U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

Via Electronic Mail
Return Receipt Requested

September 9, 2024

Mr. Georgio Francia
Qualified Person
Industria Farmaceutica Nova Argentia
Via Carlo Porta 49
Gorgonzola, Milan
Italy

Dear Mr. Francia:

Your facility was registered with the United States Food and Drug Administration (FDA) as a manufacturer of over-the-counter (OTC) drug products. FDA has reviewed the records you submitted in response to our November 21, 2023 and April 3, 2024 requests for records and other information pursuant to section 704(a)(4) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for your facility, Industria Farmaceutica Nova Argentia, FEI 3016436027, at Via Carlo Porta 49, Gorgonzola, Milan.

This letter summarizes violations of Current Good Manufacturing Practice (CGMP) regulations for finished pharmaceuticals. See Title 21 Code of Federal Regulations, parts 210 and 211 (21 CFR, parts 210 and 211).

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your drug products are adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 351(a)(2)(B)).

704(a)(4) Request for Records and Related CGMP Violations

Following review of records and other information provided pursuant to section 704(a)(4) of the FD&C Act, violations were observed including, but not limited to, the following:

1. Your firm failed to have, for each batch of drug product, appropriate laboratory determination of satisfactory conformance to final specifications for the drug product, including the identity and strength of each active ingredient, prior to release (21 CFR 211.165(a)).

You failed to conduct adequate finished product testing as part of the specifications for batch release. For example, (b) (4) Ointment" has the following active ingredients listed on the product label: (b) (4) (b) %), (b) (4) ((b) (4) %) and (b) (4) ((b) (4) %). In response to our requests for records, assay testing for these active ingredients was not included as part of your finished product release specifications.

In response to this letter, provide the following:

- A list of chemical and microbial specifications, including test methods, used to analyze each lot of your drug products before a batch disposition decision.
  - An action plan and timelines for conducting full chemical and microbiological testing of retain samples to determine the quality of all batches of drug product distributed to the United States that are within expiry as of the date of this letter.
  - A summary of all results obtained from testing retain samples from each batch. If such testing reveals substandard quality drug products, take rapid corrective actions, such as notifying customers and product recalls.

2. Your firm failed to conduct at least one test to verify the identity of each component of a drug product (21 CFR 211.84(d)(1)).

Your firm failed to test all incoming raw materials for identity prior to their use in finished drug products. For example, in your response to our requests for records, you did not provide evidence that the (b) (4), (b) (4), is tested for identity upon receipt.

In response to this letter, provide the following:

- A comprehensive, independent review of your material system to determine whether all suppliers of components, containers, and closures, are each qualified and the materials are assigned appropriate expiration or retest dates. The review should also determine whether incoming material controls are adequate to prevent use of unsuitable components, containers, and closures.

- The chemical and microbiological quality control specifications you use to test and release each incoming lot of components for use in manufacturing.

- A description of how you will test each component lot for conformity with all appropriate specifications for identity, strength, quality, and purity. If you intend to accept any results from your supplier's Certificates of Analysis (COA) instead of testing each component lot for strength, quality, and purity, specify how you will robustly establish the reliability of your supplier's results through initial validation as well as periodic re-validation. In addition, include a commitment to always conduct at least one specific identity test for each incoming component lot.

- A summary of your program for qualifying and overseeing contract facilities that test the drug products you manufacture.

3. Your firm failed to establish and follow an adequate written testing program designed to assess the stability characteristics of drug products (21 CFR 211.166(a)).

Your firm failed to establish an ongoing stability program for your finished drug product. Your response to our requests for records stated that you performed a long-term stability study with

(b) (4) batches to establish an expiration date and did not place any batches into an ongoing stability program.

In response to this letter, provide the following:

- A comprehensive, independent assessment and CAPA plan to ensure the adequacy of your stability program. Your remediated program should include, but not be limited to:
  - Stability indicating methods.
  - Stability studies for each drug product in its marketed container-closure system before distribution is permitted.
  - An ongoing program in which representative batches of each product are added each year to the program to determine if the shelf-life claim remains valid.
  - Detailed definition of the specific attributes to be tested at each station (timepoint).

- All procedures that describe these and other elements of your remediated stability program.

Parametric Release

Your firm releases purportedly sterile finished drug products using a parametric release approach instead of sterility testing. FDA considers a properly qualified and maintained parametric release program to encompass multiple, integrated CGMP systems that are in a state of control, including 1) sterilization process validation and control, 2) verification by suitable load monitor(s), 3) a validated container/closure system, and 4) an effective Quality System. Failure to meet any one of these criteria could disqualify the parametric release program.

The CGMP violations described throughout this letter demonstrate an ineffective Quality System. Consequently, FDA is concerned you do not have appropriate oversight for a parametric release approach for your finished drug products.

Drug Production Ceased

We acknowledge your commitment to cease production of "(b) (4) Ointment" drugs for the U.S. market. In response to this letter, clarify whether you intend to resume manufacturing drugs for the U.S. market at this facility in the future.

If you plan to resume any manufacturing operations regulated under the FD&C Act, notify this office before resuming your drug manufacturing operations. You are responsible for resolving all deficiencies and systemic flaws to ensure your firm is capable of ongoing CGMP compliance. In your notification to the Agency, provide a summary of your remediations to demonstrate that you have appropriately completed all corrective action and preventive action (CAPA).

Conclusion

The violations cited in this letter are not intended to be an all-inclusive list of violations that exist at your facility. You are responsible for investigating and determining the causes of any violations and for preventing their recurrence or the occurrence of other violations.

This letter notifies you of our findings and provides you an opportunity to address the above deficiencies. After you receive this letter, respond to this office in writing within 30 working days. Specify what you have done to address any violations and to prevent their recurrence. In response to this letter, you may provide additional information for our consideration as we continue to assess your activities and practices. If you cannot complete corrective actions within 30 working days, state your reasons for delay and your schedule for completion.

Send your electronic reply to CDER-OC-OMQ-Communications@fda.hhs.gov. Identify your response with FEI 3016436027 and ATTN: Sarah Rhoades.

Sincerely,

/s/

Francis Godwin
Director
Office of Manufacturing Quality
Office of Compliance
Center for Drug Evaluation and Research