



May 14, 2024

Roche Molecular Systems, Inc.
Gaila Balniene
Regulatory Affairs Manager
4300 Hacienda Drive
Pleasanton, California 94588-2722

Re: P100020/S055
Trade/Device Name: cobas HPV Test
Product Code: MAQ

P190028/S009
Trade/Device Name: cobas HPV
Product Code: MAQ

Filed: July 13, 2023
Amended: March 29, 2024

Dear Gaila Balniene:

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) supplement for the cobas HPV Test and the cobas HPV (hereafter referred to as Roche cobas HPV tests) for expanding the indications to include vaginal specimens self-collected in healthcare settings.

The cobas HPV Test (P100020/S055) is indicated for:

The cobas HPV Test for use on the cobas 4800 System (cobas HPV Test) is a qualitative in vitro test for the detection of high-risk Human Papillomavirus. This test detects the high-risk HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68 in the specimens listed below.

Clinician-collected cervical specimens should be obtained using an endocervical brush/spatula or broom and placed in the ThinPrep Pap Test PreservCyt Solution or using a cervical broom and placed in SurePath Preservative Fluid.

Self-collected vaginal specimens, obtained in a healthcare setting, can be tested as an alternative specimen type when cervical sampling is either contraindicated or cervical samples otherwise cannot be obtained.

The cobas HPV Test is indicated for use for routine cervical cancer screening as per professional medical guidelines, including triage of ASC-US cytology, co-testing (or adjunctive screen) with cytology, and HPV primary screening of individuals with a cervix to assess the risk for cervical precancer and cancer. Patients

should be followed-up in accordance with professional medical guidelines, results from prior screening, medical history, and other risk factors.

The cobas HPV (P190028/S009) is indicated for:

cobas HPV for use on the cobas 5800/6800/8800 Systems (cobas HPV) is a qualitative in vitro test for the detection of high-risk Human Papillomavirus. This test detects the high-risk HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68 in the specimens listed below.

Clinician-collected cervical specimens should be obtained using an endocervical brush/spatula or broom and placed in the ThinPrep Pap Test PreservCyt Solution.

Self-collected vaginal specimens, obtained in a healthcare setting, can be tested as an alternative specimen type when cervical sampling is either contraindicated or cervical samples otherwise cannot be obtained.

cobas HPV is indicated for use for routine cervical cancer screening as per professional medical guidelines, including triage of ASC-US cytology, co-testing (or adjunctive screen) with cytology, and HPV primary screening of individuals with a cervix to assess the risk for cervical precancer and cancer.

Patients should be followed-up in accordance with professional medical guidelines, results from prior screening, medical history, and other risk factors.

Based upon the information submitted, the PMA supplement 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 is 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.

Expiration dating for this device has been established and approved in P100020 and P190028.

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. The post-approval study, will be coordinated by NCI Cervical Center as part of the NCI Cervical Cancer 'Last Mile' Initiative: Self-collection for HPV testing to Improve Cervical Cancer Prevention (SHIP) Trial. The study contains two protocols, the "SHIP Sub-Protocol LMI-001-A-S02" and "SHIP Sub-Protocol LMI-001-A-S03", each designed to evaluate the performance of a specific self-collection device with the cobas HPV tests. Each protocol will enroll at least 500 individuals with a cervix, 25 years or older, with referrals to colposcopy based on previous positive HPV test or abnormal cytology results. The study will provide additional data regarding clinical performance of the cobas HPV tests with vaginal specimens in a U.S. population. The clinical sensitivity, clinical specificity, and false positive rate in detecting precancer/cancer, as well as the corresponding ratio between vaginal and cervical specimens will be evaluated. Additionally, the concordance of the cobas HPV tests results between the two specimen types will be evaluated. The protocols were received by FDA via email dated May 5, 2024.

For each study protocol, from the date of the PMA approval letter, you must meet the following timelines for study subject enrollment:

- First subject enrolled within 4 months
- 20% of subjects enrolled within 6 months
- 50% of subjects enrolled within 8 months
- 100% of subjects enrolled within 12 months

In addition, for each study protocol, you must submit separate periodic reports on the progress of the study 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 "SHIP Sub-Protocol LMI-001-A-S02" or "SHIP Sub-Protocol LMI-001-A-S03" as well as 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 initiation, enrollment, and completion requirements 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 John McManus at 240-402-7964 or John.McManus@fda.hhs.gov.

Sincerely,

 **Himani Bisht -S** for

Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health