DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202788/S-001
NDA 202788/S-003

SUPPLEMENT APPROVAL

Insys Therapeutics, Inc.
(c/o) The Weinberg Group, Inc.
1129 Twentieth Street, NW
Suite 600
Washington, DC 20036

Attention: Lauren H. Wind, MPH
Senior Consultant
The Weinberg Group, Inc.

Dear Ms. Wind:

Please refer to your Supplemental New Drug Applications (sNDA) dated January 18, and February 8, 2012, and received January 18, and February 8, 2012, and identified as S-001 and S-003, respectively. These sNDAs were submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Subsys (fentanyl sublingual spray).

We also acknowledge receipt of your risk evaluation and mitigation strategy (REMS) assessment dated February 8, 2012.

These "Prior Approval" supplemental new drug applications provide for the following:

S-001: Addition of a 30-unit secondary package (i.e., shelf carton) for each strength as well as minor editorial changes to the full package insert.

S-003: Modifications to the approved REMS for Subsys which are part of the single shared system REMS, the transmucosal immediate-release fentanyl (TIRF) REMS Access Program.

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 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, submitted on January 18, 2012, 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 was originally approved on January 4, 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 modifications to the TIRF REMS consist of edits to the Patient-Prescriber Agreement Form, the addition of the Closed System Pharmacy Enrollment Form and minor editorial changes. Additionally, the TIRF REMS Access Program "go-live" placeholder date has been updated with the actual "go-live" date of March 12, 2012.

Your proposed modified REMS, submitted on February 8, 2012, and appended to this letter, is approved.

The TIRF REMS Access program includes the following products:

NDA 020747	Actiq (fentanyl citrate) oral transmucosl 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 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 was amended to correspond with the TIRF REMS Access Program timetable for submission of assessments approved on December 28, 2011. The first assessment is due June 28, 2012, and the second assessment is due December 28, 2012, and assessments are due annually thereafter.

There are no changes to the REMS assessment plan described in our January 4, 2012, letter.

We remind you that assessments of an approved REMS must include, under section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. With respect to any such postapproval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such postapproval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any material or significant updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

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

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 Health 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
Carton and Container 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
06/05/2012