DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022569/ S-012/ S-015/ S-017

SUPPLEMENT APPROVAL

Depomed, Inc
Suite 300
7999 Gateway Blvd.
Newark, CA 94560

Attention: Hayley Lewis, RAC
Senior Director, Regulatory Affairs

Dear Ms. Lewis:

Please refer to your Supplemental New Drug Applications (sNDAs) dated September 14 (S-012), and 28 (S-015), 2012, and September 23 (S-017), 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Lazanda (fentanyl) nasal spray.

We acknowledge receipt of your amendments dated February 22, August 16, and October 29, 2013 (S-012), and September 10, and October 21, and 29, 2013 (S-015), and your risk evaluation and mitigation strategy (REMS) assessment dated December 21, 2012.

These supplemental new drug applications provide for the following:

S-012 Changes to sections 2 (DOSAGE AND ADMINISTRATION), 16 (HOW SUPPLIED/STORAGE AND HANDLING), and 17 (PATIENT COUNSELING INFORMATION) of the package insert, and the Medication Guide, due to modifications to the in-use shelf-life of Lazanda.

S-015 Modifications to the approved REMS for Lazanda, which is part of the single shared system REMS, the Transmucosal Immediate-Release Fentanyl (TIRF) REMS Access Program.

S-017 Modifications to the approved package insert, carton and container labeling, and REMS for Lazanda resulting from the transfer of the NDA to Depomed.

We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

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 http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling text for the package insert and Medication Guide, with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and immediate container labels that are identical to the enclosed carton and immediate container labels submitted on September 10, 2013, 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 *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 022569/S-017**." Approval of this submission by FDA is not required before the labeling is used.

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

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Lazanda (fentanyl) nasal spray was originally approved on June 30, 2011. The REMS was last modified on June 5, 2012. The REMS consists of a Medication Guide, elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS.

Your proposed modification to the TIRF REMS, including appended REMS materials as applicable, consists of the following:

- Revised terminology, processes, and definitions for outpatient pharmacies
- Revised attestations for physicians and patients to address concerns regarding patient access
- Revised Program Overview and Frequently Asked Questions to improve clarity and content
- Updated REMS materials to reflect the completion of the transition phase for the TIRF REMS Access Program

Your proposed modified REMS, submitted on September 26, 2012, jointly amended on September 24, 2013, by the TIRF REMS Industry Group (TRIG), and appended to this letter, is approved.

The TIRF REMS Access Program includes the following products:

NDA 020747 Actiq (fentanyl citrate) oral transmucosal lozenge and its authorized generic
NDA 021947 Fentora (fentanyl buccal tablets)
NDA 022266 Onsolis (fentanyl buccal soluble film)
NDA 022510 Abstral (fentanyl) sublingual tablets
NDA 022569 Lazanda (fentanyl) nasal spray
NDA 202788 Subsys (fentanyl) sublingual spray
ANDA 077312 Fentanyl Citrate Oral Transmucosal Lozenge
ANDA 078907 Fentanyl Citrate Oral Transmucosal Lozenge

Other products may be added in the future if additional TIRF NDAs or ANDAs are approved.

We remind you that section 505-1(f)(8) of FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

The timetable for submission of assessments of the REMS will remain the same as that approved on June 5, 2012.

There are no changes to the REMS assessment plan described in our December 28, 2011, letter.

In addition to the assessments submitted according to the timetable included in this approved REMS, you must submit a REMS assessment when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of the FDCA.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

NDA 022569 REMS CORRESPONDENCE
(insert concise description of content in bold capital letters, e.g.,
UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT METHODOLOGY

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

Prominently identify any submission containing the REMS assessments or proposed modifications with the following wording in bold capital letters at the top of the first page of the submission:

NDA 022569
REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 022569: NEW INDICATION OF USE
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

If you do not submit electronically, please send 5 copies of REMS-related submissions.

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 Matthew Sullivan, Senior Regulatory Project Manager, at 301-796-1245.

Sincerely,

{See appended electronic signature page}

Judith A. Racoosin, M.D., M.P.H.
Deputy Director for Safety
Division of Anesthesia, Analgesia, and Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures:
Content of Labeling
REMS

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JUDITH A RACOOSIN
11/07/2013