

Meetings with Industry and Investigators on the Research and Development of Tobacco Products (Revised*)

Guidance for Industry and Investigators

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-2012-D-0429.

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. ET.

Additional copies are available online at <http://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/ucm281147.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, Document Control Center, Bldg. 71, Rm. G335, 10903 New Hampshire Ave., Silver Spring, MD 20993-2000.

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

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See additional PRA statement on page 8 of this guidance.

* This is a revision to the first edition of this guidance, which issued in May 2012.

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

Guidance for Industry and Investigators¹

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 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.

II. BACKGROUND

The manufacture, sale, and distribution of tobacco products are subject to the Food, Drug, and Cosmetic Act (“FD&C Act” or “the Act”), as amended by the Family Smoking Prevention and Tobacco Control Act (the “Tobacco Control Act” or “TCA”).² Among other things, the Act sets forth requirements for authorization to market a new tobacco product through one of three pathways:

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

² Unless otherwise stated, references to statutory sections (identified with §) in this guidance are to sections of the FD&C Act.

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- An application to market a new tobacco product under § 910(b) (“premarket tobacco application” or “PMTA”)³
- A report showing the product is substantially equivalent to a predicate tobacco product that (i) was commercially marketed (other than for test markets) in the United States as of February 15, 2007, or (ii) FDA has issued an order of substantial equivalence under § 910(a)(2)(A)(i).⁴
- A request for exemption from substantial equivalence requirements, which requires a report showing the product meets the requirements for exemption.⁵

The Act also sets forth requirements for authorization to market a modified-risk tobacco product (“MRTP”) (§ 911).⁶

In support of a PMTA, a report showing substantial equivalence, a request for exemption from substantial equivalence requirements, or an application to market an MRTP, a manufacturer may undertake research studies (“investigations”).⁷ Such investigations may utilize tobacco products intended for investigational use (“investigational tobacco products”).⁸ Manufacturers and investigators who undertake investigations may have questions about FDA requirements, or about the use of investigational tobacco products.⁹

FDA staff intends to participate in many meetings with industry and investigators who seek information relating to the research and development of tobacco products, including studies involving investigational 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.

³ For information on how to submit a PMTA, see *Draft Guidance for Industry, Applications for Premarket Review of New Tobacco Products* (September 2011). This and all guidances cited in this document are available at <http://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/ucm281147.htm>.

⁴ See § 905(j)(1) and § 910(a). For additional information regarding how to submit a substantial equivalence report, see *Guidance for Industry, Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products* (January 2011) and *Guidance for Industry, Demonstrating the Substantial Equivalence of a New Tobacco Product: Responses to Frequently Asked Questions* (September 2015).

⁵ See § 905(j)(3) and 21 CFR 1107.1, “Exemptions.” Also, after receiving a “Found Exempt” order, applicants seeking exemption from substantial equivalence must submit a report under § 905(j)(1)(A)(ii) at least 90 days prior to the introduction or delivery for introduction of the new tobacco product into interstate commerce.

⁶ For information about the MRTP application process, see *Draft Guidance for Industry, Modified Risk Tobacco Product Applications* (March 2012).

⁷ For example, see § 910(c)(5)(A), which reads: “For purposes of [the determination under] paragraph (2)(A), whether permitting a tobacco product to be marketed would be appropriate for the protection of the public health shall, when appropriate, be determined on the basis of well-controlled investigations, which may include 1 or more clinical investigations by experts qualified by training and experience to evaluate the tobacco product.”

⁸ For more information about investigational tobacco products, see *Draft Guidance for Industry and Investigatory, Use of Investigational Tobacco Products* (Sept. 2015).

⁹ However, in most circumstances, FDA does not intend to meet to discuss submissions that are under review. See section III.D., below.

III. 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 the Office of Science within the Center for Tobacco Products regarding their research and development plans related to tobacco products.

B. Which FDA staff would likely attend this meeting?

Staff from CTP's Office of Science would attend this meeting. Staff from other parts of FDA may also participate as appropriate, e.g., CTP's Office of Compliance and Enforcement.

C. How do I request a meeting?

Any tobacco product manufacturer, researcher, importer, or investigator involved in the research, 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 either be securely transmitted electronically via the FDA Electronic Submissions Gateway ("ESG") using the eSubmitter tool¹⁰ or sent by mail or courier. Please refer to discussion section III.L. in this document for the mailing address.

D. When should I submit my meeting request?

A meeting request should be submitted prior to submission of a tobacco product application because the purpose of the meeting is to answer questions about the design and conduct of investigations intended to support an application. In most circumstances, FDA does not intend to grant meetings to discuss the content of applications under review. Occasionally, however, a meeting request is submitted during the review of an application. For example, an applicant can request a meeting to discuss the appropriate design of post-marketing studies during the review of a pending modified risk tobacco product application.

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:

- Product name and FDA-assigned Submission Tracking Number (if applicable);
- Product category, e.g., cigarettes, smokeless tobacco (if applicable);
- Product use (indicate for consumer use or for further manufacturing);
- Contact information for an authorized point of contact for the company requesting the meeting;

¹⁰ 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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- The topic of the meeting being requested, e.g., a new tobacco product application, an application for authorization to market an MRTP, or proposed investigational use of a new tobacco product;
- 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;
- A preliminary list of the specific objectives/outcomes expected from the meeting;
- A preliminary proposed agenda, including an estimate of the time needed and a designated speaker for each agenda item;
- A preliminary list of specific questions, grouped by discipline, e.g., chemistry, clinical, nonclinical;
- A list of all individuals who will attend meeting on your behalf, including titles and responsibilities;
- When you expect to submit the meeting information package, described below;
- Suggested format of the meeting, e.g., conference call, in person meeting at FDA offices, video conference, or written response, and suggested dates and times for the meeting. Meetings are usually scheduled for 1 hour.

F. How will FDA to respond to my request?

In general, FDA intends to respond to meeting requests in writing within 21 calendar days of receipt. If FDA agrees to the meeting, the written response should include the following:

- The date, time, format, and location of the meeting;
- The expected FDA participants;
- 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?

Yes. If FDA denies your initial request, you may submit another request. A subsequent request should include any information that was lacking in your initial request, and otherwise address the stated reasons for FDA's denial of the initial request. FDA will consider a subsequent meeting request to be a new request.

H. Could FDA decide that a face-to-face meeting or teleconference is unnecessary?

Yes. FDA may determine that a face-to-face meeting or teleconference is unnecessary, and instead provide written responses to the questions raised in the meeting request. If you believe that the written responses are insufficient, you may submit a subsequent request for a meeting.

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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 the Office of Science, who will likely be a Regulatory Health Project Manager. This employee will be your point of contact for additional questions regarding the meeting.

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 information 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 based on the product, phase of tobacco product development, and issues to be discussed, the meeting information package should generally include (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);

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8. A list of specific questions grouped by issue/study;
9. Product composition and design data summary;
10. Manufacturing and process control data summary;
11. Nonclinical data summary;
12. Clinical data summary;
13. Behavioral and product use data summary;
14. User and non-user perception data summary;
15. Investigational plans for studies and surveillance of the tobacco product, including a summary of proposed study protocols containing the following information:
 - Study objective(s);
 - Study hypotheses;
 - Study design;
 - Study population (inclusion/exclusion criteria, comparison group(s));
 - Human subject protection information, including Institutional Review Board (IRB) information;
 - Primary and secondary endpoints (definition and success criteria);
 - Sample size calculation;
 - Data collection procedures;
 - Duration of follow-up and baseline and follow-up assessments;
 - Data analysis plan(s).

The content of your meeting information package should include any 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 meeting information package where appropriate to reflect the most current and accurate information available to you. For specific guidance regarding the contents of the meeting information package, contact the point-of-contact person listed on FDA's response to your meeting request.

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

You should submit your meeting request to the Director, Office of Science, CTP, at FDA. The request should be prominently identified as "OS Meeting Request" and can be securely transmitted via the FDA Electronic Submissions Gateway (ESG) using the eSubmitter tool.¹¹

Alternatively, you may send your meeting request via U.S. Mail or courier to the following address:

Food and Drug Administration
Center for Tobacco Products
Document Control Center
Building 71, Room G335

¹¹ 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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10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

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.

M. What if I am unable to provide adequate supporting documentation in my meeting information package no later than 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 contact your CTP 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 paper copies to the meeting 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 meeting information package. FDA staff may not be able to provide comments on data or information not previously submitted in the meeting information package. 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 often helpful to ensure this information is preserved for meeting attendees and future reference. FDA generally 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.

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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 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.

IV. PAPERWORK REDUCTION ACT OF 1995

This guidance contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520).

The time required to complete this information collection is estimated to average 5 hours per response, including the time to review instructions, search existing data sources, gather the data needed, and complete and review the information collection. Send comments regarding this burden estimate or suggestions for reducing this burden to:

Food and Drug Administration
Center for Tobacco Products
Document Control Center
Building 71, Room G335
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. The OMB control number for this information collection is 0910-0731 (expires 06/30/2019).

Document History

May 2012 – Guidance is published.

July 2016 – This is a revision to the May 2012 edition of this guidance. Revisions include:

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- The background section of this guidance was updated to reflect the publication of *Draft Guidance for Industry and Investigators, Use of Investigational Tobacco Products* (9/24/2015) and *Guidance for Industry, Demonstrating the Substantial Equivalence of a New Tobacco Product: Responses to Frequently Asked Questions* (9/8/2015). The background section was also shortened to replace brief background information about §§ 905, 910, and 911 with citations to the current guidances that provide detailed information about each provision. The definitions section was removed, as the terms listed in the previous version were relevant to the removed text.
- Additional line items were added to the list of information one should include in the meeting package: (1) product composition and design data summary, and (2) manufacturing and process control data. These line items take the place of “Chemistry, manufacturing, and control data summary,” which was removed. Finally, the line item, “preclinical data summary” was changed to “nonclinical data summary.”