DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202788/S-005
NDA 202788/S-006

SUPPLEMENT APPROVAL

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

Attention: Willene Brondum
Senior Manager, Refdgulatory Affairs

Dear Ms. Brondum:

Please refer to your Supplemental New Drug Applications (sNDAs) dated and received June 27, 2012, (S005) and September 7, 2012, (S006) submitted pursuant to section 505(b)(2) 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 amendments to S005 dated January 17, and June 11, 21, and 27, 2013, and your risk evaluation and mitigation strategy (REMS) assessment dated December 21, 2012.

Supplement 005 is a "Prior Approval" supplemental new drug application which proposes initial dosing recommendations to assist prescribers in converting patients from Actiq (fentanyl citrate) lozenges to Subsys (fentanyl sublingual spray), as well as a modification 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.

Supplement 006 is a "Changes Being Effected in 30 days" supplemental new drug application, which provides for new 10 count carton configurations of the previously approved devices.

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 container labels that are identical to the enclosed carton labels as soon as they are available, but no more than 30 days after they are printed.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Subsys (fentanyl sublingual spray) was originally approved on January 4, 2012 and at that time became part of the single shared system REMS, the Transmucosal Immediate-Release Fentanyl (TIRF) REMS Access Program. 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 REMS, including appended REMS materials as applicable, consists of a revised TIRF REMS Knowledge Assessment and TIRF REMS Education Program to include initial dosing recommendations to assist prescribers in converting patients from Actiq (fentanyl citrate) lozenges to Subsys (fentanyl sublingual spray).

Your proposed modified REMS, submitted on January 17, 2013, amended June 11, 21, and 27, 2013, 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.

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
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

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 Matt Sullivan, Senior Regulatory Project Manager, at (301) 796-1245.

Sincerely,

{See appended electronic signature page}

Bob A. Rappaport, M.D.
Director
Division of Anesthesia, Analgesia, and
Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling
Carton 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/

BOB A RAPPAPORT
07/31/2013