Dear Ms. English:

Please refer to your New Drug Application (NDA) dated and received March 7, 2012, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Adrenalin (epinephrine injection), 1 mg/mL.

We acknowledge receipt of your amendments dated:

- April 9, 2012 (2)
- May 16, 2012 (2)
- June 19, 2012 (2)
- August 2, 2012 (2)
- September 5, 2012 (3)
- November 9, 2012 (4)
- November 30, 2012 (2)
- December 6, 2012 (2)

- April 18, 2012
- May 17, 2012 (2)
- July 3, 2012 (2)
- August 21, 2012 (2)
- October 15, 2012 (2)
- November 28, 2012
- December 4, 2012 (2)
- December 7, 2012 (2)

- May 15, 2012
- June 4, 2012
- July 20, 2012 (2)
- August 22, 2012
- October 22, 2012
- November 29, 2012 (2)
- December 5, 2012 (2)

NDA 204200 provides for the use of Adrenalin (epinephrine injection), 1 mg/mL for the following indications which, for administrative purposes, we have designated as follows:

- NDA 204200/Original 1 – Emergency treatment of allergic reactions (Type 1), including anaphylaxis
- NDA 204200/Original 2 – Induction and maintenance of mydriasis during ocular surgery

The subject of this action letter is NDA 204200/Original 1 and NDA 204200/Original 2.
We have completed our review of this application as amended. It is approved, effective on the
date of this letter, for use as recommended in the enclosed agreed-upon labeling text, which is
identical to the labeling text submitted on December 6, 2012.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of
labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA
automated drug registration and listing system (eLIST), as described at
of labeling must be identical to the enclosed labeling text for the package insert. Information on
submitting SPL files using eLIST may be found in the guidance for industry SPL Standard for
Content of Labeling Technical Qs and As, available at
CM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE-CONTAINER LABELS

Submit final printed carton and container labels that are identical to the enclosed carton and
immediate container labels which are identical to the carton and immediate container labels
submitted on December 6, 2012, as soon as they are available, but no more than 30 days after
they are printed. Please submit these labels electronically according to the guidance for industry
titled “Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product
Applications and Related Submissions Using the eCTD Specifications (June 2008).”
Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on
heavy-weight paper or similar material. For administrative purposes, designate this submission
“Final Printed Carton and Container Labels for approved NDA 204200.” Approval of this
submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text may render the
product misbranded and an unapproved new drug.

ADVISORY COMMITTEE

Your application for Adrenalin was not referred to an FDA advisory committee because the
application did not raise significant public health questions on the role of Adrenalin in the
diagnosis, cure, mitigation, treatment, or prevention of a disease.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new
active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of
administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

This product is appropriately labeled for use in all relevant pediatric populations. Therefore, no additional pediatric studies are needed at this time.

**POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B**

We remind you of your postmarketing commitment:

1977-1 Evaluate formulation and process improvements to reduce the levels of impurities with Adrenalin (epinephrine injection). In your evaluation, conduct at least one study to determine the possible cause(s) of formation and take appropriate measures to minimize the level of this impurity. Using the results from these investigations, re-evaluate the acceptance limits for and and lower the limits for these impurities. As part of an interim report, include your evaluation of the formulation/process improvements undertaken to mitigate the level of impurities, in particular and , as well as a summary of all technical work performed using the results of the conducted study(ies). The interim report should also include a proposed development plan for future batches which will ensure consistency and reliability of product quality.

The timetable you submitted on December 7, 2012, states that you will conduct this study according to the following schedule:

- **Final Protocol Submission:** January 2013
- **Interim Report Submission:** April 2013
- **Study/Trial Completion:** March 2014
- **Final Report Submission:** May 2014

Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled “Postmarketing Commitment Protocol,” “Postmarketing Commitment Final Report,” or “Postmarketing Commitment Correspondence.”
PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Prescription Drug Promotion (OPDP)  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Carol Hill, Regulatory Project Manager, at (301) 796-1266.

Sincerely,

{See appended electronic signature page}

Lydia I. Gilbert-McClain, MD, FCCP  
Deputy Director  
Division of Pulmonary, Allergy, and Rheumatology Products  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research

Renata Albrecht, MD  
Director  
Division of Transplant and Ophthalmology Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

Enclosures:  
Content of Labeling  
Carton and Container Labeling
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

RENEA ALBRECHT
12/07/2012

LYDIA I GILBERT MCCLAIN
12/07/2012