DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202788/S-010

SUPPLEMENT APPROVAL

Insys Therapeutics, Inc.
444 South Ellis St
Chandler, AZ 85224

Attention: Willene Brondum
Senior Manager, Regulatory Affairs

Dear Ms. Brondum:

Please refer to your Supplemental New Drug Application (sNDA) dated September 25, 2012, received September 25, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Subsys (fentanyl sublingual spray), 100, 200, 400, 600, and 800 mcg.

We acknowledge receipt of your amendment dated October 17, 2013, and your risk evaluation and mitigation strategy (REMS) assessment dated December 21, 2012.

This supplemental new drug application provides for modifications to the approved REMS for Subsys (fentanyl sublingual spray), which is part of the single shared system REMS, the Transmucosal Immediate-Release Fentanyl (TIRF) REMS Access Program.

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Subsys (fentanyl sublingual spray was originally approved on January 4, 2012. 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 January 4, 2012, 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 202788 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 202788
REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 202788: 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:
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