DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022510/S-013

SUPPLEMENT APPROVAL

Galena Biopharma, Inc.
4640 SW Macadam Ave., Suite 270
Portland, OR 97239

Attention: Patricia Murphy
Vice President of Regulatory Affairs

Dear Dr. Murphy:

Please refer to your Supplemental New Drug Application (sNDA) dated March 12, 2014, received March 12, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Abstral (fentanyl) sublingual tablets, 100, 200, 300, 400, 600 and 800 mcg.

We also refer to our approval letter dated November 4, 2014, which contained the following errors: a footnote following Table 1 in the Package Insert contained incorrect text related to appropriate dose titration, and the Table in the Abstral REMS entitled *Products Covered Under This Program* contained a related error.

We additionally refer to your submission dated December 9, 2014, which incorporates corrections to the Abstral REMS, as indicated above.

Your proposed modified REMS, submitted on July 25, 2014, amended December 9, 2014, and appended to this letter, is approved.

This replacement approval letter incorporates the correction of the errors. The effective approval date will remain November 4, 2014, the date of the original approval letter. The corrected Package Insert and REMS materials are attached to this letter.

This "Prior Approval" supplemental new drug application provides for modification to the approved risk evaluation and mitigation strategy (REMS) and proposes to add language to the DOSAGE AND ADMINISTRATION section of the prescribing information, Medication Guide, and REMS materials indicating that patients may be directly converted from Actiq (fentanyl citrate) lozenges to Abstral (fentanyl) sublingual tablets.

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. It is 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, 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.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Abstral (fentanyl) sublingual tablets was originally approved on January 7, 2011, and a REMS modification was approved on December 28, 2011, as part of the approval of the transmucosal immediate-release fentanyl (TIRF) REMS single-shared system. The TIRF REMS was last modified on November 7, 2013. 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 modifications to the REMS consist of changes to the Abstral (fentanyl) Medication Guide and REMS materials including the *Education Program for Prescribers and Pharmacists* and the *TIRF REMS Knowledge Assessment*. These modifications are to align the content of the REMS materials with the aforementioned changes to the product labeling to

enable conversion from Actiq (fentanyl citrate) transmucosal lozenges to Abstral (fentanyl) sublingual tablets.

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.

A revised REMS Assessment Plan was attached to our August 21, 2014, REMS Assessment Acknowledgment/REMS Assessment Plan Revisions letter.

In addition to the assessments submitted according to the timetable included in the 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 022510 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 the submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

NDA 022510 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 022510
PROPOSED REMS MODIFICATION

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 022510
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

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 Kimberly Compton, RPh, Senior Regulatory Project Manager at 301-796-1191.

Sincerely,

{See appended electronic signature page}

Sharon Hertz, MD
Acting Director
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/

SHARON H HERTZ
11/04/2014