June 15, 2026

Croma-Pharma GmbH
℅ John Smith
Partner
Hogan Lovells US LLP
Columbia Sq.
555 Thirteenth St., NW
Washington, District of Columbia 20004

Re: P250021
Trade/Device Name: saypha® ChiQ™
Product Code: LMH
Filed: June 26, 2025
Amended: April 24, 2026

Dear John Smith:

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 the saypha® ChiQ™. This device is indicated for use in cheek augmentation and restoring midface volume deficit in adults 22 years of age and older. The device is indicated to be administered by subcutaneous and/or supraperiosteal injection. Based upon the information submitted, 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.

Expiration dating for this device has been established and approved at 36 months when stored at 5–25°C/ 41–77°F, in a dry place and protected from sunlight, heat and frost.

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.

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.

You must obtain approval of your post-approval study (PAS) protocol(s) within 60 days from the date of this order. Within 30 days of your receipt of this letter, you must submit PMA supplements that include complete protocols of your post-approval studies described below. Your PMA supplements should be clearly labeled as a "PMA Post-Approval Study Protocol" as noted below and submitted to the CDRH Portal. Please reference the PMA number above to facilitate processing. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement.

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

1. PAS/FST is a prospective, multicenter, U.S., open-label, single-arm post-approval safety study in subjects with Fitzpatrick Skin Types V and VI treated with saypha® ChIQ™ for moderate to severe midface volume deficit to further characterize the safety profile in this subpopulation.

Study purpose: To further characterize the safety profile of saypha® ChIQ™ in subjects with Fitzpatrick Skin Types V and VI treated for moderate to severe midface volume deficit.

Study design (specify control, randomization, etc.): Single arm, no comparator

Total number of subjects: Up to 50 screened; 45 treated subjects to be included in the Safety Analysis Set (SAF)

Length of follow-up and frequency of assessments: Approximately 28 weeks per subject (up to 2-week screening period + baseline treatment + optional touch-up at Week 2 + 24-week follow-up). Total expected study duration is approximately 12 months, including an approximately 6-month recruitment period. Subjects will be followed for 24 weeks after the last injection (Visit 8, Week 24 = End of Study Visit). Subjects will attend in-clinic visit at Visit 3b (Week 2), Visit 4 (Week 4), Visit 5 (Week 8), Visit 6 (Week 16) and Visit 7 (Week 24), all times calculated as of after last injection. Safety will be assessed throughout the investigation. Patient diaries will be used to capture injection site reactions and symptoms of interest (including vision changes) after treatment. Protocol-defined visual examinations will be performed at each visit to assess ocular safety. Visual examinations will be performed by trained site personnel according to standardized study procedures. Standardized photography will be obtained at baseline, treatment and follow-up visits. Interim safety data (number of subjects enrolled, sites enrolled, summary of AEs/AESIs) will be submitted to FDA as part of the 6-month PAS Progress Reports.

Endpoint(s):

Primary Safety Endpoint: Incidence, severity, seriousness, relatedness, and outcome of treatment-emergent device- and/or procedure-related adverse events through Week 24

Secondary Safety Endpoint: Injection site reactions as recorded in the subject diaries during the first 4 weeks (28 days) after each treatment (i.e., either 4 weeks after baseline or 6 weeks in case of touch-up treatment). Injection site reactions will be assessed overall and for each side of the midface (i.e., left and right side separately). Subject evaluation of pain after each treatment on an 11-point NPRS (0 = no pain; 10 = worst pain imaginable)

High-level description of the data analysis plan for the primary endpoints:

Analysis Population: The Safety Analysis Set (SAF) is defined as all subjects who received at least one treatment with saypha® ChIQ™. The Full Analysis Set (FAS) similarly includes all subjects who received at least one treatment with saypha® ChIQ™.

Descriptive Methods: For categorical parameters, counts and percentages will be presented. For continuous parameters, descriptive statistics will include n, mean, standard deviation, median, and range. Two-sided 95% confidence intervals will be calculated for key incidence rates. Injection site reactions, patient diary findings, visual assessment findings, and predefined events of special interest will be summarized descriptively. No general imputation methods will be applied; methods will be described for each variable separately in the Statistical Analysis Plan (SAP).

Reference to protocol: Study outline received May 26, 2026 - VOLIDO-PAS

Plan for interim data release: Interim safety data (number of subjects enrolled, sites enrolled, summary of AEs/AESIs) will be submitted to FDA as part of the 6-month PAS Progress Reports.

2. PAS/Scale Validation is described below:

Study purpose/objectives: The objective of this study is to determine the inter-rater and intra-rater reliability of the Croma Midface Volume Deficit Severity Scale when utilized in live subject ratings and to confirm that a 1-point difference on the scale is clinically relevant across all FST.

Study design: This is a single-center, non-interventional study designed to provide supplemental data to pool with the original validation data of the Croma MVDSS.

Total number of subjects: Live validation: Approximately 50 subjects; target 5 FST I, 13 FST V, 15 FST VI. Clinical Relevance (CR): 30 image pairs will be selected; target 10 0-point difference, 10 1-point difference, 5 2-point difference, 3 3-point difference, and 2 – 4 point difference; target 5 FST I, 15 FST V, 10 FST VI.

Length of follow-up and frequency of assessments: The Live Validation will consist of two (2) Rounds, two (2) weeks apart.

Endpoint(s):

Live Validation (LV)

Intra-rater: Overall Cicchetti-Allison and Fleiss Cohen weighted kappa coefficients of the three (3) Live Validation (LV) Raters based on MVDSS scores assigned by LV raters during LV Rounds 1 and 2. Data will be presented independently from this study and if appropriate pooled across the original and supplemental studies.

Cicchetti-Allison weighted kappa is provided as a supportive sensitivity analysis to demonstrate the robustness of the reliability conclusions across alternative weighting approaches.

Inter-rater: Median pairwise Cicchetti-Allison and Fliess Cohen weighted kappa coefficients for each pairwise combination of the three (3) LV Raters based on MVDSS scores assigned by LV Raters during LV Round 1. Data will be presented independently from this study and if appropriate pooled across the original and supplemental studies.

Cicchetti-Allison weighted kappa is provided as a supportive sensitivity analysis to demonstrate the robustness of the reliability conclusions across alternative weighting approaches.

Clinical Relevance (CR)

Difference (and corresponding 95% CI) in estimated marginal means of MVDSS scores assigned by CR Reviewers, for image pairs with 0-point True Grade difference versus pairs with 1-point True Grade difference, modeling rater and image pair as random effects.

High-level description of the data analysis plan for the primary endpoints:

A statistical approach to test poolability will be conducted for both studies prior to pooling data.

The Live Validation will consist of two (2) Rounds, two (2) weeks apart. Each rater will assign a score for MVD severity of zero (0) to four (4) based on the photonumeric scale. For analysis, the primary endpoint will be analyzed on the pooled data. Additionally, a sensitivity subgroup analysis will be conducted to assess the consistency of model performance between the original live validation and the supplementary validation.

Clinical Relevance consisted of two rounds: a comparative assessment where clinicians rated image pairs as clinically different or not and a static Image review where reviewers graded each image independently using the Croma MVDSS. This exercise was designed to show that a 1-point difference on the scales represents a clinically meaningful difference. The exercise will be carried out on a new set of thirty (30) image pairs

Reference to protocol: Study outline received May 26, 2026 - Re: CROMA Midface Volume Deficit Severity Scale – Supplementary Study Protocol Synopsis

Plan for interim data release: 6-month PAS progress reports

From the date of study protocol approval, you must meet the following timelines for PAS/FST and PAS/Scale Validation:

- First subject enrolled within 6 months
- 20% of subjects enrolled within 12 months
- 50% of subjects enrolled within 18 months
- 100% of subjects enrolled within 24 months

In addition, you must submit separate periodic reports on the progress of PAS/FST and PAS/Scale Validation 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 CDRH Portal 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 initiation, enrollment, and reporting 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 Management System Regulation (QMSR) (21 CFR Part 820), which includes, but is not limited to, ISO 13485 clause 7.3 (Design controls),

ISO 13485 clause 8.3 (Nonconforming product), ISO 13485 clause 8.5.2 (Corrective action), and ISO 13485 clause 8.5.3 (Preventative action). Please note that regardless of whether a change requires premarket review, the QMSR requires device manufacturers to review and approve changes to device design and production (ISO 13485 clause 7.3 and ISO 13485 clause 7.5) and document changes and approvals in the Medical Device File (ISO 13485 clause 4.2.3).

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 to the CDRH Portal and should reference the above PMA number to facilitate processing. For more information on the CDRH Portal, please visit https://www.fda.gov/medical-devices/industry-medical-devices/send-and-track-medical-device-premarket-submissions-online-cdrh-portal.

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

Sincerely,

RACHANA VISARIA -S

Rachana Visaria, Ph.D.
Acting Director
DHT4B: Division of Plastic and
Reconstructive Surgery Devices
OHT4: Office of Surgical and
Infection Control Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health