Department of Health and Human Services

Public Health Service
Food and Drug Administration
Silver Spring, MD 20993

Warning Letter

WL: 320-15-14

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

August 6, 2015

Mr. Rajiv Malik
President
Mylan
1000 Mylan Boulevard
Canonsburg, PA 15317

Dear Mr. Malik:

The U.S. Food and Drug Administration (FDA) inspected the following three pharmaceutical manufacturing facilities.

A. February 6-13, 2015: Mylan Laboratories Limited OTL, Plot No. 284-B (19A) Bommasandra Jigani Link Road, Ind. Area, Anekal Taluk, Bangalore, 560 105
B. September 23, 2014 through October 3, 2014: Agila Specialties Private Ltd., Specialty Formulation Facility (SFF) 19A, Plot No. 284-B/1 Bommasandra Jigani Link Road, Anekal Taluk, Bangalore 560 105
C. August 1-8, 2014: Agila Specialties Private Ltd., Sterile Product Division, Opp II M, Bilekahalli, Bannerghatta Road, Bangalore, Karnataka, 560 076

At all three sites, we identified significant violations of current good manufacturing practice (CGMP) regulations for finished pharmaceuticals, Title 21, Code of Federal Regulations, Parts 210 and 211.

These violations cause your drug products to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. 351(a)(2)(B). The methods used in, or the facilities or controls used for, their manufacture, processing, packing, or holding do not conform to, or are not operated or administered in conformity with, CGMP.

We reviewed your firm's responses of August 29 and October 27, 2014, and March 9, 2015, in detail. We note that they lack sufficient corrective actions. We received your additional

correspondence of November 14, November 26, December 16, and December 19, 2014; and January 19, February 13, March 16, and April 20, 2015.

Our investigators observed specific violations during the inspections, including, but not limited to, the following.

A. **Mylan Laboratories Limited OTL (FEI: 3007512701)**

1. Your firm failed to establish and follow appropriate written procedures that are designed to prevent microbiological contamination of drug products purporting to be sterile, and that include validation of all aseptic and sterilization processes (21 CFR 211.113(b)).

a. Non-integral **(b)(4)** gloves were used in Suites **(b)(4)** and **(b)(4)** for conducting aseptic processing operations.

For example, on February 12, 2015, we found that 15 of **(b)(4)** gloves in Suite **(b)(4)**, and 4 of **(b)(4)** gloves from Suite **(b)(4)**, were non-integral. **(b)(4)** gloves used for aseptic processing had tears and pin holes. Glove S2C8 had large cuts in two different fingers. Your firm was aware that non-integral **(b)(4)** gloves were being used in Suite **(b)(4)**.

Additionally, certain records indicated that you were testing **(b)(4)** gloves for integrity, but the integrity data indicated testing for **(b)(4)** gloves. You did not follow your procedure PDN/039/R10, "Leak Testing of **(b)(4)** Glove" for testing glove integrity. You did not test each glove represented in your firm's analytical data, as required by the SOP. Instead, you repeatedly used the results for your **(b)(4)** gloves to falsely represent the results of your **(b)(4)** gloves.

The same SOP, PDN/039/R10 "Leak Testing of **(b)(4)** Glove," states that **(b)(4)** gloves are to be replaced after **(b)(4)** cycles. However, according to your "**(b)(4)** Log Sheet," the **(b)(4)** gloves in use when we inspected Suite **(b)(4)** had been **(b)(4)** replaced after no more than **(b)(4)** cycles.

During the inspection, we reviewed environmental monitoring (EM) data that showed excursions in your ISO 5 area, which you attributed to gloves. Finally, during the inspection, we observed unidentified white particles on **(b)(4)** gloves exposed to critical areas inside the RABS.

(b)(4) gloves are worn during critical interventions such as making aseptic connections, clearing jams, clearing fallen vials, **(b)(4)** sterile primary and secondary closures, purging filling needles, adjusting equipment, and changing environmental monitoring plates. Because **(b)(4)** gloves are worn during these critical interventions, using non-integral gloves for aseptic processing is an unacceptable practice. It is a direct risk to product sterility. To minimize risks to sterile products, you should implement an adequate monitoring and maintenance program to identify and eliminate non-integral gloves.

b. There is a lack of assurance that you maintain your manufacturing environment in a state of control suitable for aseptic processing.

Environmental Monitoring

For example, you did not utilize environmental monitoring data to identify environmental control issues and identify appropriate follow-up actions. There were repeated out-of-action-level (OAL) results from microbial testing, but you did not examine the data for trends or take appropriate follow-up action. Your SOP "No. MIP/047/R7 Microbiological Evaluation of Clean Rooms and Other Controlled Environments of Suite **(b)(4)** Area" describes OALs as **(b)(4)** CFU for setting plates inside the RABS (ISO 5) and **(b)(4)** CFUs for your ISO 6 area.

In 2014, you reported 375 OAL results **(b)(4)** or more CFUs in your ISO 6 area. Then, on January 31, 2015, you obtained OAL results of **(b)(4)** or more CFUs during the manufacture of **(b)(4)** Injection (**(b)(4)**) in Suite **(b)(4)**. You also obtained OAL levels from the settle plates inside the RABS (**(b)(4)** CFU near the **(b)(4)**), and **(b)(4)** CFUs were recovered from the air sampling point near the **(b)(4)**. From February 6-7, 2015, you obtained OAL results of **(b)(4)** or more colony-forming unit (CFU) in three critical ISO 5 areas of Suite **(b)(4)** during the manufacture of **(b)(4)** Injection (**(b)(4)**):

- **(b)(4)**—**(b)(4)** CFUs;
- **(b)(4)**—**(b)(4)** CFUs (fungi);
- **(b)(4)**—**(b)(4)** CFUs

Personnel Monitoring
Deficiencies in your operators' practices indicate that your manufacturing personnel monitoring program is deficient. For example, in your video of **(b)(4)** batch **(b)(4)** manufacturing, we observed an operator entering the RABS and in contact with **(b)(4)** gloves without sanitizing his gloved hands. These **(b)(4)** gloves were later worn for aseptic connections, purging filling needles, and interventions on the filling machine. Furthermore, you do not monitor these operators when they exit the area, so you have no way to determine whether the operators who enter RABS without sanitizing compromise the aseptic environment.

Additionally, on video and in person, we observed employees with **(b)(4)** on their hands before EM checks. Sanitizing gloved hands just before sampling is unacceptable because it can prevent recovery of microorganisms. This undermines the reliability of personnel monitoring data.

We are also concerned about your failure to review the results of microbial tests to identify possible trending problems in environmental control in aseptic processing areas. Your response in this regard was inadequate because it did not include a retrospective assessment to ensure that microbial test results reported are reliable. In your response to this letter, please describe your evaluation of the potential effects of the OAL results and personnel monitoring deficiencies discussed above on the quality of products you have already manufactured and distributed. Also provide the improvements you have made to your written procedures to address these violations and describe any other actions you have taken or plan to take to correct the problems and prevent their recurrence.

c. Aseptic garments worn in the filling area were also non-integral. We observed 7 of **(b)(4)** sterile gowns with tears or holes; 8 of **(b)(4)** had loose threads. We observed 2 of **(b)(4)** sterile hoods with tears or holes; 12 of **(b)(4)** had loose threads. We observed 8 of **(b)(4)** sterile booties with tears or holes; 11 of **(b)(4)** had loose threads.

Procedure PDN/013/R8 "Handling of Aseptic Area Garments" required production personnel to examine the garments for tears, holes, and loose threads, but our investigator found that these checks were not being performed.

In response to this letter, explain how your production management will ensure that gowns are suitable for aseptic processing in the future.

2. Your firm failed to establish laboratory controls that include scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality, and purity (21 CFR 211.160(b)).

a. You failed to follow your SOP MIA/007/R11 “Monitoring of Water for Microbiological Quality” for collecting water samples. During our inspection, we documented that the scheduled water drop points for **(b)(4)** and **(b)(4)** water were not sampled.

However, according to the analytical raw data work sheet, microbiological testing was performed for water sampling points **(b)(4)**. We confirmed during the inspection that these samples were not, in fact, collected by your microbiologist.

b. Your environmental monitoring data is not reliable because of the materials you use to conduct EM tests.

On February 6, 2015, our investigator observed **(b)(4)** environmental monitoring plates previously incubated at **(b)(4)** C being used for surface and personnel monitoring. Three of **(b)(4)** plates showed signs of desiccation. Media was shrinking away from the edge of microbial plates.

On February 13, 2015, our investigator observed signs of drying on three of **(b)(4)** plates used for water samples and four of **(b)(4)** plates used for bio-burden.

These observations indicate that your media's growth promotion potential may be compromised. In your response to this letter, inform us if you will be discontinuing this practice of pre-incubating plates.

3. Your firm failed to establish an adequate system for monitoring environmental conditions in aseptic processing areas (21 CFR 211.42(c)(10)(iv)).

a. You do not have a scientific rationale for the environmental monitoring sampling locations in aseptic filling Suites **(b)(4)**. You did not include factors such as smoke study findings, number and location of operators, and historical microbial data in your assessment of hazardous points.

For example, we found that settling plates are not appropriately placed in critical areas. Your smoke study showed that during set-up and filling, air flows toward the front (when **(b)(4)** open)

or back of the RABS. However, two relevant sampling points were recently eliminated. As a result, these points of increased risk are not monitored.

b. During our inspection, we noted that you have no justification for two different action levels for finger dab results. While you have an ISO 5 action level of **(b)(4)** CFU for set-up personnel, you use an ISO 6 action level of **(b)(4)** CFU for operators who do not routinely participate in aseptic processing operations using the RABS.

However, the inspection found that these "ISO 6 operators" made ISO 5 interventions, including within the **(b)(4)** laminar airflow hood (LAF) and the RABS. Notably, when >**(b)(4)** CFU was recovered from an "ISO 6 operator" who had accessed the RABS during an intervention, your firm did not consider the result to be outside the action limit.

Detecting sources of contamination during aseptic processing operations is critical to safeguard product sterility. In response to our inspection, you followed a Product Quality Assessment (PQA) protocol and found visible foreign particulate matter within your examined lots. In March and April, 2015, you voluntarily recalled seven "for Injection" lots of Gemcitabine 200 mg/vial, Gemcitabine 2g, Gemcitabine 1 g, Carboplatin 10 mg/mL, Methotrexate 25 mg/mL, and Cytarabine 20 mg/mL. In June, 2015, you expanded your recall to an additional eight lots of Gemcitabine and Methotrexate. However, other lots released into distribution may have been compromised by this manufacturing issue.

In response to this letter, send a progress report on your search for the root cause of this particulate contamination problem. Describe your product quality assessment protocol, including analysis of retain samples, corrective actions and preventive actions, and risk assessments to evaluate the product quality effects of your inadequate aseptic processing activities and inadequate environmental monitoring program.

B. **Agila Specialties Pvt Ltd (SFF) (FEI: 3007648351)**

1. Your firm failed to establish and follow appropriate written procedures that are designed to prevent microbiological contamination of drug products purporting to be sterile, and that include validation of all aseptic and sterilization processes (21 CFR 211.113(b)).

Your process simulation (media fill) studies are inadequate.

a. During our review of several media fill batch records (MFBR), we documented that integral vials identified as "jam rejects" or "other rejects" were rejected without assignable causes, and not incubated. For example,

- MFBR #MFLY-14010, July 12, 2014, 18 jam rejects
- MFBR #MFVL-13001,March 11, 2014, 176 other rejects
- MFBR #MFVL-14002, March 28, 2014, 138 jam rejects
- MFBR #MFVL-14009, May 5, 2014, 92 jam rejects

We observed your practice of rejecting and not incubating vials in all **(b)(4)** filling suites.

Your media fill practices and procedures are insufficient to justify excluding integral units in such circumstances. We acknowledge that you have committed to revising your commercial production and media fill SOPs. These written procedures should prescribe clear, specific, and justifiable production practices.

Your firm does not document the actual number of aseptically-filled units transferred to the **(b)(4)**, or the reasons you reject media fill vials. Without this information, you cannot reconcile the number of units filled and **(b)(4)** with the number needed to be incubated.

This violation is recurrent and long-standing. Your firm was cited for inadequate media fills and rejection of media fills units without justification in our Warning Letter WL-320-13-26 issued to your facility on September 9, 2013.

In your response to this letter, please submit your updated SOPs on the removal of units during media fills and commercial operations, including a description of improved recordkeeping that reflects an improved reconciliation process and justification for not incubating units.

b. You have no smoke studies for the **(b)(4)** air flow units used to transfer sterilized material to manufacturing areas and aseptic fill rooms under dynamic conditions and during routine interventions. You also have no smoke studies under dynamic conditions that demonstrate that unidirectional airflow and air quality is maintained as employees move in and out of your aseptic fill rooms.

In your response of October 27, 2014, you committed to conduct a gap analysis of aseptic processes in your facility by November 30, 2014, and to conduct smoke studies under rest and dynamic conditions. You also proposed to perform additional studies to ensure acceptable airflow in the **(b)(4)** airflow units by January 15, 2015. You should assure that all of your aseptic processing and aseptic transfer activities have been shown to provide robust unidirectional airflow. In your response to this letter, provide a summary of your re-evaluation of the airflow in all of these ISO 5 areas and specify any additional corrective actions and preventive actions you are implementing.

2. Your firm failed to establish an adequate system for monitoring environmental conditions in aseptic processing areas (21 CFR 211.42(c)(10)(iv)).

a. Your firm does not have a robust sampling plan as part of its environmental monitoring program.

No representative non-viable particle (NVP) monitoring data supports your current ISO-5 classification for the product path from the **(b)(4)** to the **(b)(4)**, which transfers product to the **(b)(4)** during aseptic processing of finished drug products.

During our inspection, we documented that your NVP probes are placed **(b)(4)** surface instead of near the working area. Placing the probe **(b)(4)** instead of near the working area means you are unable to detect NVPs where sterile drugs are exposed during aseptic processing.

Additionally, transferring **(b)(4)** vials from the filling suite to the **(b)(4)** can take up to **(b)(4)**. This extended exposure time may increase contamination hazards. However, your firm lacks adequate environmental monitoring of this part of the operation. It is essential that your sampling plan include areas where **(b)(4)** and product are exposed to the environment, and at greater risk of contamination.

b. In your ISO-5 and ISO-7 environments, the building management system (BMS) monitoring differential pressure and the non-viable particle monitoring system (NVPMS) for non-viable particles appear to be out of control. For example:

- We found 456,201 alarmed events registered in the computer system monitoring differential air pressures between your ISO-5, ISO-7, and ISO-8 manufacturing environments from February 14, 2013, through September 26, 2014.
- We also found 16,415 alarmed events registered in NVPMS for Suite **(b)(4)** ISO-5 areas, and 17,809 for Suite **(b)(4)**, from October 2012 to September 2014.

You did not conduct a comprehensive evaluation and risk assessment to determine how these frequent events affecting the aseptic processing areas may have compromised product quality.

Please perform a comprehensive assessment and summarize your findings in response to this letter.

c. Your firm failed to identify the source of gram-negative contamination in your ISO 7 area and to implement appropriate corrective actions and preventive actions.

In your ISO-7 Suite **(b)(4)**, you identified *Pseudomonas,* sp. during passive air sampling collected from your passage way, in **(b)(4)** rooms **(b)(4)** and **(b)(4)**. You did not evaluate the potential routes of contamination.

Your evaluation of environmental microbial data should not be narrowly limited to specific lots or events. Trend analysis, identifying sources of contamination, and risk assessment are essential to maintain adequate microbiological control.

This violation is recurrent. On September 9, 2013, we cited your firm in Warning Letter 320-13-26 for failure to establish an adequate environmental monitoring system. To assure drug sterility, it is vital for you to vigilantly maintain environmental control throughout aseptic operations.

We acknowledge your commitment to make corrections to these problems. You should diagram the viable and non-viable air sampling locations in all clean areas, including critical areas. In your response to this letter, summarize your retrospective review of microbiological out-of-level results to identify adverse trends. Describe any pertinent corrective actions and preventive actions you have completed or still plan to implement.

3. Your firm failed to exercise appropriate controls over computer or related systems to assure that only authorized personnel can change master production and control records, or other records (21 CFR 211.68(b)).

Your Siemens computer-based BMS and NVPMS do not require passwords to access the network and servers. Your contractors' access is uncontrolled. Responsibilities for system administrators are undefined.

This violation is recurrent. On September 9, 2013, we cited your firm in Warning Letter 320-13-26 for failure to exercise appropriate controls over computer or related systems.

C. **Agila Specialties Pvt Ltd (SPD) (FEI: 3003813519)**

1. Your firm failed to thoroughly investigate any unexplained discrepancy or failure of a batch or any of its components to meet any of its specifications, whether or not the batch has already been distributed (21 CFR 211.192).

a. In 2012, you received two complaints about discolored **(b)(4)** for Injection, USP **(b)(4)** mg/ml vials. After testing the complaint and retention lots, you found lots **(b)(4)**, with discoloration. Three lots **(b)(4)** failed assay with low values. These lots also failed impurity specifications, with high values for **(b)(4)**, and individual unknown impurities.

Your investigation was inadequate.

Although you attributed the discoloration to **(b)(4)** caused by **(b)(4)**, you did not evaluate or test other **(b)(4)** products manufactured using the same equipment. You concluded that out-of-specification assay and impurity results were due to **(b)(4)** caused by **(b)(4)**, but you did not appear to identify or remediate the root cause of this alleged **(b)(4)** problem.

In your response, you indicated that **(b)(4)** was most likely due to **(b)(4)** sticking intermittently to the **(b)(4)** during **(b)(4)**. You did not include evidence to support this conclusion. Your corrective actions and preventive actions (CAPA) include enhanced detection of **(b)(4)** and improved monitoring of **(b)(4)** at the **(b)(4)** of cap sealing. We note that you already had a system to detect and reject vials with **(b)(4)** when you produced the discolored lots of **(b)(4)**.

Enhanced detection on its own does not resolve the root cause of the problem.

In your response to this letter, please detail how your firm is resolving the mechanical or other problem causing **(b)(4)** of your injectable products. Explain what you have done to correct the problem and prevent its recurrence.

Also, describe the differences between your existing and proposed detection systems. Since the existing system already detects **(b)(4)** at a level of **(b)(4)** or more, describe how the new system is superior. Also, provide details to demonstrate that your proposed **(b)(4)** monitoring sampling approach is representative.

You conducted forced degradation studies on other products that could have been compromised. You concluded that, compared to **(b)(4)**, other **(b)(4)** products exhibited minimal sensitivity to **(b)(4)**, so they were unaffected. Your response lacks evidence to support this conclusion.

The "**(b)(4)** Study" included in your response indicates a "significant increase" of **(b)(4)** in the impurity profile of **(b)(4)** Injection, with an "increase" of impurity **(b)(4)** and unknown impurities in **(b)(4)** Injection. You noted a "marginal increase" of unknown impurities in **(b)(4)** Injection and impurity **(b)(4)** in **(b)(4)** Injection.

In your response to this letter, provide your quantitative results, and your plans for these products that may also **(b)(4)** as demonstrated by the changed impurity profiles. You noted changes in impurity profiles without changes in coloration. This suggests that **(b)(4)** in other **(b)(4)** products as a result of **(b)(4)** may not be readily detectable by discolored vials. Also explain whether the **(b)(4)** problem may also result in other **(b)(4)** integrity issues, such as non-sterility.

b. On February 16, 2013, your firm received Complaint No. 2013SP002530 for **(b)(4)** mg. This complaint, which reported a **(b)(4)** adverse reaction, also reported that the product was **(b)(4)**. You did not investigate this defect to determine the root cause of the **(b)(4)**.

c. On February 26, 2013, your firm received Complaint No. 2013SP002695 for **(b)(4)** mg. This complaint, which reported **(b)(4)**, stated that the product was also discolored and took too long to **(b)(4)**. You did not investigate the root cause of product discoloration and slow **(b)(4)** time. You did not evaluate the qualitative attributes of the product to determine if discoloration was due to **(b)(4)**, or if the assay and impurities were within specification.

2. Your firm failed to establish an adequate system for monitoring environmental conditions in aseptic processing areas (21 CFR 211.42(c)(10)(iv)).

a. You did not have settling plates located where the risk of product contamination was greatest. For example, your EM program did not include placement of settling plates near the filling zone, the stopper **(b)(4)**, or the incoming track for **(b)(4)**. The **(b)(4)** filling line settling plate was positioned where filled **(b)(4)** had already been stoppered.

b. On August 6, 2014, when collecting finger dab samples of the **(b)(4)** gloves, your microbiologist failed to ensure that each finger touched the surface of the **(b)(4)** sampling plate.

We acknowledge your firm's commitment to implement corrective actions. You also state that you performed a retrospective assessment of **(b)(4)** filling area environmental monitoring trends over the last two years (August 2013 to the present). You concluded that the trends were acceptable, with no effect on product quality. However, the basis of your assessment is flawed. Sound evaluation of environmental monitoring data relies on sufficient sampling plans and techniques.

3. Your firm failed to follow appropriate written procedures that are designed to prevent microbiological contamination of drug products purporting to be sterile, and that include validation of all aseptic and sterilization processes (21 CFR 211.113(b)).

a. We observed that operators moving in and out of the classified areas were not slow and deliberate during the set-up and filling of batch **(b)(4)**. We often saw operators bump into each other during filling operations.

Your firm was previously cited for inadequate ISO 5 behaviors and procedures during our August 2013 inspection. We acknowledge your firm's proposed CAPA, and will review your aseptic practices on our next inspection to determine its effectiveness.

b. In the **(b)(4)** filling line, barrier **(b)(4)** remain open after activities inside the filling barrier are completed. We observed open barrier **(b)(4)** during and after the **(b)(4)** line setup. For example, **(b)(4)** were open while the microbiologist collected samples, after the operator left to change his gloves, and after the microbiologist left the area. We saw other operators in the area, but barrier **(b)(4)** remained open. A flashing light indicating opened barrier **(b)(4)** was ignored.

This is an example of your failure to operate in accordance with basic RABS concepts that are designed to restrict access and reduce the risk of product contamination from human interventions.

Conclusion

Violations cited in this letter are not intended as an all-inclusive list. You are responsible for determining the causes of these violations, for preventing their recurrence, and for preventing other violations.

These items found at three different sites, together with other deficiencies found by our investigators, raise questions about the ability of your current corporate quality system to achieve overall compliance with CGMP. Furthermore, several violations are recurrent and long-standing. Although we acknowledge that the Agila facilities were acquired by Mylan recently, you were on notice of the violations in Warning Letter 320-13-26, dated September 9, 2013. Even without this Warning Letter, your corporate quality system should have detected and corrected the forgoing violations without FDA intervention.

As a result of receiving this warning letter or for other reasons, if you are considering a decision that could reduce the number of active pharmaceutical ingredients produced by your manufacturing facility, please contact CDER's Drug Shortages Staff immediately at drugshortages@fda.hhs.gov. We can work with you on the most effective ways to bring your operations into compliance with the law. Contacting the Drug Shortages Staff allows you to meet any obligations you may have to report discontinuances in your drug manufacture under 21 U.S.C. 356C(a)(1). As soon as possible, FDA must consider what actions, if any, may be needed to avoid shortages and protect patients who depend on your products. In appropriate cases, you may take corrective action while avoiding or limiting drug shortages.

Until you complete all corrections and we confirm your corrections and compliance with CGMP, FDA may withhold approval of any new applications or supplements listing your firm as a drug product manufacturer. Under Section 801(a)(3) of the Act, 21 U.S.C. 381(a)(3), failure to correct these violations may also result in FDA refusing admission into the United States of articles manufactured at:

A. Mylan Laboratories Limited OTL, Plot No. 284-B (19A) Bommasandra Jigani Link Road, Ind. Area, Anekal Taluk, Bangalore, 560105
B. Agila Specialties Private Ltd., Specialty Formulation Facility (SFF) 19A, Plot No. 284-B/1 Bommasandra Jigani Link Road, Anekal Taluk, Bangalore 560 105
C. Agila Specialties Private Ltd., Sterile Product Division, Opp II M, Bilekahalli, Bannerghatta Road, Bangalore, Karnataka, 560 076

Within 15 working days of receipt of this letter, please notify this office, in writing, of the specific steps that you have taken to correct and prevent the recurrence of violations. Provide supporting documentation.

If you cannot complete corrective actions within 15 working days, state the reasons for the delay and the date by which you will have completed the corrections. If you no longer manufacture or distribute the drug product(s) at issue, provide the date(s) and reason(s) you ceased production. Send your reply to:

Rebecca Parrilla, M.S.
Compliance Officer/CSO
Office of Manufacturing Quality
Division of Drug Quality I
Global Compliance Branch 2
U.S. Food and Drug Administration
White Oak, Building 51 Room 4326
10903 New Hampshire Ave.
Silver Spring, MD 20993

and

Rafael Arroyo, M.S.
Compliance Officer/CSO
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Global Compliance Branch 2
U.S. Food and Drug Administration
White Oak, Building 51 Room 4235
10903 New Hampshire Ave.
Silver Spring, MD 20993

Please identify your response with FEI #3007512701, FEI #3007648351, and FEI #3003813519.

Sincerely,
/S/
Thomas J. Cosgrove, J.D.
Director
Office of Manufacturing Quality
Office of Compliance
Center for Drug Evaluation and Research