTP point of contact will advise you on the number of paper copies you should submit for the planned FDA meeting attendees.

P. How will the meeting be conducted?

Your presentations should be limited to information included in the information package. FDA staff may not be able to provide comments on new data.

Before the end of the meeting, attendees should summarize the important discussion points, agreements, clarifications, and action items. FDA intends to ask the meeting participant(s) to present the summary to ensure that there is mutual understanding of meeting outcomes and actions. FDA staff should then add or further clarify any important points not covered in the summary. The summary can be done at the end of the meeting or after the discussion of each question.

Q. Will FDA provide any documentation to summarize the meeting?

Documentation of meeting outcomes, agreements, disagreements, and action items is helpful for ensuring that this information is preserved for meeting attendees and future reference. FDA intends to provide the official minutes of the meeting to summarize the important discussion points, decisions, recommendations, agreements, disagreements, issues for further discussion, and action items. We intend to send you the official minutes within 45 days of the meeting.

R. What should I do if I have a question or concern regarding the official meeting minutes?

If you have a question or concern regarding the meeting minutes, you should get in touch with your CTP point of contact. If you disagree with the accuracy of FDA's minutes, you should send

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your comments and suggested changes, including your recommendations and rationale, to your point of contact for our consideration. If FDA deems it appropriate to change the official minutes, the Agency intends to document this change in an addendum to the official minutes. FDA also intends to include any areas of continued objection to the accuracy of the minutes in such an addendum.

S. Can I submit or discuss confidential information with FDA prior to, during, or after the meeting?

You may choose to submit nonpublic, trade secret, or confidential commercial information prior to a meeting or to discuss such information prior to, during, or after the meeting. FDA abides by the federal laws governing confidentiality, including sections 301(j) and 906(c) of the FD&C Act (21 U.S.C. 331(j) and 387f(c)), the Trade Secrets Act (18 U.S.C. 1905), and the Freedom of Information Act (5 U.S.C. 552), as well as FDA's implementing regulations.