DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Center for Tobacco Products
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

OMB No. 0910-xxxx
Expiration Date: mm/dd/yyyy
(See Paperwork Reduction Act Statement on Page 4)

Month dd, yyyy

Submission Tracking Number (STN): [RDXXXXXXX]

INTERNAL DRAFT DELIBERATIVE

[Address Block]

Dear [Sir or Madam]:

Under section 904(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), FDA is requesting that manufacturers of tobacco products submit documents relating to research on the effects of pH of smokeless tobacco products. This request applies to research relating to the effects of pH on all such tobacco products and their components, parts, or accessories, including those products for research, investigational use, developmental studies, test marketing, and/or commercial marketing.

I. Submission Content

A. Submission of Documents Pursuant to a Section 904(b) Request

In accordance with section 904(b) of the FD&C Act, FDA requests that you submit all documents (including underlying scientific and financial information) relating to research activities and research findings conducted, supported, or possessed by you or your agents relating to a specified set of topics, as set forth below. The request includes, but is not limited to, documents relating to research findings and activities, if any, that you possess as the result of acquiring or merging with another company. For purposes of this request, "research" may include, but is not limited to, focus groups, surveys, experimental clinical studies, toxicological and biochemical assays, in vivo and in vitro assays including animal testing, laboratory formulation and processing testing, taste panels, and assessments of the effectiveness of product marketing practices. The request applies to research relating to any and all smokeless tobacco products, including the components, parts, or accessories of such products, including but not limited to products for research, investigational use, developmental studies, test marketing, and/or commercial marketing.

For products not manufactured in the United States, the request applies to the extent you have imported such products into the United States. An importer of a tobacco product not manufactured in the United States is required to supply the information requested by FDA from the manufacturer of that product.

1. Topics

Pursuant to section 904(b), FDA requests all documents (including underlying scientific and financial information) relating to research activities, research findings, and marketing research for smokeless tobacco products developed since January 1, 1980, subject to the limitations in section I.A.2 of this letter, on *all* of the following topics:

1. The effect of product pH on the ratio of free/bound (unprotonated/protonated) nicotine;
2. The effect of product pH on user behavior;
3. The effect of product pH on user subjective effects and experiences including, but not limited to, sensory effects in the mouth and throat, liking, craving and withdrawal symptoms, stimulation, concentration, and anxiety;
4. The effect of product pH on user physiological responses including, but not limited to, heart rate, blood pressure, temperature, and nicotine pharmacokinetics;
5. For smokeless tobacco products that have a pH of 7.2 or less, marketing research (including underlying financial information) that includes attractiveness or appeal to new users, inexperienced users, and/or to persons under the age of 25.

Research and development of methodology for adjusting the pH of smokeless tobacco products is specifically excluded from this 904(b) request.

2. Limitations — types of documents and information

With respect to the topics listed above, FDA requests the following documents and information:

- Study proposals, original implemented protocols (including all amendments), analysis plans, agreements, notebooks, data collection tools, including, but not limited to, forms and assessment scales for planned, ongoing, or completed studies, surveys, and other research, whether for external release or internal use;
- Final data analyses and reports regarding studies, surveys, data compilations, or other research, whether for external or internal use (if there were no final analyses, interim data analyses should be submitted);
- Posters and/or presentations exhibited or to be exhibited at external meetings or conferences if the underlying data has not been presented in other documents and information within this request;
- Manuscripts, articles, editorials, and letters that have been submitted for publication but not yet published (e.g., in review, accepted, rejected);
- Underlying data (e.g., in the form of spreadsheets, datasets, charts, tables, and diagrams) analyzed to produce any of the data analyses, reports, posters, manuscripts, or articles requested above.

With respect to documents, FDA requests only the final version, or in the absence of a final version, the most recent draft of each document. Please do not submit (a) past iterations of a completed or more recent document, (b) document duplicates, or (c) near duplicates that only vary in minor ways (e.g., differences in addressee or changes in letterhead). Published (publicly available) press releases, abstracts, editorials, letters, manuscripts, material safety data sheets (MSDS), and HHS correspondences are not requested, although we would appreciate a list of such publications provided as a separate appendix. Electronic mail should be in portable document format (.pdf) and responsive to the above topic areas. Transmittal email should not be included.

Data supporting summary reports are included in this request. FDA asks that spreadsheets or datasets be submitted both in pdf and in a file type and structured format that allows for meaningful review and analysis of the data (e.g., Excel (.xls), comma separated values (.csv), or SAS transport (.xpt) file formats). Where relevant, data submissions should be accompanied by the name and version of software used to create the file, names and definitions of variables, and copies of programs and macros needed to generate your analyses. Your submission should include any data analyses that stratify scientific results by gender, race/ethnicity, age, or other similar factors.

As an option, information responsive to this 904(b) request that has been previously provided to FDA under sections 904(a)(l), 904(a)(3), 904(c)(l), 904(c)(2), or 904(c)(3) of the FD&C Act does not have to be re-submitted as long as the document is fully referenced in the metadata load file.

3. Date for submission of documents

All information for this request is to be received by FDA no later than 60 days from the date of this letter. **If you do not have any documents responsive to this request, inform FDA of this in writing by [Month, dd, yyyy]**. If you anticipate difficulties with this document production, please contact FDA within 30 days of the date of this letter so that we may assist you in resolving any technical difficulties you may have and facilitate compliance with the above timeline.

Failure to provide information requested by FDA in accordance with section 904(b) of the FD&C Act is a violation of the FD&C Act and subject to regulatory and enforcement action by FDA.

B. Submission of Additional Information

To provide context and background for the 904(b) requests in section I.A of this letter, FDA also asks that you voluntarily submit the following additional information, as applicable:

6. A summary (one to five pages in length) for each of the topics in section I.A that includes the number and type of documents included, and a high-level overview of the content;
7. Explanations of the scientific and business reasons, rationale, or justifications for developing and marketing smokeless tobacco products with different pH values, including expected and observed perception and behavior of current and potential consumers.

II. Submission Instructions

Consistent with applicable statutes and regulations, the confidentiality of trade secret and confidential commercial information submitted to FDA pursuant to this request will be preserved.

We encourage you to submit your response in an electronic format on CD-ROM, DVD, or hard drive. Please see the enclosed document for guidance in preparing your submission to FDA.

Your submission should be prominently identified with the manufacturer's or importer's name, the label "FDA MM-YYYY pH Request for [RDXXXXXXX]" and sent to the following address:

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

If you have questions regarding this document request, please contact XXXXXX, Regulatory Health Project Manager, at xxx-xxx-xxxx.

Sincerely,

[Signatory]

Paperwork Reduction Act Statement

The public reporting burden for this collection of information has been estimated to average between 5 and 175 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing burden to:

Department of Health and Human Services
Food and Drug Administration
Office of the Deputy Commissioner for Operations
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

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 number.

Enclosure

Enclosure: Submission Information

A. General Instructions

We request that you submit documents and related material on a CD-ROM, DVD, or hard drive. Documents should be in text-searchable PDF file(s) per FDA guidance on electronic submissions, the FDA eSubmitter User Manual, and the National Archives and Records Administration (NARA) Technical Guidelines for Digitizing Archival Materials for Electronic Access, for document preservation of content and format. The files should include a signed cover letter prominently identified as "FDA MM-YYYY pH Request for [RDXXXXXXX]," and should also identify the software (name, version, and company) that you used to confirm the submission is free of viruses or other malware. The cover letter should include the number of documents you are submitting for each of the topics. The electronic media should be labeled with your company name, a contact phone number, "FDA MM-YYYY pH Request for [RDXXXXXXX]," submission date, and series number (e.g., "disc 1 of 2").

In order for FDA to accept, access, review, and archive the documents, all documents are to be submitted in their native color and files, including compressed files and archives, and cannot be password protected. File formats that should be avoided are proprietary, requiring specialized software to read, and active content that can contain macros or change the content upon opening the file. Ensure all documents are text-searchable and restriction settings under Document Properties are set to "allowed." If you submit PDF files, they should not contain any attached, embedded, or bundled files. If any documents are scanned, you should verify the accuracy of optical character recognition and legibility of the document. In addition, multi-page documents should be properly unitized, instead of several single-page files.

B. Instructions for Information Submitted Under Section I.A

To ensure accessibility of your documents and facilitate more fluent and efficient communication between you and FDA regarding your submissions, FDA recommends that you take the following steps:

- Uniquely number all pages of your submission, a process commonly referred to in the litigation context as Bates numbering; and
- Translate all foreign language documents into English.
- Create and submit a glossary or explanation of any abbreviations, jargon, or internal names (e.g., code names).

To provide context and background for each document, FDA recommends inclusion of a load file containing the following metadata for each document:

- Manufacturer filing the document;
- Document date;
- Document author(s);
- Document recipient(s);
- Document custodian;
- Document title or identification number;
- Beginning and ending Bates numbers;

- Bates number ranges for other documents physically or digitally attached to the document;
- OCR text (for scanned paper documents);
- Identify each document as one of the following document types: Email, Briefing slides, Publication, Memo, Report, Meeting minutes, Proposal, Study design, Other
- Topic(s) (i.e., the topic or topics listed in section I.A.1 of the attached letter to which the document relates);
- Product name(s) (e.g., brand or sub-brand, or a unique, consistent identifying name for any tobacco product in research or development);
- Product identification number; Identify the presence of each document in the University of California San Francisco Legacy Tobacco Documents Library (LTDL) as one of the following: present with the Bates number (begin Bates number to end Bates number), not present, or unknown; and if applicable
- For information previously provided to FDA:
    - Date of previous FDA submission;
    - Regulatory section under which the document was submitted;
    - File name;
    - File extension;
    - Bates number (begin Bates number to end Bates number);
    - Relevant page numbers.

FDA requests that load files containing metadata be submitted in a comma delimited ASCII format and be organized so that data fields will appear in the same order as they appear here, i.e., "Manufacturer filing the document" should be the first field, and "Identification of document presence in LTDL" should be the last field. Metadata load file delimiters should be as follows:

Metadata Load File Delimiters

Field separator:	**Vertical Pipe (ASCII 124)**
Field encapsulate:	**Carat (ASCII 094)**
Return value in data:	**Tilde (ASCII 126)**
Multi-value field:	**Semi Colon (ASCII 059)**
Dates format:	**MM/DD/YYYY**

Hard Returns should appear only at the end of each record.

If you scan paper documents for digital production, please use optical character recognition software (OCR) technology to extract searchable text data from the document image. Any extracted searchable text should be produced with the document as metadata.

The instructions in this enclosure are based on communications that FDA has received from industry and our evaluation of submissions received under the FD&C Act to date. If you have questions about how to prepare your submission, please contact us.