

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: June 1, 2012

TO: Division of Anesthesia, Analgesia, and Addiction Products; Office of Generic Drugs

FROM: Division of Risk Management; Office of Regulatory Policy

SUBJECT: Documentation of sponsor agreement for TIRF REMS modification #1

APPLICATION/DRUG:

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

This memo serves as documentation of agreement between OSE/DRISK and the sponsors of the TIRF REMS Access program for the first modification of the single, shared system TIRF REMS.

The proposed REMS modification supplemental application was received in February 2012 for each of the above applications. The modified REMS and its appended materials approved for this modification supplement have additional changes to those proposed in the February submission. The attached documentation includes email correspondence and track changed documents indicating that FDA and the TRIG agreed on the modified REMS.

The rationale for this memo of documentation is due to the time constraints of the above sponsors submitting the current modified REMS to their individual files as amendments to their supplemental applications, which could take up to two weeks. The modified REMS contains a closed system pharmacy enrollment form that must be approved in order to complete enrollment of the closed system pharmacies, formally termed integrated health care systems. Our enforcement discretion letter to the TIRF sponsors, dated March 20, 2012, says “after June 30, 2012, all Integrated Health Care Systems are enrolled in the TIRF REMS Access Program”.

In addition to this memo, cross-reference the DRISK review dated June 1, 2012 authored by Megan Moncur.

Attached Documentation Table of Contents:

1. Memorandum from TIRF REMS Industry Working Group (TRIG)	page 4
2. Email to TRIG dated May 15, 2012 proposing changes to REMS	page 5
a. Clean REMS document- May 15, 2012	page 6
b. Tracked REMS document- May 15, 2012	page 22
c. Clean Patient-Prescriber Agreement Form- May 15, 2012	page 38
d. Tracked Patient-Prescriber Agreement Form- May 15, 2012	page 41
e. Clean Closed System Pharmacy Enrollment Form- May 15, 2012	page 44
f. Tracked Closed System Pharmacy Enrollment Form- May 15, 2012	page 47
3. Email from TRIG dated May 30, 2012 accepting tracked proposals and proposing new tracked changes	page 50
a. Tracked REMS document- May 30, 2012	page 51
b. Tracked Patient-Prescriber Agreement Form- May 30, 2012	page 67
c. Tracked Closed System Pharmacy Enrollment Form- May 30, 2012	page 70
4. Email to TRIG dated May 31, 2012 stating DRISK agreement with the additional revisions proposed by the TRIG on May 30 th	page 73

May 31, 2012

Bob Rappaport, M.D., Director
Division of Anesthesia, Analgesia and Addiction Products
Food and Drug Administration
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

**Re: Transmucosal Immediate Release Fentanyl (TIRF) REMS - Modification 1
(Original Submissions dated February 2012)**

Dear Dr. Rappaport:

In connection with the Amendment to the Approved REMS submitted by the individual companies which compose the TIRF REMS Industry Working Group (TRIG) in early February 2012, reference is made to the telephone communication dated May 25, 2012 between FDA, Nancy Dickinson and Megan Moncur, and myself on behalf of the TIRF REMS Industry Working Group (TRIG) in which the TRIG's feedback was requested for the following documents previously provided by Darrell Jenkins in his email to Christine Kampf of the TRIG dated May 15, 2012:

- REMS
- Closed System Pharmacy Enrollment Form
- PPAF

Further reference is made to the e-mail response containing the TRIG's feedback on the REMS documents submitted by myself on behalf of the TRIG on May 30, 2012 and FDA's subsequent email dated May 31, 2012 from Mark Liberatore of FDA indicating the Agency's acceptance of the TRIG's proposed modifications to the abovementioned documents.

The TRIG (see list below) unanimously agrees with the final versions of the documents forwarded to Mr. Liberatore on May 31 and respectfully requests approval for TIRF REMS Modification 1.

Sincerely,



Willene M. Brondum
Senior Manager, Regulatory Affairs

cc: Archimedes Pharma, Cephalon / Teva Pharmaceuticals, Covidien,
Endo Pharmaceuticals, Insys Therapeutics, Inc., Meda Pharmaceuticals, Par Pharmaceutical Inc.,
ProStrakan, Sandoz Inc.

From: [Jenkins, Darrell](#)
To: [Compton, Kimberly](#); [Sullivan, Matthew](#); [Auth, Doris](#); [Liberatore, Mark](#); [Everett, Kristen](#); [Dickinson, Nancy Clark](#); [Lemley, Carrie](#); [Moncur, Megan](#); [Miller, Kristen](#); [Jenkins, Darrell](#); [Won, Katherine](#); [Racoosin, Judith A](#)
Subject: FW: Documents for TRIG
Date: Tuesday, May 15, 2012 6:45:15 PM
Attachments: [120515 + fda clean rem.doc.docx](#)
[120515 + fda redline rem.doc.pdf](#)
[120515 + fda redline patient-prescriber-agreement-form.pdf](#)
[120515 + fda clean patient-prescriber-agreement-form.docx](#)
[120515 +fda clean Closed System Pharmacy Enrollment Form.docx](#)
[120515 +fda redline Closed System Pharmacy Enrollment Form.pdf](#)

fyi

From: Jenkins, Darrell
Sent: Tuesday, May 15, 2012 6:41 PM
To: 'Christine Kampf'; 'Ottinger, James'
Cc: Jenkins, Darrell; Liberatore, Mark
Subject: Documents for TRIG

Please review the attached documents and let us know as soon as you can whether you have any questions, comments, and/or revisions. Once these documents are agreed upon, we can approve the REMS Modification (including the closed system enrollment form).

Redline and clean versions of the following documents are attached (note: the base documents for the redline versions are noted in the document):

1. [REMS document](#)
2. [Patient-prescriber-agreement-form](#)
3. [Closed system enrollment form](#)

Thanks. Darrell.

FOLLOWING THIS PAGE, FDA_6144 TO FDA_6187 WITHHELD IN FULL AS B(4)/CCI (PROPOSED/DRAFT REMS WEB MATERIALS)

From: [Willene Brondum](#)
To: [Liberatore, Mark](#); [Jenkins, Darrell](#); [Bradley, Sean](#)
Cc: [Dickinson, Nancy Clark](#)
Subject: TRIG Submission re: 5/15 forms
Date: Wednesday, May 30, 2012 11:18:33 AM
Attachments: [120515 REMS - TRIG Feedback - Redline.docx](#)
[120515 Closed System Pharmacy Enrollment Form - TRIG Feedback - Redline.docx](#)
[120515 patient-prescriber-agreement-form - TRIG Feedback - Redline.docx](#)
Importance: High

Mr. Liberatore,

On the TRIG, attached please find the TRIG redline versions of the following documents FDA previously updated on May 15 to include closed system pharmacies:

- REMS
- Closed System Pharmacy Enrollment Form
- PPAF

The TRIG apologizes for the delay in returning these documents. Please do not hesitate to contact me if there are any other adjustments needed to these documents. If the documents are satisfactory as redlined, please advise and I will return the memo requested by Nancy Dickinson and Megan Moncur in our telephone conversation last Friday, May 25.

Thanks very much!

Willy Brondum
Senior Manager, Regulatory Affairs



10220 South 51st Street, Suite 2, Phoenix, AZ 85044
P: (602) 910-2617 Ext. 9022 * F: (602) 910-2627 * C: (602) 750-8039
wbrondum@insysrx.com * www.insysrx.com

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FOLLOWING THIS PAGE, FDA_6189 TO FDA_6210
WITHHELD IN FULL AS B(4)/CCI (PROPOSED/DRAFT REMS
WFR MATERIAL S)

FDA_6188

From: [Liberatore, Mark](#)
To: ["Willene Brondum"](#)
Cc: [Dickinson, Nancy Clark](#); [Moncur, Megan](#); [Jenkins, Darrell](#); [Bradley, Sean](#)
Subject: RE: TRIG Submission re: 5/15 forms
Date: Thursday, May 31, 2012 9:54:47 AM

Hi Willy,

The team has looked at the emailed documents from the TRIG, and agree with the proposals. Would you please send us a memo with all of the sponsors listed which states that the sponsors also agree?

Please contact me via email with any questions.

Thank You,
-Mark

From: Willene Brondum [mailto:wbrondum@insysrx.com]
Sent: Wednesday, May 30, 2012 11:18 AM
To: Liberatore, Mark; Jenkins, Darrell; Bradley, Sean
Cc: Dickinson, Nancy Clark
Subject: TRIG Submission re: 5/15 forms
Importance: High

Mr. Liberatore,

On the TRIG, attached please find the TRIG redline versions of the following documents FDA previously updated on May 15 to include closed system pharmacies:

- REMS
- Closed System Pharmacy Enrollment Form
- PPAF

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Thanks very much!

Willy Brondum
Senior Manager, Regulatory Affairs



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

/s/

MEGAN M MONCUR

06/01/2012

concur