May 3, 2024

Geneoscopy, Inc.
Erica Barnell, M.D., Ph.D.
Chief Science Officer
2220 Welsch Industrial Court
St. Louis, MO 63146

Re: P230001
Trade/Device Name: ColoSense®
Product Code: SBB
Filed: January 20, 2023
Amended: September 27, 2023, April 22, 2024

Dear Erica Barnell:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for ColoSense®. This device is indicated for:

> ColoSense is intended for the qualitative detection of colorectal neoplasia associated RNA markers and for the presence of occult hemoglobin in human stool. ColoSense is for use with the ColoSense Collection Kit, the ColoSense Test Kit, the ColoSense Software, and the following instruments: Polymedco iFOBT Analyzer; bioMérieux EMAG Nucleic Acid Extraction System; and Bio-Rad QXDx ddPCR System. ColoSense is a single-site test performed at Geneoscopy, Inc.
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> A positive ColoSense result may indicate the presence of colorectal cancer (CRC), advanced adenomas (AA), or serrated precancerous lesions (SPL), and should be followed by a colonoscopy. ColoSense is indicated as a screening test for adults, 45 years of age or older, who are at typical average-risk for developing CRC. ColoSense is not a replacement for diagnostic colonoscopy or surveillance colonoscopy in high-risk individuals.

We are pleased to infom you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below. Although this letter refers to your product as a device, please be aware that some approved products may instead be combination products. The Premarket Approval Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm identifies combination product submissions.

The sale and distribution of this device are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). FDA has determined that these restrictions on sale and distribution are necessary to provide reasonable assurance of the safety and effectiveness of the device. Your device is therefore a restricted device subject to the

requirements in sections 502(q) and (r) of the act, in addition to all other applicable requirements, including those governing the manufacture, distribution, and marketing of devices.

Continued approval of the PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA. This report, identified as "Annual Report" and bearing the applicable PMA reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and must include the information required by 21 CFR 814.84.

In addition to the above, and in order to provide continued reasonable assurance of the safety and effectiveness of the PMA device, under 21 CFR 814.82(a)(9), the Annual Report must include, separately for each model number (if applicable), the number of devices sold and distributed during the reporting period, including those distributed to distributors. The distribution data will serve as a denominator and provide necessary context for FDA to ascertain the frequency and prevalence of adverse events, as FDA evaluates the continued safety and effectiveness of the device.

In addition to the Annual Report requirements, you must provide the following data in post-approval study (PAS) reports for PAS listed below.

1. Geneoscopy Inc. must conduct a study to expand the total number of colorectal cancer (CRC) cases evaluated by Colosense. You have agreed to the ColoSense Post-Approval Study (PAS), Protocol ID: CT-PRT-0004 by email dated April 10, 2024 which is a prospective, multisite, decentralized study evaluating the sensitivity and specificity of the Colosense screening test for colorectal cancer, using colonoscopy as the reference method. Lesions will be confirmed as malignant by histopathologic examination. The post-approval study (PAS) must meet the study requirements meeting these criteria below:
    - The primary objective of this post-approval study (PAS) is to continue to evaluate the clinical effectiveness of ColoSense by obtaining at least 23 CRC cases (23 cases in addition to the 27 obtained in CRC-PREVENT for a total of 50 CRC cases) to have an adequate number of CRC subjects that are part of the intended use population (average risk) to provide more certainty in the test performance.
    - In total, this study will enroll 12,500 subjects. The ColoSense test will be performed in advance of an average risk screening colonoscopy. With an estimate that 65% of enrolled patients would complete all study requirements, Geneoscopy anticipates approximately 8,125 viable results. Geneoscopy expects to obtain an additional 33 patients with CRC. Of the 33 subjects with CRC, 23 are expected to have no family history of CRC.
    - The study length will be 36 months with 24 months of follow-up:
        - The first subject will be enrolled within 12 months of the study protocol approval date.
        - 20% of subjects enrolled within 20 months of the study protocol approval date.
        - 50% of subjects enrolled within 28 months of the study protocol approval date.
        - 100% of subjects enrolled within 36 months of the study protocol approval date.
    - Data from the original CRC-PREVENT trial will be pooled with the post-approval study to assess primary endpoints. The primary endpoints for this study are ColoSense sensitivity for colorectal cancer, ColoSense sensitivity for advanced adenomas, ColoSense sensitivity for serrated precancerous lesions, and ColoSense specificity for all other findings. Criteria for success requires that the combined sensitivity of CRC (CRCs observed in the CRC-PREVENT clinical trial and CRCs

observed in the PAS) must be greater than 90% and the lower bound of the 95% two-sided confidence interval must be greater than 80% when the data is pooled with the results of the CRC-PREVENT post-approval study.

- The post-approval study will include four co-primary performance measures:
  - Colosense sensitivity for subjects with Colorectal Cancer (CRC) (category 1.0)
  - ColoSense sensitivity for subjects with Advanced Adenomas (AA) (categories 2.1-2.3)
  - ColoSense sensitivity for serrated precancerous lesions (SPL) (category 2.4) and
  - ColoSense specificity for subjects with negative findings (categories 3.1-6.2)

  The post-approval study will include three co-secondary performance measures:
  - ColoSense sensitivity for subjects with high-grade dysplasia or >10 adenomas (category 2.1)
  - ColoSense sensitivity for subjects with tubulovillous adenomas (category 2.2)
  - ColoSense sensitivity for subjects with advanced adenomas (AA) and serrated precancerous lesions (SPL) (categories 2.1-2.4)
- FDA tracks and evaluates the conduct of a PAS through review of study reports submitted to the Agency. Reporting requirements include Enrollment Status Reports, PAS Progress Reports which must be submitted every six months until subject enrollment has been completed, and annually thereafter, from the date of the approval order, unless otherwise specified by FDA, as well as a Final Report. You must follow the reporting schedule, as required by the PMA approval order, until you have submitted the Final PAS Report FDA requires all applicants to provide one electronic copy (eCopy) of PAS submissions to the following address: http://www.fda.gov/cdrhsubmissionaddress

From the date of study protocol approval, you must meet the following timelines:

- The first subject will be enrolled within 12 months of the study protocol approval date.
- 20% of subjects enrolled within 20 months of the study protocol approval date.
- 50% of subjects enrolled within 28 months of the study protocol approval date.
- 100% of subjects enrolled within 36 months of the study protocol approval date.

In addition, you must submit separate periodic reports on the progress of the PAS as follows:

- PAS Progress Reports every six (6) months until subject enrollment has been completed, and annually thereafter, from the date of the PMA approval letter, unless otherwise specified by FDA.
- If any enrollment milestones are not met, you must begin submitting quarterly enrollment status reports every 3 months in addition to your periodic (6-month) PAS Progress Reports, until FDA notifies you otherwise.
- Submit the Final PAS Report three (3) months from study completion (i.e., last subject's last follow-up date).

Each PAS report should be submitted to the address below identified as a "PMA Post-Approval Study Report" in accordance with how the study is identified above and bearing the applicable PMA reference number.

Be advised that failure to comply with any post-approval requirement, including study objective, sample size, study endpoints and performance metrics outlined above, constitutes grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.82(c) and 814.46(a)(2).

Be advised that the failure to conduct any such study in compliance with the good clinical laboratory practices in 21 CFR part 58 (if a non-clinical study subject to part 58) or the institutional review board regulations in 21 CFR part 56 and the informed consent regulations in 21 CFR part 50 (if a clinical study involving human subjects) may be grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.46(a)(3)-(4).

Be advised that protocol information, interim and final results will be published on the Post-Approval Studies Program Database Webpage, available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma_pas.cfm.

In addition, the results from any post approval study should be included in the labeling as these data become available. Under 21 CFR 814.39, any updated labeling must be submitted to FDA in the form of a PMA Supplement. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by Premarket Approval Application Order" (https://www.fda.gov/media/71327/download).

This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final Unique Device Identification (UDI) rule. These provisions include the requirement to provide a UDI on the device label and packages (21 CFR 801.20), format dates on the device label in accordance with 21 CFR 801.18, and submit data to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). Additionally, 21 CFR 814.84 (b)(4) requires PMA annual reports submitted after September 24, 2014, to identify each device identifier currently in use for the subject device, and the device identifiers for devices that have been discontinued since the previous periodic report. It is not necessary to identify any device identifier discontinued prior to December 23, 2013. Combination Products may also be subject to UDI requirements (see 21 CFR 801.30). For more information on these requirements, please see the UDI website available at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-udi-system.

Before making any change affecting the safety or effectiveness of the PMA device, you must submit a PMA supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39. All PMA supplements and alternate submissions (30-day notice) must comply with the applicable requirements in 21 CFR 814.39. Additional information about changes that may require a PMA supplement are provided in the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" https://www.fda.gov/media/81431/download.

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production and process controls (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52 for devices or post-marketing safety reporting (21 CFR Part 4, Subpart B) for combination products, you are required to report adverse events for this device. Manufacturers of medical

devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or

2. Has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems and on combination product post-marketing safety reporting is available at https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products.

In accordance with the recall requirements specified in 21 CFR 806.10 for devices or the post-marketing safety reporting requirements (21 CFR Part 4, Subpart B) for combination products, you are required to submit a written report to FDA of any correction or removal of this device initiated by you to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device which may present a risk to health, with certain exceptions specified in 21 CFR 806.10(a)(2). Additional information on recalls is available at https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/industry-guidance-recalls.

CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve your PMA by making available, among other information, a summary of the safety and effectiveness data upon which the approval is based. The information can be found at https://www.fda.gov/medical-devices/device-approvals-denials-and-clearances/pma-approvals. Written requests for this information can also be made to the Food and Drug Administration, Dockets Management Branch, (HFA-305), 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by submitting a petition for review under section 515(g) of the act and requesting either a hearing or review by an independent advisory committee. FDA may, for good cause, extend this 30-day filing period.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a PMA. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with a copy of all final labeling. Final labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by a cover letter stating that the final labeling is identical to the labeling approved in draft form. If the final labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Control Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact Caryl Giuliano at Caryl.Giuliano@fda.hhs.gov .

Sincerely,

Donna M. Roscoe -S

Donna Roscoe, Ph.D.
Acting Director
Division of Molecular Genetics and Pathology
OHT7: Office of In Vitro Diagnostics
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