

legislative requirement. In Spring 2015, the FDA–NIH (National Institutes of Health) Joint Leadership Council identified the harmonization of terms used in translational science and medical product development as a priority need, with a focus on terms related to study endpoints and biomarkers (see <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm614359.htm>). Working together with the goals of improving communication, aligning expectations, and improving scientific understanding, the two agencies developed the BEST Resource. The current phase of BEST comprises a glossary that clarifies use of important terms in the context of biomarkers and related scientific concepts and describes some of the hierarchical relationships, connections, and dependencies among the terms it contains. For example, the BEST glossary aims to capture distinctions between biomarkers and clinical assessments and to describe their distinct roles in biomedical research, clinical practice, and medical product development. FDA refers the public to the following web page for additional background information as well as a link to the BEST glossary of terms: <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm614359.htm>. FDA has previously discussed taxonomy for biomarkers used in drug development at its public meeting on Drug Development Tool Process on December 11, 2018, and invited comment on the BEST taxonomy in guidance published on December 12, 2018, on the evidentiary framework for biomarker qualification.

## II. Establishment of a Docket and Issues for Consideration

To help FDA determine the utility of the BEST glossary of terms, develop future iterations, and identify best methods for conveying this information, FDA is soliciting public comments on the BEST glossary that can be found on the following web page: <https://www.ncbi.nlm.nih.gov/books/NBK338448/?report=reader>. The BEST glossary is meant to be a resource that will be periodically updated with additional terms and clarifying information. Specifically, FDA welcomes comments concerning: (1) The utility of the BEST glossary; (2) specific proposed edits, including additions and removal of terms, with a rationale supporting these proposed edits; (3) the best approach for developing future iterations of the glossary; and (4) questions pertaining to the BEST glossary that you would like

FDA to address in future communications. As the glossary is refined, the goal is to elaborate on these terms, so they will remain relevant, thus fostering consistent usage. Ultimately, FDA hopes that the BEST glossary will help to accelerate development and refinement of medical products, which will lead to improvements in health outcomes. The Agency will consider comments submitted to the docket as it revises the BEST glossary of terms.

Dated: July 22, 2019.

**Lowell J. Schiller,**

*Principal Associate Commissioner for Policy.*

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**BILLING CODE 4164–01–P**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

[Docket No. FDA–2019–N–0994]

#### Modified Risk Tobacco Product Applications for VLN™ King and VLN™ Menthol King, Combusted, Filtered Cigarettes, Submitted by 22nd Century Group, Inc.

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice of availability.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing the availability for public comment of modified risk tobacco product applications (MRTPAs) for VLN™ King and VLN™ Menthol King, combusted, filtered cigarettes, submitted by 22nd Century Group, Inc.

**DATES:** Electronic or written comments on the application may be submitted beginning July 25, 2019. FDA will establish a closing date for the comment period as described in section I.

**ADDRESSES:** You may submit comments as follows:

#### Electronic Submissions

Submit electronic comments in the following way:

- **Federal eRulemaking Portal:** <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or

confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see “Written/Paper Submissions” and “Instructions”).

#### Written/Paper Submissions

Submit written/paper submissions as follows:

- **Mail/Hand delivery/Courier (for written/paper submissions):** Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in “Instructions.”

**Instructions:** All submissions received must include the Docket No. FDA–2019–N–0994 for “Modified Risk Tobacco Product Applications for VLN™ King and VLN™ Menthol King, Combusted, Filtered Cigarettes Submitted by 22nd Century Group Inc.” Received comments will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

- **Confidential Submissions—**To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not

in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

**Docket:** For access to the docket to read the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

**FOR FURTHER INFORMATION CONTACT:** Paul Hart, Center for Tobacco Products, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. G335, Silver Spring, MD 20993-0002, 1-877-287-1373, [AskCTP@fda.hhs.gov](mailto:AskCTP@fda.hhs.gov).

#### SUPPLEMENTARY INFORMATION:

##### I. Background

Section 911 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 387k) addresses the marketing and distribution of modified risk tobacco products (MRTPs). 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. Section 911(a) of the FD&C Act prohibits the introduction or delivery for introduction into interstate commerce of any MRTP unless an order issued by FDA pursuant to section 911(g) of the FD&C Act is effective with respect to such product.

Section 911(d) of the FD&C Act describes the information that must be included in a MRTPA, which must be filed and evaluated by FDA before an applicant can receive an order from FDA. FDA is required by section 911(e) of the FD&C Act to make a MRTPA available to the public (except for matters in the application that are trade secrets or otherwise confidential commercial information) and to request comments by interested persons on the information contained in the application and on the label, labeling, and advertising accompanying the application. The determination of whether an order is appropriate under section 911 of the FD&C Act is based on the scientific information submitted by the applicant as well as the scientific evidence and other information that is

made available to the Agency, including through public comments.

Section 911(g) of the FD&C Act describes the demonstrations applicants must make to obtain an order from FDA under either section 911(g)(1) or (g)(2). The applicant, 22nd Century Group, Inc., is seeking an order under section 911(g)(2) of the FD&C Act.

FDA may issue an order under section 911(g)(2) of the FD&C Act with respect to a tobacco product that does not satisfy the section 911(g)(1) standard. A person seeking an order under section 911(g)(2) of the FD&C Act must show that:

- Such an order would be appropriate to promote the public health;
- any aspect of the label, labeling, and advertising for the product that would cause the product to be an MRTP is limited to an explicit or implicit representation that the tobacco product or its smoke does not contain or is free of a substance or contains a reduced level of a substance, or presents a reduced exposure to a substance in tobacco smoke;

- scientific evidence is not available and, using the best available scientific methods, cannot be made available without conducting long-term epidemiological studies for an application to meet the standards for obtaining an order under section 911(g)(1);

- the scientific evidence that is available without conducting long-term epidemiological studies demonstrates that a measurable and substantial reduction in morbidity or mortality among individual tobacco users is reasonably likely in subsequent studies;

- the magnitude of overall reductions in exposure to the substance or substances which are the subject of the application is substantial, such substance or substances are harmful, and the product as actually used exposes consumers to the specified reduced level of the substance or substances;

- the product as actually used by consumers will not expose them to higher levels of other harmful substances compared to the similar types of tobacco products then on the market unless such increases are minimal and the reasonably likely overall impact of use of the product remains a substantial and measurable reduction in overall morbidity and mortality among individual tobacco users;

- testing of actual consumer perception shows that, as the applicant proposes to label and market the product, consumers will not be misled into believing that the product is or has

been demonstrated to be less harmful or presents or has been demonstrated to present less of a risk of disease than one or more other commercially marketed tobacco products; and

- issuance of an order with respect to the application is expected to benefit the health of the population as a whole taking into account both users of tobacco products and persons who do not currently use tobacco products.

Section 911(g)(4) of the FD&C Act describes factors that FDA must take into account in evaluating whether a tobacco product satisfies the requirements in section 911(g)(2).

FDA is issuing this notice to inform the public that the MRTPAs for the following products submitted by 22nd Century Group, Inc. have been filed and are being made available for public comment:

- MR0000140: VLN™ King
- MR0000141: VLN™ Menthol King

FDA will post the application documents, including any amendments, to its website for the MRTPAs (see section II) for public comment on a rolling basis as they are redacted in accordance with applicable laws. In this document, FDA is announcing the availability of the first batch of application documents for public comment. FDA intends to establish a closing date for the comment period that is both at least 180 days after the date of this notice and at least 30 days after the final documents from the applications are made available for public comment. FDA will announce the closing date at least 30 days in advance. FDA believes that this comment period is appropriate given the volume and complexity of the applications being posted.

FDA will notify the public about the availability of additional application documents and the comment period closing date via the Agency’s web page for the MRTPAs (see section II) and by other means of public communication, such as by email to individuals who have signed up to receive email alerts. FDA does not intend to issue additional notices in the **Federal Register** regarding the availability of additional application documents, including amendments, or the comment period for these MRTPAs. To receive email alerts, visit FDA’s email subscription service management website (<https://updates.fda.gov/subscriptionmanagement>), provide an email address, scroll down to the “Tobacco” heading, select “Modified Risk Tobacco Product Application Update,” and click “Submit.” To encourage public participation

consistent with section 911(e) of the FD&C Act, FDA is making the redacted MRTPAs that are the subject of this notice available electronically (see section II).

**II. Electronic Access**

Persons with access to the internet may obtain the documents at <https://www.fda.gov/tobacco-products/advertising-and-promotion/22nd-century-group-inc-modified-risk-tobacco-product-mrtp-applications>.

Dated: July 19, 2019.

**Lowell J. Schiller,**

*Principal Associate Commissioner for Policy.*

[FR Doc. 2019-15831 Filed 7-24-19; 8:45 am]

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**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

[Docket No. FDA-2008-D-0031]

**Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Clinical Laboratory Improvement Amendments Waiver Applications**

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

**DATES:** Fax written comments on the collection of information by August 26, 2019.

**ADDRESSES:** To ensure that comments on the information collection are received,

OMB recommends that written comments be faxed to the Office of Information and Regulatory Affairs, OMB, Attn: FDA Desk Officer, Fax: 202-395-7285, or emailed to [oir\\_submission@omb.eop.gov](mailto:oir_submission@omb.eop.gov). All comments should be identified with the OMB control number 0910-0598. Also include the FDA docket number found in brackets in the heading of this document.

**FOR FURTHER INFORMATION CONTACT:**

Amber Sanford, Office of Operations, Food and Drug Administration, Three White Flint North, 10A-12M, 11601 Landsdown St., North Bethesda, MD 20852, 301-796-8867, [PRASStaff@fda.hhs.gov](mailto:PRASStaff@fda.hhs.gov).

**SUPPLEMENTARY INFORMATION:** In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

**Clinical Laboratory Improvement Amendments Waiver Applications**

*OMB Control Number 0910-0598—Extension*

Congress passed the Clinical Laboratory Improvement Amendments (CLIA) (Pub. L. 100-578) in 1988 to establish quality standards for all laboratory testing. The purpose was to ensure the accuracy, reliability, and timeliness of patient test results regardless of where the test took place. CLIA requires that clinical laboratories obtain a certificate from the Secretary of Health and Human Services (the Secretary), before accepting materials derived from the human body for laboratory tests (42 U.S.C. 263a(b)). Laboratories that perform only tests that are “simple” and that have an “insignificant risk of an erroneous result” may obtain a certificate of waiver (42 U.S.C. 263a(d)(2)). The Secretary has delegated to FDA the

authority to determine whether particular tests (waived tests) are “simple” and have “an insignificant risk of an erroneous result” under CLIA (69 FR 22849).

On January 30, 2008, FDA published a guidance document entitled “Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices—Guidance for Industry and FDA Staff” (<https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm079632.htm>). This guidance describes recommendations for device manufacturers submitting to FDA an application for determination that a cleared or approved device meets this CLIA standard (CLIA waiver application). The guidance recommends that CLIA waiver applications include a description of the features of the device that make it “simple”; a report describing a hazard analysis that identifies potential sources of error, including a summary of the design and results of flex studies and conclusions drawn from the flex studies; a description of fail-safe and failure alert mechanisms and a description of the studies validating these mechanisms; a description of clinical tests that demonstrate the accuracy of the test in the hands of intended operators; and statistical analyses of clinical study results.

In the **Federal Register** of March 26, 2019 (84 FR 11307), FDA published a 60-day notice requesting public comment on the proposed collection of information. No comments were received.

FDA estimates the burden of this collection of information as follows:

TABLE 1—ESTIMATED ANNUAL REPORTING BURDEN <sup>1</sup>

Activity	Number of respondents	Number of responses per respondent	Total annual responses	Average burden per response	Total hours	Total operating and maintenance costs
CLIA Waiver Application .....	13	1	13	1,200	15,600	\$350,000

<sup>1</sup> There are no capital costs associated with this collection of information.

TABLE 2—ESTIMATED ANNUAL RECORDKEEPING BURDEN <sup>1</sup>

Activity	Number of recordkeepers	Number of records per recordkeeper	Total annual records	Average burden per recordkeeping	Total hours
CLIA Waiver Records .....	13	1	13	2,800	36,400

<sup>1</sup> There are no capital costs or operating and maintenance costs associated with this collection of information.