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CARACO
PHARMACEUTICAL LABORATORIES, LTD.

June 19, 2008

Ms. Joanne Givens, District Director
Detroit District Office
Food and Drug Administration
300 River Place, Suite 5900
Detroit, Michigan 48207

Re: FDA 483 issued June 11, 2008 to Caraco Pharmaceutical Laboratories, Ltd.

Dear Ms. Givens,

I wanted to send an initial response letter to you to explain that Caraco management is committed to making quality system improvements in order to meet full compliance with the GMP regulations. Caraco considers this the top priority for the company and is committed to providing the necessary resources to accomplish our compliance initiatives expeditiously and effectively. We take the FDA observations from the GMP inspection initiated on May 1, 2008 very seriously and are already identifying and implementing corrective action plans. These corrective actions will not only address the specific findings on the FDA Form 483 but also will address other improvements to Caraco's quality systems and processes. As part of our corrective action plan we will make improvements to our management review process and provide increased Quality Assurance oversight to strengthen our quality system. Caraco management will monitor the effectiveness of these quality system improvements and make adjustments as indicated. A summary of our system level improvements are provided below and will address the following topics:

- Contract Regulatory Consulting
- Management Review Process
- Organizational Changes
- Internal Audits
- Investigation Process
- Training

Contract Regulatory Consulting

Caraco recognizes the need for qualified experts outside of our internal framework. We expect to gain best practice improvements to identify, make recommendations for and implement corrective actions and continuous improvements. Therefore, we have hired [redacted] to assist with all of the improvements outlined in this letter. [redacted] are already on site working with our Quality Assurance team and management to effect changes necessary. Their team is comprised of former FDA employees who also have industry experience. (b)(4)

Management Review Process

Currently our management review process includes at a minimum [redacted] Quality Review Board (QRB) meetings in accordance with Caraco SOP [redacted] The QRB includes members of Caraco senior management from each functional group. The QRB meeting is initiated and chaired by Quality and (b)(4)

includes an agenda, meeting minutes, and action items. We have determined that our current QRB process needs to be strengthened in order to adequately address our quality system. Therefore, we have made the following improvements:

- increased our QRB meetings to bi-weekly
- the meetings include [redacted] as a part of the review process (b)(4)
- the meetings identify and commit the resources needed to implement the corrective actions and continuous improvement activities

Organizational Changes

On May 1, 2008 prior to the FDA arrival at Caraco we made two major organizational changes. First the Dispensing department moved from Commercial Materials Management's responsibility to the Manufacturing department's responsibility. The second organizational change was to move our Technical Services group that is responsible for investigations from Manufacturing to Quality. These changes improve the alignment of our internal expertise and priorities in both Manufacturing and Quality. We also doubled the number of employees in the Technical Services group responsible for investigations. Other organizational changes have yet to be determined or finalized.

At the end of March we hired an Associate Director of Manufacturing to focus on the corrective and preventative actions necessary for improved performance and compliance. We also hired a Senior Manager of Manufacturing who is also focused on corrective and preventative actions. We have hired additional manufacturing managers including most recently a new Dispensing Manager. These changes provide increased oversight and management to our critical cGMP processes and allow us to be more proactive in preventative measures for an improved outcome. We anticipate hiring additional Quality Assurance personnel to improve our oversight and have already devoted QA staff for oversight to assist Manufacturing in the transition of managing the dispensing staff.

Internal Audits

[redacted] will be conducting a comprehensive audit of all critical areas. [redacted] will present their findings and recommendations for corrective actions to the QRB and assist with implementation of the corrective actions for the observations noted and for other areas of improvement. (b)(4) [redacted] will provide customized training deemed necessary for the investigators on staff. We will be recruiting additional Quality Assurance Auditors who will work closely with [redacted] as an opportunity for training.

Investigation Process

Caraco senior management has formed a task force consisting of managers from various departments responsible for evaluating, documenting and closing all outstanding investigations. Quality management is responsible for monitoring the performance of this task force. This will also be reviewed as part of the QRB meetings. In addition, the task force is responsible for assuring that the appropriate change control and corrective actions are implemented. [redacted] will assist with investigational techniques, tools, and training for each investigator to improve the overall scope and depth of the investigations. (b)(4)

As mentioned above, we have doubled the number of employees in the Technical Services group responsible for investigations in order to meet the [redacted] day procedural requirement for incident closure. Critical investigations are to be reviewed at the [redacted] QRB meeting to assure senior management visibility and involvement. (b)(4)

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Training

[redacted] will develop and give customized cGMP training to all employees to supplement training that has already been provided. In addition, the Quality department has revised the training matrix for the Dispensing Operator position to better define the precise job profile and eliminate unrelated training material. All Dispensing Operators and management are being re-trained on all appropriate procedures. (b)(4)

Other

Although Caraco considers all observations critical, we feel it is necessary to respond to Observation 2 immediately since this observation calls into question the quality of product that has been commercially released. We have conducted testing on [redacted]s cited in Observation 2. We placed all remaining inventory of these lots on hold based on the observation until further evaluation was completed. As an extension to the [redacted] cross contamination incidents involving Metoprolol Tartrate and Tramadol HCl, additional studies were performed to investigate the possibility of any further cross contamination that may have occurred during the time period of January 25 through January 29, 2008 when the incidents occurred. Quality Control reviewed the lot release data for the [redacted] manufactured during this time period. Any impurities outside the known raw material impurity peaks would have been detected by the following release tests: Related Substances, Identification, and Uniformity. The review concluded that none of the [redacted] had abnormal results which would indicate cross contamination. (b)(4)

Additional studies were conducted to verify the lot release results. The lots were first evaluated for Metoprolol Tartrate contamination using Metoprolol Tartrate chromatography conditions in order to optimize the detection of Metoprolol Tartrate as a contaminant. All lots of non-Metoprolol Tartrate products were found to be free of Metoprolol Tartrate. The lots were then evaluated for possible cross contamination involving [redacted] different API's used in the commercial drug products manufactured during the contamination incidents. Either Metoprolol Tartrate or Tramadol HCl chromatography conditions were used depending on the API being studied. If required, additional chromatography conditions were used to separate the peaks further. In conclusion, the study showed that no drug products were found to be cross contaminated. (b)(4)

As indicated to the FDA Inspectors during the closeout meeting, we will be forwarding a detailed response and corrective action plan for each observation in the FDA Form 483 on or before July 11, 2008. I want to convey to you that we are already working diligently to correct these issues. We are committed to eliminate these issues with efficiency and resolve. We will expend the necessary resources to meet every timeline outlined in our forthcoming corrective action plan without fail for both near-term and long-term corrections, regardless of their criticality. With the help of new employees, our core employees and [redacted], I am sure that our actions will be swift and comprehensive. As previously stated we will have definitive dates for the completion of all [redacted] plans. It is my intention to update you [redacted] once our corrective action plan is submitted to you. Should you have any questions about our complete response, please do not hesitate to contact my office directly at [redacted] (b)(6) Furthermore, I would be happy to meet with you to discuss any concerns that you may have. I appreciate this opportunity to respond. (b)(4)

Sincerely,

Daniel Movens, CEO
Caraco Pharmaceutical Laboratories, Ltd.

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