Supplementary Online Content

Rollman JE, Heyward J, Olson L, Lurie P, Sharfstein J, Alexander GC. Assessment of the FDA Risk Evaluation and Mitigation Strategy for transmucosal immediate-release fentanyl products [published February 19, 2019]. *JAMA*. doi:10.1001/jama.2019.0235

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This supplementary material has been provided by the authors to give readers additional information about their work.

Technical Appendix

Supplemental Materials

TECHNICAL APPENDIX

Patient, prescriber and pharmacist surveys

Patients, prescribers and pharmacists enrolled in the TIRF REMS program were surveyed by the sponsor at the 12, 24, 36, 48 and 60-month time periods, in fulfillment of the annual TRIG assessment reports required by the FDA. The TRIG sent out initial survey invitations by postal mail to actively enrolled REMS participants from each group, followed by a second mailing to non-responders, and then final contact via fax and email (pharmacists and prescribers). Participants were invited to call a phone number or visit a website to complete the survey; following completion, participants received a $50 gift card (prescribers received $125). Previous survey respondents and those with family members who work for the TRIG were excluded. The survey generally took place over several months in the fall of each year and the first approximately 300 in each group who responded were surveyed. These results were included in the sponsor's REMS assessments and were subsequently compiled by the authors into these tables. Responses generally included three options: true/yes, false/no and don't know. Though all of these values were reported, only the correct response (true/yes OR false/no) included 95% confidence intervals. TRIG reports indicated that "A correct response rate of 65% or greater was considered to represent adequate understanding of each concept or key risk message."

Assessment of Opioid Tolerance

In accordance with a request from the FDA in its response to the 36-month assessment, the 48-month REMS assessment included an analysis of IMS Longitudinal Prescription Database (LRx) commercial claims data focusing on the proportion of TIRF patients who were opioid tolerant. In these analyses, opioid tolerance was defined based on an individual having "at least 7 continuous days of sufficient daily dose [of another, non-TIRF opioid] immediately preceding the TIRF prescription". Among individuals filling a TIRF between October 29, 2014 and October 28, 2015, 12,406 of 25,322 individuals, or 49.0%, were opioid tolerant, according to the TRIG's REMS assessment. (A different, unspecified calculation discussed in the FDA evaluation of the 48-month report found that approximately 58% of patients were opioid tolerant.) In its review of the 48-month REMS assessment, the FDA requested additional analyses to be performed and results submitted as part of the 60-month REMS assessment, including product-specific analyses of opioid tolerance to be submitted to individual NDA/ANDAs. The results of these additional analyses indicated that between 44.6% - 65.4% of TIRF patients were opioid tolerant, though the proportion opioid-tolerant among those prescribed Subsys, calculated using a different algorithm, was significantly higher (77%), prompting the FDA to ask for validation of the algorithms used to determine opioid tolerance and to conduct analyses of the rates of adverse events among opioid non-tolerant TIRF patients.

TIRF REMS Provider Knowledge Assessment

Transmucosal Immediate Release Fentanyl (TIRF) REMS Access Program

Knowledge Assessment

For real-time processing of this Knowledge Assessment, please go to www.TIRFREMSaccess.com.

To submit this form via fax, please answer all questions below, fill in the fields at the bottom of the form, and fax all pages to 1-866-822-1487. You will receive enrollment confirmation via email or fax.

Question 1

The patients described are all experiencing breakthrough pain, but ONE is not an appropriate patient for a TIRF medicine. Which patient should not receive a TIRF medicine?

Select one option.

A. 12-year-old sarcoma patient, using transdermal fentanyl for her underlying persistent cancer pain.

B. Adult female with advanced breast cancer; on 60 mg of oral morphine daily for the past 4 weeks.

C. Adult male with advanced lung cancer; his underlying persistent pain is managed with 25 mcg/hour transdermal fentanyl patches for the past 3 months.

D. Adult male with multiple myeloma who has bone pain currently managed with 50 mg oral oxymorphone daily for the last 2 weeks.

Question 2

The patients described are experiencing breakthrough pain. A TIRF medicine is NOT appropriate for one of them. Which patient should not receive a TIRF medicine?

Select one option.

A. Adult male with advanced lung cancer; underlying persistent cancer pain managed with 25 mcg/hour transdermal fentanyl patches for the past 2 months.

B. Adult female with localized breast cancer; just completed a mastectomy and reconstructive surgery; persistent cancer pain managed with 30 mg oral morphine daily for the past 6 weeks.

C. Adult male patient with advanced prostate cancer who, over the last 2 weeks, has been prescribed 100 mg oral morphine daily for pain due to bone metastasis.

D. Adult female with advanced sarcoma who has been taking a daily dose of 12 mg oral hydromorphone for the last 3 weeks.

DEA Number or Chain ID: _____

Question 3

Certain factors may increase the risk of abuse and/or diversion of opioid medications. Which of the following is most accurate?

Select one option.

A. A history of alcohol abuse with the patient or close family members.

B. The patient has a household member with a street drug abuse problem.

C. The patient has a history of prescription drug misuse.

D. All of the above.

Question 4

A patient is already taking a TIRF medicine but wants to change their medicine. His/her doctor decides to prescribe a different TIRF medicine (that is not a bioequivalent generic version of a branded product) in its place. How should the prescriber proceed?

Select one option.

A. The prescriber can safely convert to the equivalent dosage of the new TIRF medicine, as it has the same effect as other TIRF medicines.

B. The prescriber must not convert from the equivalent TIRF medicine dose to another TIRF medicine because they have different absorption properties and this could result in a fentanyl overdose.

C. Convert from the other TIRF medicine to the new TIRF medicine at half of the dose.

D. The prescriber should base the starting dose of the newly prescribed TIRF medicine on the dose of the opioid medicine used for their underlying persistent cancer pain.

Question 5

A patient is starting titration with a TIRF medicine. What dose must they start with?

Select one option.

A. An appropriate dose based on the dose of the opioid medicine used for underlying persistent cancer pain.

B. The dose that the prescriber believes is appropriate based on their clinical experience.

C. The lowest available dose, unless individual product Full Prescribing Information provides product-specific guidance.

D. The median available dose.

DEA Number or Chain ID: _____

Question 6

A prescriber has started titrating a patient with the lowest dose of a TIRF medicine. However, after 30 minutes, the breakthrough pain has not been sufficiently relieved. What should they advise the patient to do?

Select one option.

A. Take another (identical) dose of the TIRF medicine immediately.

B. Take a dose of an alternative rescue medicine.

C. Provide guidance based on the product-specific Medication Guide because the instructions are not the same for all TIRF medicines.

D. Double the dose and take immediately.

Question 7

A patient is taking a TIRF medicine and the doctor would like to prescribe erythromycin, a CYP3A4 inhibitor. Which of the following statements is true?

Select one option.

A. The patient can't be prescribed erythromycin, because using it at the same time as a TIRF medicine could be fatal.

B. Use of a TIRF medicine with a CYP3A4 inhibitor may require dosage adjustment; carefully monitor the patient for opioid toxicity, otherwise such use may cause potentially fatal respiratory depression.

C. There is no possible drug interaction between CYP3A4 inhibitors and TIRF medicines.

D. The dose of the TIRF medicine must be reduced by one half if a CYP3A4 inhibitor is prescribed in the same patient.

Question 8

Before initiating treatment with a TIRF medicine, prescribers must review the Medication Guide with the patient. Which of the following counseling statements is not correct?

Select one option.

A. TIRF medicines contain fentanyl in an amount that could be fatal to children of all ages, in individuals for whom they were not prescribed, and in those who are not opioid tolerant.

B. Inform patients that TIRF medicines must not be used for acute or postoperative pain, pain from injuries, headache/migraine, or any other short-term pain.

C. Instruct patients that if they stop taking their around-the-clock opioid medicine, they can continue to take their TIRF medicine.

D. Instruct patients to never share their TIRF medicine with anyone else, even if that person has the same symptoms.

DEA Number or Chain ID: _____

Question 9

There is a risk of fatal overdose with inappropriate use of TIRF medicines. Which one of the following answers is most accurate?

Select one option.

A. TIRF medicines can be fatal if taken by children.

B. TIRF medicines can be fatal if taken by anyone for whom it is not prescribed.

C. TIRF medicines can be fatal if taken by anyone who is not opioid-tolerant.

D. All of the above.

Question 10

Which one of the following statements is most accurate regarding the safe storage and disposal of TIRF medicines?

Select one option.

A. TIRF medicines should be kept in a safe place and out of the reach of children.

B. TIRF medicines should be protected from theft.

C. Dispose of partially used or unneeded TIRF medicine by following the TIRF medicine-specific procedure specified in the Medication Guide.

D. All of the above.

Question 11

Conversion between specific TIRF medicines has been established and is described in the Prescribing Information for which products?

Select one option.

A. Actiq to Abstral

B. Actiq to Fentora

C. Actiq to Subsys

D. All of the above

Prescriber/Authorized Pharmacy Representative _____

DEA Number _____

Chain ID (If applicable) _____

eTABLE 1. PRODUCTS INCLUDED IN U.S. FOOD AND DRUG ADMINISTRATION (FDA) TIRF RISK EVALUATION AND MITIGATION STRATEGY (REMS) PROGRAM, 2011 – 2017

Product Name (active ingredient)/formulation	Current Application Holder (previous)	Follow-up Interval of Assessments				
		Initial REMS (12/28/2011)	6 months (6/28/2012)	24 months (12/28/2013)	48 months (12/28/2015)	60 months (12/28/2016)
ABSTRAL (fentanyl citrate) sublingual tablets	Sentynl Theraps INC (ProStrakan, Galena)	✓	✓	✓	✓	✓
ACTIQ (fentanyl citrate) oral transmucosal lozenge and authorized generic	Cephalon/Teva	✓	✓	✓	✓	✓
FENTORA (fentanyl citrate) buccal tablet	Cephalon/Teva	✓	✓	✓	✓	✓
LAZANDA (fentanyl citrate) nasal spray	Elefsee Pharms INTL (Archimedes, Depomed)	✓	✓	✓	✓	✓
ONSOLIS (fentanyl citrate) buccal film	BDSI (Meda)	✓	✓	✓	✓	✓
Fentanyl citrate oral transmucosal lozenge	Par Pharm	✓	✓	✓	✓	✓
Fentanyl citrate oral transmucosal lozenge	Specgx LLC/ Mallinckrodt Inc. (approved 1/4/12)		✓	✓	✓	✓
SUBSYS (fentanyl sublingual spray)	Insys Dev Co INC (approved 1/4/12)		✓	✓	✓	✓
Fentanyl buccal tablet (not yet marketed)	Mylan Labs (tentative approval 3/4/15)				✓	✓
Fentanyl buccal tablet	Watson Labs (approved 1/8/16)					✓
Fentanyl citrate	Actavis Labs FL INC (approved 11/17/17)					

12-Month Patient KAB Survey

APPENDIX A Screening and Main Questionnaire

Survey Legend

- **[PROGRAMMER]** is used to indicate directions to the programmer and is set in bold, red, uppercase letters between square brackets. **[PATIENT]** indicates text applicable to a patient when it differs from survey text for caregivers, parents and legal guardians. **[PARENT/CAREGIVER/LEGAL GUARDIAN]** indicates text applicable to parents, caregivers, and legal guardians when it differs from survey text for patients.

- **(INTERVIEWER)** is used to indicate directions to the phone interviewer and is set in bold, blue, text between parentheses. This text appears when content is to be administered by phone only (for example, spontaneous adverse event reporting).

- **[ONLINE]** indicates a question is worded specifically for administering the survey online. **[PHONE]** indicates a question is worded specifically to be read by a phone interviewer and differs from the online text.

- **[BEGIN ONLINE/PHONE SURVEY CONTENT]** and **[END SURVEY CONTENT]** are used to indicate to the programmer the type of survey administration and the beginning and end of the survey or sections within the survey content, for example, **[BEGIN ADVERSE EVENT/PRODUCT COMPLAINT]** and **[END ADVERSE EVENT/PRODUCT COMPLAINT]**.

- **[TERMINATE]** is displayed next to responses that should cause the survey to end. The following termination language will be programmed into the survey or read by the interviewer unless different language is specified with the question.

  Thank you very much for your time today. Based on your answer, you are not eligible to take this survey. We appreciate your interest in the survey.

- **[RANDOMIZE LIST]** is inserted before questions to indicate to the programmer that the responses should be randomized. Responses such as “I don’t know,” “Prefer not to answer” or “None of the above” will always appear at the end of the randomized responses.

- **[GO TO Ax]** (Skip logic) is inserted after a response to indicate to the programmer that the survey should skip to the indicated question (for example, **[GO TO Q17]** skips to question 17). If no skip logic is indicated the survey continues to the next question in the sequence.

Survey Legend

- **[MULTILINE INPUT]** indicates to the programmer that multiple lines should be provided for data entry (for example, two address lines or a free-text response).

- **[DROP-DOWN LIST INPUT WITH STATES TABLE]** indicates to the programmer that the response should be a drop-down list containing the states in the table below.

Alabama	Georgia	Massachusetts	New York	Tennessee
Alaska	Guam	Michigan	North Carolina	Texas
American Samoa	Hawaii	Minnesota	North Dakota	US Virgin Islands
Arizona	Idaho	Mississippi	Northern Mariana Islands	Utah
Arkansas	Illinois	Missouri	Ohio	Vermont
California	Indiana	Montana	Oklahoma	Virginia
Colorado	Iowa	Nebraska	Oregon	Washington
Connecticut	Kansas	Nevada	Pennsylvania	West Virginia
Delaware	Kentucky	New Hampshire	Puerto Rico	Wisconsin
District of Columbia	Louisiana	New Jersey	Rhode Island	Wyoming
Florida	Maine	New Mexico	South Carolina	
	Maryland		South Dakota	

- The following is used to categorize survey populations into standard geographic regions but it is not displayed in the survey.

Geographic Distribution (based on address) [1]: Northeast, Midwest, South, and West regions

Northeast Region

– New England Division - ME, NH, VT, MA, RI, CT
– Middle Atlantic Division - NY, NJ, PA

Midwest Region

– East North Central Division - OH, IN, IL, MI, WI
– West North Central Division - MN, IA, MO, ND, SD, NE, KS

South Region

– South Atlantic Division - DE, MD, DC, VA, WV, NC, SC, GA, FL
– East South Central Division - KY, TN, AL, MS
– West South Central Division - AR, LA, OK, TX

West

Survey Legend

- Mountain Division - MT, ID, WY, CO, NM, AZ, UT, NV
- Pacific Division WA, OR, CA, AK, HI

- The following US territories are categorized as **Other**: Puerto Rico, Northern Mariana Islands, US Virgin Islands, American Samoa, and Guam.

[1] U.S. Census Bureau, last revised Friday, 27-Jul-2001 12:59:43 EDT.

[BEGIN ONLINE/PHONE SURVEY CONTENT]

[PREAMBLE 1]

Before you begin, we would like to share some important information about this survey. The survey is being conducted by the makers of Abstral®, Actiq®, Fentora®, Lazanda®, Onsolis®, Subsys™ and the generic versions of any of these brands. These are **T**ransmucosal **I**mmediate **R**elease **F**entanyl medicines, also known as rapid onset opioids **(INTERVIEWER: Please pause briefly)** (and sometimes called "fast acting fentanyls") or TIRF medicines.

(INTERVIEWER: Pronounce "TIRF," then spell out T-I-R-F).

The information collected will help the makers of TIRF medicines know if patients and their caregivers understand important information about taking these medicines. The survey will take about 20 minutes.

There are no known risks to you in taking this survey. You may refuse to take part or withdraw at any time without penalty or loss of benefits to which you are otherwise entitled. Your answers to the questions or your decision to take part in the survey will not affect your ability to receive or take TIRF medicines.

[ONLINE ONLY]How We Use Your Information

[PHONE ONLY] Now I would like to tell you about how your contact information will be used.

Your answers to the survey questions will be combined with answers given by other people taking the survey. All answers will be put together and reported in anonymous form to manufacturers of TIRF medicines. Your name will not be used in any report. If you are eligible to take the survey, complete all the questions, and provide your contact information, you will receive a $25 gift card for your time.

Your name and address will be used only to send you the gift card, a Thank You Letter, a product-specific Medication Guide, and a copy of the correct answers to key risk message questions, after you complete the survey.

Providing a telephone number is optional. Your telephone number will be used only if there are any questions about your answers.

[ONLINE ONLY] How We Protect Your Privacy

[PHONE ONLY]Now I would like to tell you about how we protect your privacy.

We respect that the privacy of your personal information is important to you. You will not be contacted for marketing purposes based on your personal information or your answers to the survey. Neither the manufacturers of TIRF medicines nor their contractors will sell, transfer,

or rent your information. Your answers will be kept strictly confidential. Your privacy will be protected; however, research survey records may be inspected by the FDA (Food and Drug Administration) and a company called (b) (4) which is the Institutional Review Board (IRB). Your choice to allow the manufacturers of TIRF medicines to use your information is entirely voluntary, but necessary to take part in this survey.

[ONLINE ONLY] How to Learn More About Transmucosal Immediate Release Fentanyl Medicines

[ONLINE ONLY] If you have questions about the survey, or have any problems with the survey, please contact the Survey Coordinating Center at 1-877-379-3297.

[PHONE ONLY] Please feel free to ask me to repeat any questions or statements as we go through the survey.

Once you have answered a question and moved on, you cannot go back and change your answers.

If you have questions about your rights as a research participant or related concerns, you may contact the IRB at (b) (4). **[ONLINE ONLY]** Be sure to write down this telephone number; it will not be displayed again.

The information in this survey should not take the place of talking with your doctor or health care professional. If you have any questions about your condition or treatment or that of the person you care for, or if you would like more information about TIRF medicines, talk to your doctor, pharmacist, or other health care professional.

Thank you for your participation in this survey.

[END PREAMBLE 1]

1. Do you agree to take part in this survey?

   - ○ Yes
   - ○ No **[TERMINATE]**

2. Within the last 3 months, have you filled a prescription for yourself for a transmucosal immediate release fentanyl medicine (known as "TIRF medicines")? TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Onsolis®, Subsys™, and the generic versions of any of these brands.

   - ○ Yes **[GO TO Q4]**
   - ○ No
   - ○ I don't know

3. Are you a caregiver for someone who has filled a prescription for a TIRF medicine within the last 3 months? As a reminder, TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Onsolis®, Subsys™, and the generic versions of any of these brands.

   - ○ Yes
   - ○ No **[TERMINATE]**
   - ○ I don't know **[TERMINATE]**

4. Have you ever taken part in a survey about a TIRF medicine before?

   - ○ Yes **[TERMINATE ONLY IN ALL SUBSEQUENT WAVES]**
   - ○ No
   - ○ I don't know **[TERMINATE ONLY IN ALL SUBSEQUENT WAVES]**

5. Which of the following groups best describes your age?

- ○ Under 18 **[TERMINATE]**
- ○ 18 – 29
- ○ 30 – 39
- ○ 40 – 49
- ○ 50 – 59
- ○ 60 – 69
- ○ 70 or older
- ○ Prefer not to answer **[TERMINATE]**

6. **[CAREGIVER ONLY]** Which of the following groups best describes the patient's age?

- ○ Under 16
- ○ 16 – 29
- ○ 30 – 39
- ○ 40 – 49
- ○ 50 – 59
- ○ 60 – 69
- ○ 70 or older
- ○ Prefer not to answer

7. Have you or any of your immediate family members ever worked for any of the following companies or agencies? Please select all that apply.

- ○ Anesta LLC **[TERMINATE]**
- ○ Archimedes Pharma US Inc.**[TERMINATE]**
- ○ Cephalon, Inc. **[TERMINATE]**
- ○ Endo Pharmaceuticals Inc. **[TERMINATE]**

- Insys Therapeutics**[TERMINATE]**
- Mallinckrodt (a Covidien Company) **[TERMINATE]**
- Meda Pharmaceuticals **[TERMINATE]**
- Par Pharmaceutical, Inc.**[TERMINATE]**
- ProStrakan, Inc. **[TERMINATE]**
- Sandoz Inc. **[TERMINATE]**
- Teva Pharmaceuticals, Ltd. **[TERMINATE]**
- United BioSource Corporation**[TERMINATE]**
- McKesson Specialty Care Solutions**[TERMINATE]**
- RelayHealth**[TERMINATE]**
- FDA (Food and Drug Administration) **[TERMINATE]**
- No **[IF SELECTED IN ADDITION TO OTHER RESPONSES, TERMINATE]**
- I don't know **[TERMINATE]**

[PREAMBLE 2]

[PATIENT]Please answer the following questions based on information about the TIRF medicine that was most recently prescribed for you. TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Onsolis®, Subsys™, and the generic versions of these brands. Please think of the information that you read or that was provided to you by a doctor, nurse, or other healthcare professional. If you don't know the answer to any of the following questions please respond "I don't know" instead of guessing the correct response.

[CAREGIVER]Please answer the following questions based on information about the TIRF medicine that was most recently prescribed for the patient. TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Onsolis®, Subsys™, and the generic versions of these brands. Please think of the information that you read or that was provided to you or to the patient by a doctor, nurse, or other healthcare professional. If you don't know the answer to any of the following questions please respond "I don't know" instead of guessing the correct response.

8. **[PATIENT]** Did the doctor, nurse, or other healthcare professional in the doctor's office ever talk to you about the risks and possible side effects of the TIRF medicine that was most recently prescribed for you? TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Onsolis®, Subsys™, and the generic versions of these brands.

[CAREGIVER] Did the doctor, nurse, or other healthcare professional in the doctor's office ever talk to you about the risks and possible side effects of the TIRF medicine that was most recently prescribed to the patient? TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Onsolis®, Subsys™, and the generic versions of these brands.

- ○ Yes
- ○ No
- ○ I don't know

9. **[PATIENT]** For which of the following conditions should I use a TIRF medicine?

[CAREGIVER] For which of the following conditions should the person I take care of use a TIRF medicine?

	[RANDOMIZE LIST]	**Yes**	**No**	**I don't know**
9a.	Headache or migraine pain	○	○	○
9b.	Breakthrough pain from cancer	○	○	○
9c.	Dental pain	○	○	○
9d.	Acute or post-operative pain	○	○	○
9e.	Chronic non-cancer pain	○	○	○

10. Please answer True, False, or I don't know for the following statement:

TIRF medicines should only be taken by patients who are opioid tolerant.

- ○ True
- ○ False
- ○ I don't know

11. Please answer True, False, or I don't know for each of the following statements.

	[RANDOMIZE LIST]	True	False	I don't know
11a.	Opioid tolerant means that a patient is already taking other opioid pain medicines around the clock and their body is used to these medicines.	○	○	○
11b.	If a patient stops taking around-the-clock opioid pain medicine, they must also stop taking the TIRF medicine.	○	○	○
11c.	It is safe to switch to another medicine that contains fentanyl without talking to a healthcare provider first.	○	○	○
11d.	A patient may give TIRF medicines to another person if they have the same symptoms as the patient.	○	○	○

12. **[PATIENT]** Please answer True, False, or I don't know for each statement about the TIRF medicine that was most recently prescribed for you.

[CAREGIVER] Please answer True, False, or I don't know for each statement about the TIRF medicine that was most recently prescribed for the patient.

	[RANDOMIZE LIST]	True	False	I don't know
12a.	TIRF medicines should be stored in a safe place out of the reach of children.	○	○	○
12b.	It is OK for patients to take TIRF medicines for headache pain.	○	○	○
12c.	TIRF medicines should be taken exactly as prescribed by the doctor.	○	○	○
12d.	TIRF medicines can cause life-threatening breathing problems that can lead to death.	○	○	○

13. What should you do if an adult who has not been prescribed a TIRF medicine takes a TIRF medicine? (Please select one.)

[RANDOMIZE LIST]

- ○ Wait an hour and see if the person is OK.
- ○ Get emergency help right away.
- ○ Do nothing.
- ○ I don't know

14. **[PATIENT]** Did the doctor, nurse, or other healthcare professional in the doctor's office ever tell you how to use the TIRF medicine that was most recently prescribed for you?

[CAREGIVER] Did the doctor, nurse, or other healthcare professional in the doctor's office ever tell you how to use the TIRF medicine that was most recently prescribed for the patient?

- ○ Yes
- ○ No
- ○ I don't know

15. **[PATIENT]** Did the doctor, nurse, or other healthcare professional in the doctor's office ever tell you how to store or keep the TIRF medicine that was most recently prescribed for you?

[CAREGIVER] Did the doctor, nurse, or other healthcare professional in the doctor's office ever tell you how to store or keep the TIRF medicine that was most recently prescribed for the patient?

- ○ Yes
- ○ No
- ○ I don't know

16. **[PATIENT]** Please answer True, False, or I don't know for each statement about the TIRF medicine that was most recently prescribed for you.

[CAREGIVER] Please answer True, False, or I don't know for each statement about the TIRF medicine that was most recently prescribed for the patient.

	[RANDOMIZE LIST]	**True**	**False**	**I don't know**
16a.	Selling or giving away TIRF medicines is against the law.	○	○	○
16b.	It is OK to take TIRF medicines for short-term pain that will go away in a few days.	○	○	○
16c.	TIRF medicines must be disposed of as described in the specific product's Medication Guide.	○	○	○
16d.	TIRF medicines are only available to patients through a special program (called the TIRF REMS Access program).	○	○	○
16e.	A TIRF medicine can cause an overdose and death in any child who takes it.	○	○	○

[PREAMBLE 3]

[PATIENT] The next set of questions is about the Medication Guide for the TIRF medicine that was most recently prescribed for you.

[CAREGIVER] The next set of questions is about the Medication Guide for the TIRF medicine that was most recently prescribed for the patient.

[BOTH] A Medication Guide is a paper handout that contains important information about the risks associated with the use of a TIRF medicine and how to use it safely. Medication Guides always include the title "Medication Guide" followed by the name of the medicine and its pronunciation. The Medication Guide usually has a section titled "What is the most important information I should know?" The Medication Guide is in a question-and-answer format and may be given to you by your pharmacist or doctor.

[END PREAMBLE 3]

17. **[PATIENT]** Have you ever received a Medication Guide for the TIRF medicine that was prescribed for you?

[CAREGIVER] Have you or the patient ever received a Medication Guide for the TIRF medicine that was prescribed for the patient?

- ○ Yes
- ○ No **[GO TO PREAMBLE 4]**
- ○ I don't know **[GO TO PREAMBLE 4]**

18. **[PATIENT]** Did you receive the Medication Guide from the doctor who prescribed the TIRF medicine or someone in the doctor's office?

[CAREGIVER] Did you or the patient receive the Medication Guide from the doctor who prescribed the TIRF medicine or someone in the doctor's office?

- ○ Yes
- ○ No **[GO TO Q20]**
- ○ I don't know **[GO TO Q20]**

19. **[PATIENT]** When was the Medication Guide given to you?

[CAREGIVER] When was the Medication Guide given to you or the patient?

- ○ At the first appointment with the doctor who prescribed the TIRF medicine
- ○ At the last appointment with the doctor who prescribed the TIRF medicine
- ○ I don't remember

20. **[PATIENT]** Did you receive the Medication Guide for the TIRF medicine from the pharmacy?

[CAREGIVER] Did you or the patient receive the Medication Guide for the TIRF medicine from the pharmacy?

- ○ Yes
- ○ No **[GO TO Q22]**
- ○ I don't know **[GO TO Q22]**

21. **[PATIENT]** When was the most recent time that you received a Medication Guide for the TIRF medicine at the pharmacy?

[CAREGIVER] When was the most recent time that you or the patient received a Medication Guide for the TIRF medicine at the pharmacy?

- ○ Only with the first filled prescription
- ○ Each time a prescription is filled
- ○ Other (please specify): _____
- ○ I don't know

22. Did you read the Medication Guide?

- ○ Yes
- ○ No **[GO TO Q25]**
- ○ I don't know **[GO TO Q25]**

23. How much did you read?

- ○ All of it
- ○ Most of it
- ○ Some of it
- ○ I don't know

24. How much of the Medication Guide did you understand?

- ○ All of it
- ○ Most of it
- ○ Some of it
- ○ None of it
- ○ I don't know

25. Did someone offer to explain the Medication Guide to you?

- ○ Yes
- ○ No **[GO TO Q29]**
- ○ I don't know **[GO TO Q29]**

26. Who offered to explain the Medication Guide to you? (Select all that apply.)

- ○ The doctor or another healthcare professional in the doctor's office
- ○ The pharmacist where the TIRF medicine prescription was filled
- ○ Someone else (specify the type of person but not his/her name)

_____

27. Did you accept the offer to have the Medication Guide explained to you?

- ○ Yes
- ○ No **[GO TO Q29]**
- ○ I don't know **[GO TO Q29]**

28. How much of the explanation did you understand?

- ○ All of it
- ○ Most of it
- ○ Some of it
- ○ None of it
- ○ I don't know

29. Did you or do you have any questions about the information in the Medication Guide?

- ○ Yes
- ○ No **[GO TO PREAMBLE 4]**
- ○ I don't know **[GO TO PREAMBLE 4]**

30. What are your questions? **[MULTILINE INPUT]**

[PREAMBLE 4]

The next set of questions is about the Patient-Prescriber Agreement Form for TIRF medicines. As a reminder, TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Onsolis®, Subsys™, and the generic versions of any of these brands. The Patient-Prescriber Agreement is a form that is signed by the doctor and the patient or their caregiver. This form may also be referred to as the Prescriber-Patient Agreement.

[END PREAMBLE 4]

31. Did the doctor or someone in the doctor's office explain the Patient-Prescriber Agreement Form to you?

- ○ Yes
- ○ No **[GO TO Q33]**
- ○ I don't know **[GO TO Q33]**

32. How much of the explanation did you understand?

- ○ All of it
- ○ Most of it
- ○ Some of it
- ○ None of it
- ○ I don't know

33. **[PATIENT]** Did you sign a Patient-Prescriber Agreement Form?

[CAREGIVER] Did you or the person you are caring for sign a Patient-Prescriber Agreement Form?

- ○ Yes
- ○ No **[GO TO DEMOGRAPHICS PREAMBLE]**
- ○ I don't know **[GO TO DEMOGRAPHICS PREAMBLE]**

34. Did the doctor or someone in the doctor's office give you a copy of the signed Patient-Prescriber Agreement Form?

- ○ Yes
- ○ No
- ○ I don't know

[DEMOGRAPHICS PREAMBLE]

There are just a few more questions to help us combine your answers with other answers we have received.

35. What is your gender?

- ○ Male
- ○ Female
- ○ Prefer not to answer

36. What is the highest level of education you have completed?

- ○ Less than high school
- ○ Some high school
- ○ High school graduate/GED
- ○ Some college/Associate's degree
- ○ Bachelor's degree
- ○ Master's degree
- ○ Professional or Doctoral degree
- ○ Prefer not to answer

37. What is the main language you speak at home? (Please select only one.)

- ○ English
- ○ French
- ○ Spanish
- ○ Portuguese
- ○ Italian
- ○ German
- ○ Chinese
- ○ Japanese
- ○ Korean
- ○ Other
- ○ Prefer not to answer

38. Are you Hispanic or Latino?

- ○ Yes
- ○ No
- ○ Prefer not to answer

39. For informational purposes only, which of the following U.S. census categories best describes your race? (Please select only one.)

- ○ American Indian or Alaska Native
- ○ Asian (origins of Far East, Southeast Asia or the Indian subcontinent)
- ○ Black or African American
- ○ Native Hawaiian or Other Pacific Islander
- ○ White
- ○ Other
- ○ Prefer not to answer

40. In which state do you live?

[DROP-DOWN LIST INPUT WITH STATES TABLE WITH "Prefer not to answer" AT END]

[PHONE ONLY: ADVERSE EVENT/PRODUCT COMPLAINT]

(INTERVIEWER: Please record if respondent spontaneously reported an adverse event or product complaint during the course of this interview.)

- ○ Yes
- ○ No **[GO TO CLOSING 1]**

Enter Safety Adverse Event Verbatim

[MULTILINE INPUT]

(INTERVIEWER: Indicate to the respondent that someone may call back to ask more questions about the adverse event or product complaint that was reported.)

[END ADVERSE EVENT/PRODUCT COMPLAINT]

[CLOSING 1]

You are eligible to receive a $25 gift card for your time completing the survey. In order to receive the gift card, we need to collect your name and address so that we can mail it to you. If you do not provide your name and address you will not receive the gift card for your time taking the survey.

41. Do you agree to give us your name and mailing address so we can send your payment?

- ○ Yes
- ○ No **[SKIP TO CLOSING 2]**

FIRST NAME: _____

LAST NAME: _____

ADDRESS: **[MULTILINE INPUT]**

CITY: _____

STATE: **[DROP-DOWN LIST INPUT WITH STATES TABLE]**

ZIP: _____

[CLOSING 2]

We would also like to ask for your telephone number. Providing your telephone number is optional and it will be used to contact you only if there are questions about your survey responses.

42. Do you want to provide your telephone number?

○ Yes

○ No **[SKIP TO CLOSING 3]**

Telephone: _____

[CLOSING 3]

This is the end of the survey. If you have questions about the survey, please contact the Survey Coordinating Center at 1-877-379-3297. Thank you again for your help.

[END OF SURVEY CONTENT]

APPENDIX B Sample Patient Letter of Invitation

PAT_FIRST_NAME] [PAT_LAST_NAME]
[CURR_DATE]
[PAT_STREET_ADDR]
[PAT_CITY], [PAT_STATE] [PAT_ZIP]

Dear [PAT_FULL_NAME]:

Thank you for choosing [PHARMACY] for your prescription needs. We are contacting you to invite you to participate in a survey being conducted by the manufacturers of Transmucosal Immediate Release Fentanyl medicines (TIRF medicines), as required by the FDA. The purpose of the survey is to find out if patients and/or their caregivers understand important information related to taking these medicines. The TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Onsolis®, Subsys™, and the generic versions of any of these brands.

The survey is being administered by United BioSource Corporation, on behalf of the manufacturers of TIRF medicines: Archimedes Pharma US Inc., Cephalon, Inc., Endo Pharmaceuticals Inc., Insys Therapeutics, Meda Pharmaceuticals, Mallinckrodt (a Covidien Company), Par Pharmaceutical, Inc., ProStrakan, Inc., and Sandoz Inc. Survey participants must be 18 years of age or older. A caregiver may complete the survey on behalf of patients who are unable to take the survey for themselves. Eligible individuals who complete the survey will be sent a $25 gift card to thank them for their time. The survey will take about 20 minutes.

If you are interested in participating and want to find out if you are eligible,

- Go to www.XXX.com* any time, or
- Call 1-877-379-3297, 8 a.m. to 10 p.m. Eastern Time, Monday through Friday.

Please have this letter with you when you take the survey. You will be asked to give this unique code prior to starting the survey: **[CODE_ID]**.

The survey asks questions about the type of information you received about your TIRF medication and where you get your medication information.

You do not have to take part in this survey; the decision to participate is entirely yours. Your privacy will be strictly guarded. Your answers to the survey questions will be combined with answers given by others, and your name will not be used in any written report or publication. Neither taking the survey nor your answers to the questions will affect your ability to receive or take a TIRF medicine.

Thank you in advance for your help with this important survey.

Sincerely,

[PHARMACY]

* We recommend that you take the survey on a desktop or laptop computer. Taking the survey on mobile devices, such as smart phones, tablets, and e-notebooks, is not supported.

12-Month Pharmacist KAB Survey

Appendix A Pharmacist Questionnaire

Survey Legend

- **[PROGRAMMER]** is used to indicate directions to the programmer and is set in bold, red, uppercase letters between square brackets.

- **(INTERVIEWER)** is used to indicate directions to the phone interviewer and is set in bold, blue, text between parentheses. This text appears when content is to be administered by phone only (for example, spontaneous adverse event reporting).

- **[ONLINE]** indicates a question is worded specifically for administering the survey online. **[PHONE]** indicates a question is worded specifically to be read by a phone interviewer and differs from the online text.

- **[BEGIN ONLINE/PHONE SURVEY CONTENT]** and **[END SURVEY CONTENT]** are used to indicate to the programmer the type of survey administration and the beginning and end of the survey or sections within the survey content, for example, **[BEGIN ADVERSE EVENT/PRODUCT COMPLAINT]** and **[END ADVERSE EVENT/PRODUCT COMPLAINT]**.

- **[TERMINATE]** is displayed next to responses that should cause the survey to end. The following termination language will be programmed into the survey or read by the interviewer unless different language is specified with the question.

  Thank you very much for your time today. Based on your answer, you are not eligible to take this survey. We appreciate your interest in the survey.

- **[RANDOMIZE LIST]** is inserted before questions to indicate to the programmer that the responses should be randomized. Responses such as "I don't know," "Prefer not to answer" or "None of the above" will always appear at the end of the randomized responses.

- **[GO TO Qx]** (skip logic) is inserted after a response to indicate to the programmer that the survey should skip to the indicated question (for example, **[GO TO Q17]** skips to question 17). If no skip logic is indicated the survey continues to the next question in the sequence.

- **[MULTILINE INPUT]** indicates to the programmer that multiple lines should be provided for data entry (for example, two address lines or a free-text response).

Survey Legend

- **[DROP-DOWN LIST INPUT WITH STATES TABLE]** indicates to the programmer that the response should be a drop-down list containing the states in the table below.

Alabama	Georgia	Massachusetts	New York	Tennessee
Alaska	Guam	Michigan	North Carolina	Texas
American Samoa	Hawaii	Minnesota	North Dakota	US Virgin Islands
Arizona	Idaho	Mississippi	Northern Mariana Islands	Utah
Arkansas	Illinois	Missouri	Ohio	Vermont
California	Indiana	Montana	Oklahoma	Virginia
Colorado	Iowa	Nebraska	Oregon	Washington
Connecticut	Kansas	Nevada	Pennsylvania	West Virginia
Delaware	Kentucky	New Hampshire	Puerto Rico	Wisconsin
District of Columbia	Louisiana	New Jersey	Rhode Island	Wyoming
Florida	Maine	New Mexico	South Carolina	
	Maryland		South Dakota	

- The following is used to categorize survey populations into standard geographic regions but it is not displayed in the survey.

  Geographic Distribution (based on address) [1]: Northeast, Midwest, South, and West regions

  Northeast Region
  - New England Division - ME, NH, VT, MA, RI, CT
  - Middle Atlantic Division - NY, NJ, PA

  Midwest Region
  - East North Central Division - OH, IN, IL, MI, WI
  - West North Central Division - MN, IA, MO, ND, SD, NE, KS

  South Region
  - South Atlantic Division - DE, MD, DC, VA, WV, NC, SC, GA, FL
  - East South Central Division - KY, TN, AL, MS
    West South Central Division - AR, LA, OK, TX

  West
  - Mountain Division - MT, ID, WY, CO, NM, AZ, UT, NV

Survey Legend

– Pacific Division WA, OR, CA, AK, HI

- The following US territories are categorized as **Other**: Puerto Rico, Northern Mariana Islands, US Virgin Islands, American Samoa, and Guam.

[1] U.S. Census Bureau, last revised Friday, 27-Jul-2001 12:59:43 EDT.

[BEGIN ONLINE/PHONE SURVEY CONTENT]

[PREAMBLE 1]

Before you begin, we would like to share some important information about this survey. The manufacturers of Transmucosal Immediate Release Fentanyl medicines are conducting this survey, as required by the FDA, to assess pharmacists' understanding of the safe use and dispensing of these medicines. These medicines are known as rapid onset opioids and referred to in this survey as "TIRF medicines." **(INTERVIEWER: Say "TIRF" then spell out T-I-R-F)** The TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Onsolis®, Subsys™, and generic versions of any of these brands. The manufacturers of these medicines include Archimedes Pharma US Inc., Cephalon, Inc., Endo Pharmaceuticals Inc., Insys Therapeutics, Meda Pharmaceuticals, Mallinckrodt (a Covidien Company), Par Pharmaceutical, Inc., ProStrakan, and Sandoz Inc. The survey will take 15-20 minutes.

There are no known risks to you in taking this survey. You may refuse to take part or withdraw at any time. Your answers to the questions or your decision to take part in the survey will not affect your ability to dispense TIRF medicines.

[ONLINE ONLY]How We Use Your Information

[PHONE ONLY] Now I would like to read some information about how your contact information will be used.

Your answers to the survey questions will be combined with answers given by other pharmacists taking the survey. All answers will be put together and reported in anonymous form to the manufacturers of TIRF medicines. Your name will not be used in any report. If you are eligible to take the survey, complete all the questions, and provide your contact information, you will receive a $50 honorarium for your time and participation.

Your name and address will be used to send you the honorarium after you complete the survey. Your personal information will also be used if we have questions about your survey or if we are required to use your information to comply with a federal or state law or regulation.

Providing a telephone number is optional. Your phone number will be used only if there are any questions about your survey responses.

[ONLINE ONLY] How We Protect Your Privacy

[PHONE ONLY]Now I would like to tell you some information about how we protect your privacy.

We respect that the privacy of your personal information is important to you. You will not be contacted for marketing purposes based on your personal information or your answers to the survey. Neither the manufacturers of TIRF medicines nor their contractors will sell, transfer, or rent your information. Your answers will be kept strictly confidential. Your privacy will be protected; however, research survey records may be inspected by the FDA. Your choice to allow manufacturers of TIRF medicines to use your information is entirely voluntary but necessary to take part in this survey.

[ONLINE ONLY] How to Learn More about This Survey

[ONLINE ONLY] If you have questions about the survey, or problems with the survey, please contact the Survey Coordinating Center at 1-877-379-3297. Be sure to write down this telephone number; it will not be displayed again.

[PHONE ONLY]Now I will tell you how you can learn more about this survey. Please have a pen or pencil ready to write down a telephone number you can call should you have any questions about the survey. If you have questions about the survey, please ask me at any time. If you have questions at a later time, please contact the Survey Coordinating Center at 1-877-379-3297. Please feel free to ask me to repeat any questions or statements as we go through the survey. Once you have answered a question and moved on, you cannot go back and change your answers. Thank you for your participation in this survey.

[ONLINE ONLY] Taking the Survey

[ONLINE ONLY] Once you have answered a question and moved on, you cannot go back and change your answers.

[ONLINE ONLY] Thank you for your participation in this survey.

[END PREAMBLE 1]

[BEGIN INCLUSION/EXCLUSION QUESTIONS]

1. Your agreement to participate in this survey confirms mutual understanding in connection with completion of the survey and the fair market value of the payment to be rendered in connection with those services.

   Do you agree to participate in this survey?

   - ○ Yes
   - ○ No **[TERMINATE]**

2. Have you ever taken part in this survey about TIRF medicines before? TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Onsolis®, Subsys™, and generic versions of any of these brands.

   - ○ Yes **[ONLY TERMINATE AFTER WAVE 1]**
   - ○ No
   - ○ I don't know **[ONLY TERMINATE AFTER WAVE 1]**

3. Do you work in a pharmacy that is enrolled in the TIRF REMS Access program?

   - ○ Yes
   - ○ No **[TERMINATE]**
   - ○ I don't know **[TERMINATE]**

4. Have you or any of your immediate family members ever worked for any of the following companies or agencies? Please select all that apply.

   - ○ Anesta LLC **[TERMINATE]**
   - ○ Archimedes Pharma US Inc.**[TERMINATE]**
   - ○ Cephalon, Inc. **[TERMINATE]**
   - ○ Endo Pharmaceuticals Inc. **[TERMINATE]**
   - ○ Insys Therapeutics**[TERMINATE]**
   - ○ McKesson Specialty Care Solutions**[TERMINATE]**

- Mallinckrodt (a Covidien Company) **[TERMINATE]**
- Meda Pharmaceuticals **[TERMINATE]**
- Par Pharmaceutical, Inc.**[TERMINATE]**
- ProStrakan, Inc. **[TERMINATE]**
- Teva Pharmaceuticals, Ltd. **[TERMINATE]**
- Sandoz Inc. **[TERMINATE]**
- RelayHealth **[TERMINATE]**
- United BioSource Corporation**[TERMINATE]**
- FDA **[TERMINATE]**
- None of these apply **[IF SELECTED IN ADDITION TO OTHER RESPONSES, TERMINATE]**
- I don't know **[TERMINATE]**
- Prefer not to answer **[TERMINATE]**

[END INCLUSION/EXCLUSION QUESTIONS]

5. Please select "True," "False," or "I don't know" for each of the following.

According to the labeling, patients considered opioid-tolerant are those:

[RANDOMIZE LIST]	True	False	I don't know
5a. Who are taking regular opioid therapy for underlying persistent cancer pain for one week or longer	○	○	○
5b. Who are not currently taking opioid therapy, but have taken opioid therapy before	○	○	○
5c. Who are not currently taking opioid therapy, but with no known intolerance or hypersensitivity to the drug fentanyl	○	○	○

6. Please answer "True," "False," or "I don't know" for each statement about TIRF medicines.

[RANDOMIZE LIST]	True	False	I don't know
6a. TIRF medicines are contraindicated in opioid non-tolerant patients because life-threatening respiratory depression could occur at any dose.	○	○	○
6b. Death has occurred in opioid non-tolerant patients treated with some fentanyl products.	○	○	○
6c. TIRF medicines may be used in opioid non-tolerant patients.	○	○	○
6d. Prescribers starting a patient on a TIRF medicine must begin with titration from the lowest dose available for that specific product, even if the patient has previously taken another TIRF medicine.	○	○	○
6e. It is important to monitor for signs of abuse and addiction in patients who take TIRF medicines.	○	○	○

7. Which of the following are risk factors for opioid abuse? Please answer "Yes," "No," or "I don't know" for each option.

[RANDOMIZE LIST]	Yes	No	I don't know
7a. A personal history of psychiatric illness	○	○	○
7b. A personal history of past or current alcohol or drug abuse, or a family history of illicit drug use or alcohol abuse	○	○	○
7c. A family history of asthma	○	○	○

8. For which of the following indications can TIRF medicines be prescribed to opioid tolerant patients? Answer "Yes," "No," or "I don't know" for each option.

[RANDOMIZE LIST]	Yes	No	I don't know
8a. Acute or postoperative pain	○	○	○
8b. Headache or migraine pain	○	○	○
8c. Dental pain	○	○	○
8d. Breakthrough pain from cancer	○	○	○
8e. Chronic non-cancer pain	○	○	○

9. Please answer "True," "False," or "I don't know" for each statement about TIRF medicines.

[RANDOMIZE LIST]	True	False	I don't know
9a. TIRF medicines can be abused in a manner similar to other opioid agonists.	○	○	○
9b. TIRF medicines are interchangeable with each other regardless of route of administration.	○	○	○
9c. The conversion of one TIRF medicine for another TIRF medicine may result in a fatal overdose because of differences in the pharmacokinetics of fentanyl absorption.	○	○	○
9d. Dosing of TIRF medicines is not equivalent on a microgram-to-microgram basis.	○	○	○

10. How frequently do you perform the following activities when dispensing TIRF

medicines? Please answer "Always," "Only with the first prescription," "Sometimes," "Never," or "I don't know."

	[RANDOMIZE LIST]	Always	Only with the first prescription	Sometimes	Never	I don't know
10a.	Ask patients (or their caregivers) about the presence of children in the home	○	○	○	○	○
10b.	Instruct patients (or their caregivers) not to share TIRF medicines with anyone else	○	○	○	○	○
10c.	Counsel patients (or their caregivers) that accidental exposure to TIRF medicines by a child may be fatal	○	○	○	○	○
10d.	Instruct patients (or their caregivers) to keep TIRF medicines out of the reach of children to prevent accidental exposure	○	○	○	○	○
10e.	Instruct patients (or their caregivers) about proper disposal of any unused or partially used TIRF medicines	○	○	○	○	○
10f.	Give patients (or their caregivers) the Medication Guide for their TIRF medicine	○	○	○	○	○

11. Please answer "True," "False," or "I don't know " for each statement about TIRF medicines.

	[RANDOMIZE LIST]	True	False	I don't know
11a.	TIRF medicines may be sold, loaned, or transferred to another pharmacy.	○	○	○
11b.	All pharmacy staff that dispenses TIRF medicines must be educated on the requirements of the TIRF REMS Access program.	○	○	○

11c.	TIRF medicines with the same route of administration can be substituted with each other if the pharmacy is out of stock for one product.	○	○	○

12. **[INPATIENT PHARMACIST]**Does the inpatient pharmacy where you work have an established system, order sets, protocols and/or other measures to help ensure appropriate patient selection and compliance with the requirements of the TIRF REMS Access Program?

- ○ Yes
- ○ No
- ○ I don't know

13. **[OUTPATIENT PHARMACIST]**Does the outpatient or retail pharmacy where you work process all TIRF medicine prescriptions, regardless of method of payment, through the pharmacy management system?

- ○ Yes
- ○ No
- ○ I don't know

14. **[CSP OUTPATIENT PHARMACIST]**Does the pharmacy where you work process all TIRF medicine prescriptions, regardless of method of payment, through the TIRF REMS Access Call Center?

- ○ Yes
- ○ No
- ○ I don't know

15. **[INPATIENT PHARMACIST]** Please answer "True," "False," or "I don't know" for the following statement about TIRF medicines.

	True	False	I don't know
It is OK to dispense TIRF medicines from the inpatient pharmacy inventory to an outpatient for use at home.	○	○	○

[PREAMBLE 3]

The next set of questions is about the educational materials for TIRF medicines. As a reminder, the TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Onsolis®, Subsys™, and generic versions of any of these brands.

16. Did you receive or do you have access to the Full Prescribing Information for the TIRF medicine that you dispense?

- ○ Yes
- ○ No **[GO TO Q18]**
- ○ I don't know **[GO TO Q18]**

17. Did you read the Full Prescribing Information for the TIRF medicine that you dispense?

- ○ Yes
- ○ No
- ○ I don't know

18. Did you receive or do you have access to the Medication Guide for the TIRF medicine that you dispense?

- ○ Yes
- ○ No **[GO TO Q20]**
- ○ I don't know **[GO TO Q20]**

19. Did you read the Medication Guide for the TIRF medicine that you dispense?

- ○ Yes
- ○ No
- ○ I don't know

20. Did you or do you have any questions about the information in the Full Prescribing Information or Medication Guide?

- ○ Yes
- ○ No **[GO TO DEMOGRAPHICS PREAMBLE]**
- ○ I don't know **[GO TO DEMOGRAPHICS PREAMBLE]**

21. What are your questions?**[MULTILINE INPUT]**

[DEMOGRAPHICS PREAMBLE]

There are just a few more questions to help us combine your answers with other answers we have received.

22. Are you the Pharmacist in Charge for the TIRF REMS Access Program where you work?

- ○ Yes
- ○ No
- ○ I don't know

23. On average, how many times per month have you dispensed TIRF medicines within the last 6 months?

- ○ None **[Go to DEMOGRAPHICS PREAMBLE 2]**
- ○ 1 – 2 times per month
- ○ 3 – 5 times per month

- ○ More than 5 times per month
- ○ I don't remember

24. Please select the TIRF medicines that you have dispensed within the last 6 months (select all that apply):

- ○ Abstral®
- ○ Actiq® or generic Actiq®
- ○ Fentora® or generic Fentora®
- ○ Lazanda ®
- ○ Onsolis®
- ○ Subsys™

[DEMOGRAPHICS PREAMBLE 2]

These last few questions are for demographic purposes.

25. What is your gender?

- ○ Male
- ○ Female
- ○ Prefer not to answer

26. In total, how many years have you been a practicing pharmacist?

- ○ Less than 3 years
- ○ 3 – 5 years
- ○ 6 – 10 years
- ○ 11 – 15 years
- ○ More than 15 years
- ○ Prefer not to answer

27. In which state do you practice?

[DROP-DOWN LIST INPUT WITH STATES TABLE WITH "Prefer not to answer" AT END]

[PHONE ONLY: BEGIN ADVERSE EVENT/PRODUCT COMPLAINT]

(INTERVIEWER: Please record if respondent spontaneously reported an adverse event or product complaint during the course of this interview.)

- ○ Yes
- ○ No **[GO TO CLOSING 1]**

Enter Safety Adverse Event Verbatim

[MULTILINE INPUT]

(INTERVIEWER: Indicate to the respondent that someone may call back to ask more questions about the adverse event or product complaint that was reported.)

[END ADVERSE EVENT/PRODUCT COMPLAINT]

[CLOSING 1]

We would like to send you a $50 honorarium within the next few weeks to thank you for your time, but we need your name and address to do so. If you do not provide your name and address you will not receive the honorarium for your time and participation in the survey.

Do you agree to give us your name and mailing address so we can send you the honorarium?

○ Yes

○ No **[SKIP TO CLOSING 2]**

FIRST NAME: _____

LAST NAME: _____

ADDRESS: **[MULTILINE INPUT]**

CITY: _____

STATE: **[DROP-DOWN LIST INPUT WITH STATES TABLE]**

ZIP: _____

[CLOSING 2]

We would also like to ask for your telephone number. Providing your telephone number is optional and it will be used to contact you only if there are questions about your survey responses.

Do you want to provide your telephone number?

○ Yes

○ No **[SKIP TO CLOSING 3]**

Telephone: _____

[CLOSING 3]

That ends the survey. Thank you again for your help.

[END OF SURVEY CONTENT]

Appendix B Sample Pharmacist Invitation Letter

[CURR_DATE]

[PHARMACY NAME or NAME OF PHARMACIST IN CHARGE]

[STREET_ADDR]

[CITY], [STATE] [ZIP]

Dear [NAME OF PHARMACIST IN CHARGE]:

You were selected to receive this letter because you have enrolled in the TIRF REMS Access Program. We are contacting you to inform you about a survey being conducted by the manufacturers of Transmucosal Immediate Release Fentanyl (TIRF) medicines, as required by the Food and Drug Administration (FDA). The purpose of the survey is to assess pharmacists' understanding of the safe and appropriate use of these medicines. The TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Onsolis®, Subsys™, and generic versions of any of these brands.

The manufacturers of TIRF medicines include Archimedes Pharma US Inc., Cephalon, Inc., Endo Pharmaceuticals Inc., Insys Therapeutics, Meda Pharmaceuticals, Mallinckrodt (a Covidien Company), Par Pharmaceutical, Inc., ProStrakan, Inc., and Sandoz Inc (collectively referred to as the "TIRF Industry REMS Group"). These manufacturers are looking for 200 pharmacists to complete the survey. Eligible pharmacists who complete the survey will be sent a $50 honorarium to thank them for their time. The survey will take 15-20 minutes.

Your answers will be kept strictly confidential and will be combined with the answers from other pharmacists who take this survey. Your name will not be used in the report of this survey and your contact information will only be used to send you a $50 honorarium for the time you took to complete the survey.

You are under no obligation to participate in this survey. If you are interested in participating, go to **www.XXXXXXXXXX.com** anytime or call **1-877-379-3297,** 8AM to 10PM Eastern Time Monday through Friday. You will be asked to give this unique code prior to starting the survey: **[CODE_ID]**.

Please have this letter with you at the time you take the survey. Thank you in advance for your help with this important effort.

Sincerely,

TIRF Industry REMS Group

* We recommend that you take the survey on a desktop or laptop computer. Taking the survey on mobile devices, such as smart phones, tablets, and e-notebooks, is not supported.

12-Month Prescriber KAB Survey

Appendix A Prescriber Questionnaire

Survey Legend

- **[PROGRAMMER]** is used to indicate directions to the programmer and is set in bold, red, uppercase letters between square brackets.

- **(INTERVIEWER)** is used to indicate directions to the phone interviewer and is set in bold, blue, text between parentheses. This text appears when content is to be administered by phone only (for example, spontaneous adverse event reporting).

- **[ONLINE]** indicates a question is worded specifically for administering the survey online. **[PHONE]** indicates a question is worded specifically to be read by a phone interviewer and differs from the online text.

- **[BEGIN ONLINE/PHONE SURVEY CONTENT]** and **[END SURVEY CONTENT]** are used to indicate to the programmer the type of survey administration and the beginning and end of the survey or sections within the survey content, for example, **[BEGIN ADVERSE EVENT/PRODUCT COMPLAINT]** and **[END ADVERSE EVENT/PRODUCT COMPLAINT]**.

- **[TERMINATE]** is displayed next to responses that should cause the survey to end. The following termination language will be programmed into the survey or read by the interviewer unless different language is specified with the question.

  Thank you very much for your time today. Based on your answer, you are not eligible to take this survey. We appreciate your interest in the survey.

- **[RANDOMIZE LIST]** is inserted before questions to indicate to the programmer that the responses should be randomized. Responses such as "I don't know," "Prefer not to answer" or "None of the above" will always appear at the end of the randomized responses.

- **[GO TO Qx]** (skip logic) is inserted after a response to indicate to the programmer that the survey should skip to the indicated question (for example, **[GO TO Q17]** skips to question 17). If no skip logic is indicated the survey continues to the next question in the sequence.

- **[MULTILINE INPUT]** indicates to the programmer that multiple lines should be provided for data entry (for example, two address lines or a free-text response).

Survey Legend

- **[DROP-DOWN LIST INPUT WITH STATES TABLE]** indicates to the programmer that the response should be a drop-down list containing the states and US territories in the table below.

Alabama	Georgia	Massachusetts	New York	Tennessee
Alaska	Guam	Michigan	North Carolina	Texas
American Samoa	Hawaii	Minnesota	North Dakota	US Virgin Islands
Arizona	Idaho	Mississippi	Northern Mariana Islands	Utah
Arkansas	Illinois	Missouri	Ohio	Vermont
California	Indiana	Montana	Oklahoma	Virginia
Colorado	Iowa	Nebraska	Oregon	Washington
Connecticut	Kansas	Nevada	Pennsylvania	West Virginia
Delaware	Kentucky	New Hampshire	Puerto Rico	Wisconsin
District of Columbia	Louisiana	New Jersey	Rhode Island	Wyoming
Florida	Maine	New Mexico	South Carolina	
	Maryland		South Dakota	

- The following is used to categorize survey populations into standard geographic regions but it is not displayed in the survey.

Geographic Distribution (based on address) [1]: Northeast, Midwest, South, and West regions

Northeast Region

- New England Division - ME, NH, VT, MA, RI, CT
- Middle Atlantic Division - NY, NJ, PA

Midwest Region

- East North Central Division - OH, IN, IL, MI, WI
- West North Central Division - MN, IA, MO, ND, SD, NE, KS

South Region

- South Atlantic Division - DE, MD, DC, VA, WV, NC, SC, GA, FL
- East South Central Division - KY, TN, AL, MS
- West South Central Division - AR, LA, OK, TX

Survey Legend

West

- Mountain Division - MT, ID, WY, CO, NM, AZ, UT, NV
- Pacific Division WA, OR, CA, AK, HI

- The following US territories are categorized as **Other**: Puerto Rico, Northern Mariana Islands, US Virgin Islands, American Samoa, and Guam.

[1] U.S. Census Bureau, last revised Friday, 27-Jul-2001 12:59:43 EDT.

[BEGIN ONLINE/PHONE SURVEY CONTENT]

[PREAMBLE 1]

Before you begin, we would like to share some important information about this survey. The manufacturers of Transmucosal Immediate Release Fentanyl medicines are conducting this survey, as required by the FDA, to assess prescribers' understanding of the safe use and prescribing of these medicines. These medicines are known as rapid onset opioids and referred to in this survey as "TIRF medicines." **(INTERVIEWER: Say "TIRF" then spell out T-I-R-F)** The TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Onsolis®, Subsys™, and generic versions of any of these brands. The manufacturers of these medicines include Archimedes Pharma US Inc., Cephalon, Inc., Endo Pharmaceuticals Inc., Insys Therapeutics, Meda Pharmaceuticals, Mallinckrodt (a Covidien Company), Par Pharmaceutical, Inc., ProStrakan, and Sandoz Inc. The survey will take approximately 20 minutes.

There are no known risks to you in taking this survey. You may refuse to take part or withdraw at any time. Your answers to the questions or your decision to take part in the survey will not affect your ability to prescribe TIRF medicines.

[ONLINE ONLY]How We Use Your Information

[PHONE ONLY] Now I would like to read some information about how your contact information will be used.

Your answers to the survey questions will be combined with answers given by other healthcare professionals taking the survey. All answers will be put together and reported in anonymous form to the manufacturers of TIRF medicines. Your name will not be used in any report. If you are eligible to take the survey, complete all the questions, and provide your contact information, you will receive a $125 honorarium for your time and participation. This compensation represents the fair value for your services in connection with completion of the survey. The amount of the compensation was not determined in any manner that takes into account the volume or value of any referrals or business otherwise generated by you.

Your name and address will be used to send you the honorarium after you complete the survey. Your personal information will also be used if we have questions about your survey or if we are required to use your information to comply with a federal or state law or regulation, including without limitation, reporting payments made to physicians under the federal physician payment sunshine provisions. Physicians who practice in Vermont, Massachusetts, or Minnesota should be aware that they will not be permitted to receive payment for survey completion and may elect not to complete the survey.

Providing a telephone number is optional. Your phone number will be used only if there are any questions about your survey responses.

[ONLINE ONLY] How We Protect Your Privacy

[PHONE ONLY]Now I would like to tell you some information about how we protect your privacy.

We respect that the privacy of your personal information is important to you. You will not be contacted for marketing purposes based on your personal information or your answers to the survey. Neither the manufacturers of TIRF medicines nor their contractors will sell, transfer, or rent your information. Your answers will be kept strictly confidential. Your personal information will not be used in a manner inconsistent with this document. Your privacy will be protected; however, research survey records may be inspected by the FDA. Your choice to allow manufacturers of TIRF medicines to use your information is entirely voluntary but necessary to take part in this survey.

[ONLINE ONLY] How to Learn More about This Survey

[ONLINE ONLY] If you have questions about the survey, or problems with the survey, please contact the Survey Coordinating Center at 1-877-379-3297. Be sure to write down this telephone number; it will not be displayed again.

[PHONE ONLY]Now I will tell you how you can learn more about this survey. Please have a pen or pencil ready to write down a telephone number you can call should you have any questions about the survey. If you have questions about the survey, please ask me at any time. If you have questions at a later time, please contact the Survey Coordinating Center at 1-877-379-3297. Please feel free to ask me to repeat any questions or statements as we go through the survey. Once you have answered a question and moved on, you cannot go back and change your answers. Thank you for your participation in this survey.

[ONLINE ONLY] Taking the Survey

[ONLINE ONLY] Once you have answered a question and moved on, you cannot go back and change your answers.

[ONLINE ONLY] Thank you for your participation in this survey.

[END PREAMBLE 1]

[BEGIN INCLUSION/EXCLUSION QUESTIONS]

1. Your agreement to participate in this survey confirms mutual understanding in connection with completion of the survey and the fair market value of the payment to be rendered in connection with those services.

   Do you agree to participate in this survey?

   - ○ Yes
   - ○ No **[TERMINATE]**

2. Have you ever taken part in this survey about TIRF medicines before? TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Onsolis®, Subsys™, and generic versions of any of these brands.

   - ○ Yes **[ONLY TERMINATE AFTER WAVE 1]**
   - ○ No
   - ○ I don't know **[ONLY TERMINATE AFTER WAVE 1]**

3. Are you enrolled in the TIRF REMS Access program?

   - ○ Yes
   - ○ No **[TERMINATE]**
   - ○ I don't know **[TERMINATE]**

4. Have you or any of your immediate family members ever worked for any of the following companies or agencies? Please select all that apply.

   - ○ Anesta LLC **[TERMINATE]**
   - ○ Archimedes Pharma US Inc.**[TERMINATE]**
   - ○ Cephalon, Inc. **[TERMINATE]**
   - ○ Endo Pharmaceuticals Inc. **[TERMINATE]**
   - ○ Insys Therapeutics**[TERMINATE]**

- McKesson Specialty Care Solutions**[TERMINATE]**
- Mallinckrodt (a Covidien Company) **[TERMINATE]**
- Meda Pharmaceuticals **[TERMINATE]**
- Par Pharmaceutical, Inc.**[TERMINATE]**
- ProStrakan, Inc. **[TERMINATE]**
- Sandoz Inc. **[TERMINATE]**
- Teva Pharmaceuticals, Ltd. **[TERMINATE]**
- RelayHealth**[TERMINATE]**
- United BioSource Corporation**[TERMINATE]**
- FDA **[TERMINATE]**
- None of these apply **[IF SELECTED IN ADDITION TO OTHER RESPONSES, TERMINATE]**
- I don't know **[TERMINATE]**
- Prefer not to answer **[TERMINATE]**

[END INCLUSION/EXCLUSION QUESTIONS]

5. Please select "True," "False," or "I don't know" for each of the following.

According to the labeling, patients considered opioid-tolerant are those:

	[RANDOMIZE LIST]	True	False	I don't know
5a.	Who are taking regular opioid therapy for underlying persistent cancer pain for one week or longer	○	○	○
5b.	Who are not currently taking opioid therapy, but have taken opioid therapy before	○	○	○
5c.	Who are not currently taking opioid therapy, but with no known intolerance or hypersensitivity to the drug fentanyl	○	○	○

6. Please answer "True," "False," or "I don't know" for each statement about TIRF medicines.

	[RANDOMIZE LIST]	True	False	I don't know
6a.	TIRF medicines are contraindicated in opioid non-tolerant patients because life-threatening respiratory depression could occur at any dose.	○	○	○
6b.	Death has occurred in opioid non-tolerant patients treated with some fentanyl products.	○	○	○
6c.	TIRF medicines may be used to treat opioid non-tolerant patients.	○	○	○
6d.	Prescribers starting a patient on a TIRF medicine must begin with titration from the lowest dose available for that specific product, even if the patient has previously taken another TIRF medicine.	○	○	○
6e.	It is important to monitor for signs of abuse and addiction in patients who take TIRF medicines.	○	○	○

7. Which of the following are risk factors for opioid abuse? Please answer "Yes," "No," or "I don't know" for each option.

	[RANDOMIZE LIST]	Yes	No	I don't know
7a.	A personal history of psychiatric illness	○	○	○
7b.	A personal history of past or current alcohol or drug abuse, or a family history of illicit drug use or alcohol abuse	○	○	○
7c.	A family history of asthma	○	○	○

8. For which of the following indications do you prescribe TIRF medicines to opioid tolerant patients? Please answer "Yes," "No," or "I don't know" for each option.

	[RANDOMIZE LIST]	Yes	No	I don't know
8a.	Acute or postoperative pain	○	○	○
8b.	Headache or migraine pain	○	○	○
8c.	Dental pain	○	○	○
8d.	Breakthrough pain from cancer	○	○	○
8e.	Chronic non-cancer pain	○	○	○

9. Please answer "True," "False," or "I don't know" for each statement about TIRF medicines.

	[RANDOMIZE LIST]	True	False	I don't know
9a.	TIRF medicines can be abused in a manner similar to other opioid agonists.	○	○	○
9b.	TIRF medicines are interchangeable with each other regardless of route of administration.	○	○	○
9c.	The conversion of one TIRF medicine for another TIRF medicine may result in a fatal overdose because of differences in the pharmacokinetics of fentanyl absorption.	○	○	○
9d.	Dosing of TIRF medicines is not equivalent on a microgram-to-microgram basis.	○	○	○

10. How frequently do you perform the following activities when prescribing TIRF medicines? Please answer "Always," "Only with the first prescription," "Sometimes," "Never," or "I don't know."

	[RANDOMIZE LIST]	Always	Only with the first prescription	Sometimes	Never	I don't know
10a.	Ask patients (or their caregivers) about the presence of children in the home	○	○	○	○	○
10b.	Instruct patients (or their caregivers) not to share TIRF medicines with anyone else	○	○	○	○	○
10c.	Counsel patients (or their caregivers) that accidental exposure to TIRF medicines by a child may be fatal	○	○	○	○	○
10d.	Instruct patients (or their caregivers) to keep TIRF medicines out of the reach of children to prevent accidental exposure	○	○	○	○	○
10e.	Instruct patients (or their caregivers) about proper disposal of any unused or partially used TIRF medicines	○	○	○	○	○
10f.	Give patients (or their caregivers) the Medication Guide for their TIRF medicine	○	○	○	○	○

11. The following patients described are experiencing breakthrough pain. According to the labeling, a TIRF medicine is not appropriate for one of them. Please answer "Yes," "No," or "I don't know" as to whether each patient should receive a TIRF medicine.

	[RANDOMIZE LIST]	Yes	No	I don't know
11a.	Adult male with advanced lung cancer; underlying persistent cancer pain managed with 25 mcg/hour transdermal fentanyl patches for the past two months.	○	○	○
11b.	Adult female with localized breast cancer; just completed a mastectomy and reconstructive surgery; persistent cancer pain managed with 30 mg oral morphine daily for the past 6 weeks.	○	○	○
11c.	Adult male patient with advanced prostate cancer who, over the last 2 weeks, has been prescribed 100 mg oral morphine daily for pain due to bone metastasis.	○	○	○

11d.	Adult female with advanced sarcoma who has been taking a daily dose of 12 mg oral hydromorphone for the last 3 weeks.	○	○	○

12. A patient is already taking a TIRF medicine but wants to change their medicine. The doctor decides to prescribe a different TIRF medicine (that is not a bioequivalent generic version of a branded product) in its place. How should the prescriber proceed? For each of the following scenarios, please indicate if it is a correct action for the prescriber by answering "Yes," "No," or "I don't know."

	[RANDOMIZE LIST]	**Yes**	**No**	**I don't know**
12a.	The prescriber can safely convert to the equivalent dosage of the new TIRF medicine as it has the same effect as other TIRF medicines.	○	○	○
12b.	The prescriber must not convert from the equivalent TIRF medicine dose to another TIRF medicine because they have different absorption properties and this could result in a fentanyl overdose.	○	○	○
12c.	Convert from the other TIRF medicine to the new TIRF medicine at half of the dose.	○	○	○
12d.	The prescriber should base the starting dose of the newly prescribed TIRF medicine on the dose of the opioid medicine used for their underlying persistent cancer pain.	○	○	○

13. A patient is starting titration with a TIRF medicine. What dose must they start with? Please indicate "Yes," "No," or "I don't know" for each of the following dosing scenarios.

	[RANDOMIZE LIST]	**Yes**	**No**	**I don't know**
13a.	An appropriate dose based on the dose of the opioid medicine used for underlying persistent cancer pain.	○	○	○
13b.	The dose that the prescriber believes is appropriate based on their clinical experience.	○	○	○
13c.	The lowest available dose, unless individual product Full Prescribing Information provides product-specific guidance.	○	○	○
13d.	The median available dose.	○	○	○

14. A prescriber has started titrating a patient with the lowest dose of a TIRF medicine. However, after 30 minutes the breakthrough pain has not been sufficiently relieved. What should they advise the patient to do? Please answer "Yes," "No," or "I don't know" for each of the scenarios described.

	[RANDOMIZE LIST]	Yes	No	I don't know
14a.	Take another (identical) dose of the TIRF medicine immediately.	○	○	○
14b.	Take a dose of an alternative rescue medicine.	○	○	○
14c.	Provide guidance based on the product-specific Medication Guide because the instructions are not the same for all TIRF medicines.	○	○	○
14d.	Double the dose and take immediately.	○	○	○

15. A patient is taking a TIRF medicine and the doctor would like to prescribe erythromycin, a CYP3A4 inhibitor. Please select "True," "False," or "I don't know" for each of the following statements.

	[RANDOMIZE LIST]	True	False	I don't know
15a.	The patient can't be prescribed erythromycin, because using it at the same time as a TIRF medicine could be fatal.	○	○	○
15b.	Use of a TIRF medicine with a CYP3A4 inhibitor may require dosage adjustment; carefully monitor the patient for opioid toxicity, otherwise such use may cause potentially fatal respiratory depression.	○	○	○
15c.	There is no possible drug interaction between CYP3A4 inhibitors and TIRF medicines.	○	○	○
15d.	The dose of the TIRF medicine must be reduced by one half if a CYP3A4 inhibitor is prescribed in the same patient.	○	○	○

16. Before initiating treatment with a TIRF medicine, prescribers must review the Medication Guide with the patient. Please select "True," "False," or "I don't know" for each of the following counseling statements.

	[RANDOMIZE LIST]	True	False	I don't know
16a.	TIRF medicines contain fentanyl in an amount that could be fatal to children of all ages, in individuals for whom they were not prescribed, and in those who are not opioid tolerant.	○	○	○
16b.	Inform patients that TIRF medicines must not be used for acute or postoperative pain, pain from injuries, headache/migraine, or any other short-term pain.	○	○	○
16c.	Instruct patients that, if they stop taking their around - the-clock opioid medicine, they can continue to take their TIRF medicine.	○	○	○
16d.	Instruct patients to never share their TIRF medicine with anyone else, even if that person has the same symptoms.	○	○	○

[PREAMBLE 2]

The next set of questions is about the educational materials for TIRF medicines and the TIRF Patient-Prescriber Agreement. As a reminder, the TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Onsolis®, Subsys™, and generic versions of any of these brands.

17. Did you receive or do you have access to the Full Prescribing Information for the TIRF medicine that you prescribe?

- ○ Yes
- ○ No **[GO TO Q19]**
- ○ I don't know **[GO TO Q19]**

18. Did you read the Full Prescribing Information for the TIRF medicine that you prescribe?

- ○ Yes
- ○ No
- ○ I don't know

19. Did you receive or do you have access to the Medication Guide for the TIRF medicine that you prescribe?

- ○ Yes
- ○ No **[GO TO Q21]**
- ○ I don't know **[GO TO Q21]**

20. Did you read the Medication Guide for the TIRF medicine that you prescribe?

- ○ Yes
- ○ No
- ○ I don't know

21. Did you or do you have any questions about the information in the Full Prescribing Information or Medication Guide?

- ○ Yes
- ○ No **[GO TO Q23]**
- ○ I don't know **[GO TO Q23]**

22. What are your questions?**[MULTILINE INPUT]**

23. Do you review the Patient-Prescriber Agreement Form with each of your patients for whom you prescribe TIRF medicines or their caregiver?

- ○ Yes
- ○ No **[GO TO Q25]**
- ○ I don't know **[GO TO Q25]**

24. Do you and the patient or their caregiver sign the Patient-Prescriber Agreement Form for TIRF medicines after you have reviewed it with him/her?

- ○ Yes
- ○ No
- ○ I don't know

25. Do you give a copy of the Patient-Prescriber Agreement Form for TIRF medicines to the patient or their caregiver?

- ○ Yes
- ○ No
- ○ I don't know

[DEMOGRAPHICS PREAMBLE]

There are just a few more questions to help us combine your answers with other answers we have received.

26. On average, how many times per month have you prescribed the TIRF medicines within the last 6 months?

- ○ None **[GO TO DEMOGRAPHICS PREAMBLE 2]**
- ○ 1 – 2 times per month
- ○ 3 – 5 times per month
- ○ More than 5 times per month
- ○ I don't remember

27. Please select the TIRF medicines that you have prescribed within the last 6 months: (select all that apply)

- ○ Abstral®
- ○ Actiq® or generic Actiq®
- ○ Fentora® or generic Fentora®
- ○ Lazanda®
- ○ Onsolis®
- ○ Subsys™

[DEMOGRAPHICS PREAMBLE 2]These last few questions are for demographic purposes.

28. What is your gender?

- ○ Male
- ○ Female
- ○ Prefer not to answer

29. What is your medical degree?

- ○ MD
- ○ DO
- ○ Nurse Practitioner **[Go to Q31]**
- ○ Physician Assistant **[Go to Q31]**
- ○ Prefer not to answer

30. In total, how many years have you been practicing medicine, since completing your post-graduate education?

- ○ Less than 3 years
- ○ 3 – 5 years
- ○ 6 – 10 years
- ○ 11 – 15 years
- ○ More than 15 years
- ○ Prefer not to answer

31. In which state do you practice?

[DROP-DOWN LIST INPUT WITH STATES TABLE WITH "Prefer not to answer" at END]

32. What is your medical specialty?

- ○ Oncology
- ○ Primary care
- ○ Pain management
- ○ Other (please specify): _____

[PHONE ONLY: BEGIN ADVERSE EVENT/PRODUCT COMPLAINT]

(INTERVIEWER: Please record if respondent spontaneously reported an adverse event or product complaint during the course of this interview.)

- ○ Yes
- ○ No **[GO TO CLOSING 1]**

Enter Safety Adverse Event Verbatim

[MULTILINE INPUT]

(INTERVIEWER: Indicate to the respondent that someone may call back to ask more questions about the adverse event or product complaint that was reported.)

[END ADVERSE EVENT/PRODUCT COMPLAINT]

[CLOSING 1]

We would like to send you a $125 honorarium within the next few weeks to thank you for your time, but we need your name and address to do so. If you do not provide your name and address you will not receive the honorarium for your time and participation in the survey. As a reminder, physicians who practice in Vermont, Massachusetts, or Minnesota should be aware that they will not be permitted to receive payment for survey completion.

Do you agree to give us your name and mailing address so we can send you the honorarium?

- ○ Yes
- ○ No **[SKIP TO CLOSING 2]**

FIRST NAME: _____

LAST NAME: _____

ADDRESS: **[MULTILINE INPUT]**

CITY: _____

STATE: **[DROP-DOWN LIST INPUT WITH STATES TABLE]**

ZIP: _____

[CLOSING 2]

We would also like to ask for your telephone number and NPI number. Providing your telephone number and NPI number is optional. Your telephone number will be used to contact you only if there are questions about your survey responses.

Do you want to provide your telephone number?

○ Yes

○ No **[SKIP TO NPI NUMBER QUESTION]**

Telephone: _____

[NEW PAGE]

Do you want to provide your NPI number?

○ Yes

○ No **[SKIP TO CLOSING 3]**

NPI #: _____

[CLOSING 3]

That ends the survey. Thank you again for your help.

[END OF SURVEY CONTENT]

Appendix B Sample Prescriber Invitation Letter

[CURR_DATE]

[PRESCRIBER NAME]

[STREET_ADDR]

[CITY], [STATE] [ZIP]

Dear [PRESCRIBER NAME]:

You were selected to receive this letter because you have enrolled in the TIRF REMS Access Program. We are contacting you to invite you to participate in a survey being conducted by the manufacturers of Transmucosal Immediate Release Fentanyl (TIRF) medicines, as required by the Food and Drug Administration (FDA). The purpose of the survey is to assess prescribers' understanding of the safe and appropriate use of these medicines. The TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Onsolis®, Subsys™, and generic versions of any of these brands.

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Your answers will be kept strictly confidential and will be combined with the answers from other prescribers who take this survey. Your name will not be used in the report of this survey and your contact information will only be used to send you a $125 honorarium for the time you took to complete the survey and if required to comply with a federal or state law or regulation, including without limitation, reporting payments made to physicians under the federal physician payment sunshine provisions. Physicians who practice in Vermont, Massachusetts, or Minnesota should be aware that they will not be permitted to receive payment for survey completion and may elect not to complete the survey.

You are under no obligation to participate in this survey. If you are interested in participating, go to **www.XXXXXXXXXX.com** anytime or call **1-877-379-3297,** 8AM to 10PM Eastern Time Monday through Friday. You will be asked to give this unique code prior to starting the survey: **[CODE_ID]**.

Please have this letter with you at the time you take the survey. Thank you in advance for your help with this important effort.

Sincerely,

TIRF REMS Industry Group

* We recommend that you take the survey on a desktop or laptop computer. Taking the survey on mobile devices, such as smart phones, tablets, and e-notebooks, is not supported.

60-Month Patient KAB Survey

APPENDIX A Screening and Main Questionnaire

Survey Legend

[PROGRAMMER] is used to indicate directions to the programmer and is set in bold, red, uppercase letters between square brackets.

[PATIENT] indicates text applicable to a patient when it differs from survey text for caregivers, parents and legal guardians.

[OTHER] indicates text applicable to parents, caregivers, and legal guardians when it differs from survey text for patients.

(INTERVIEWER) is used to indicate directions to the telephone interviewer and is set in bold, blue, text between parentheses. This text appears when content is to be administered by telephone only (for example, spontaneous adverse event reporting).

[ONLINE] indicates a question is worded specifically for administering the survey online. **[PHONE]** indicates a question is worded specifically to be read by a telephone interviewer and differs from the online text.

[BEGIN SURVEY CONTENT] and **[END SURVEY CONTENT]** are used to indicate to the programmer the type of survey administration and the beginning and end of the survey or sections within the survey content, for example, **[BEGIN ADVERSE EVENT/PRODUCT COMPLAINT]** and **[END ADVERSE EVENT/PRODUCT COMPLAINT]**.

[TERMINATE] is displayed next to responses that should cause the survey to end. The following termination language will be programmed into the survey or read by the interviewer unless different language is specified with the question.

> *Thank you very much for your time today. Based on your answer, you are not eligible to take this survey. We appreciate your interest in the survey.*

[RANDOMIZE LIST] is inserted before questions to indicate to the programmer that the responses should be randomized. Responses such as “I don’t know,” “Prefer not to answer” or “None of the above” will always appear at the end of the randomized responses.

[GO TO Qx] (Skip logic) is inserted after a response to indicate to the programmer that the survey should skip to the indicated question (for example, **[GO TO Q17]** skips to question 17). If no skip logic is indicated the survey continues to the next question in the sequence.

Response options for questions that allow multiple responses must be indicated with check

Survey Legend

boxes (□). At least one option must be selected for the question to be considered answered.

If any response option requires text to be collected and does not need another question label, show **[FREE TEXT]** after the response option~~.~~, if applicable.

Response options for questions that allow only one response must be indicated with radio buttons (○).

If any response option requires text to be collected and does not need another question label, show **[FREE TEXT]** after the response option, if applicable.

[FREE TEXT] indicates to the programmer that one line should be provided for data entry.

[MULTILINE INPUT] indicates to the programmer that multiple lines should be provided for data entry (for example, two address lines).

[DROP-DOWN LIST INPUT WITH STATES TABLE] indicates to the programmer that the response should be a drop-down list containing the states in the table below.

Alabama	Georgia	Massachusetts	New York	Tennessee
Alaska	Guam	Michigan	North Carolina	Texas
American Samoa	Hawaii	Minnesota	North Dakota	US Virgin Islands
Arizona	Idaho	Mississippi	Northern Mariana Islands	Utah
Arkansas	Illinois	Missouri	Ohio	Vermont
California	Indiana	Montana	Oklahoma	Virginia
Colorado	Iowa	Nebraska	Oregon	Washington
Connecticut	Kansas	Nevada	Pennsylvania	West Virginia
Delaware	Kentucky	New Hampshire	Puerto Rico	Wisconsin
District of Columbia	Louisiana	New Jersey	Rhode Island	Wyoming
Florida	Maine	New Mexico	South Carolina	
	Maryland		South Dakota	

The following is used to categorize survey populations into standard geographic regions but it is not displayed in the survey.

Geographic Distribution (based on address) [1]: Northeast, Midwest, South, and West regions

Survey Legend

Northeast Region

- New England Division - ME, NH, VT, MA, RI, CT
- Middle Atlantic Division - NY, NJ, PA

Midwest Region

- East North Central Division - OH, IN, IL, MI, WI
- West North Central Division - MN, IA, MO, ND, SD, NE, KS

South Region

- South Atlantic Division - DE, MD, DC, VA, WV, NC, SC, GA, FL
- East South Central Division - KY, TN, AL, MS
- West South Central Division - AR, LA, OK, TX

West

- Mountain Division - MT, ID, WY, CO, NM, AZ, UT, NV
- Pacific Division WA, OR, CA, AK, HI

The following US territories are categorized as **Other**: Puerto Rico, Northern Mariana Islands, US Virgin Islands, American Samoa, and Guam.

[1] U.S. Census Bureau, last revised Friday, 27-Jul-2001 12:59:43 EDT.

[BEGIN SURVEY CONTENT]

[BEGIN ONLINE PREAMBLE 1]

Before you begin, we would like to share some important information about this survey. The survey is being conducted by UBC on behalf of the Transmucosal Immediate Release Fentanyl (TIRF) Risk Evaluation and Mitigation Strategy (REMS) Access ~~Program (“~~program (TIRF REMS Access ~~Program”~~program or Program), sponsors of which include the makers of Abstral®, Actiq®, Fentora®, Lazanda®, Subsys® and the generic versions of any of these brands. These TIRF Medicines are also known as rapid onset opioids ~~(~~and sometimes called ~~“~~fast acting fentanyls~~”).~~ Please note that references to the TIRF REMS Access ~~Program~~program in this introduction include the sponsors of the Program, as well as its retained agents or contractors, including UBC.

The information collected will help the makers of TIRF Medicines know if patients and their caregivers understand important information about taking these medicines. The survey will take about 20 minutes.

There are no known risks to you in taking this survey. You may refuse to take part or withdraw at any time without penalty or loss of benefits to which you are otherwise entitled. Your answers to the questions or your decision to take part in the survey will not affect your ability to receive or take TIRF Medicines.

How We Use Your Information

The terms of the TIRF REMS Access ~~Program~~program Patient-Prescriber Agreement Form (PPAF) on file and the Patient Privacy Notice contained therein, provide that the TIRF REMS Access ~~Program~~program may receive, use, and share your health information, using a unique identifier instead of your name, in order to evaluate the proper use of TIRF Medicines and report to the Food and Drug Administration (FDA) about the effectiveness of the Program. Should you choose to participate in the survey, you agree that any information you provide during the course of the survey may be used or shared with the TIRF REMS Access ~~Program~~program according to these terms.

Your answers to the survey questions will be combined with answers given by other people taking the survey. All answers will be collected by UBC, compiled, and reported in anonymous form to the TIRF REMS Access ~~Program~~program and the FDA. Your name will not be used in any report. If you are eligible to take the survey, complete all the questions, and provide your contact information, you will receive a $50 gift card for your time.

Your name and address will be received only by UBC and will be used only to send you the gift card, a Thank You Letter, a product-specific Medication Guide, and a copy of the correct answers to key risk message questions, after you complete the survey.

Providing a telephone number is optional. Your telephone number will be used only if there are any questions about your answers.

How We Protect Your Privacy

We respect that the privacy of your personal information is important to you. You will not be contacted for marketing purposes based on your personal information or your answers to the survey. The TIRF REMS Access ~~Program~~program will not sell, transfer (except in connection with reporting to the FDA), or rent your information. Your privacy will be protected; however, research survey records may be inspected by the FDA and a company called Sterling Independent Services, Inc., which is the Institutional Review Board (IRB) that looks out for the interest of survey participants. Your choice to allow the TIRF REMS Access ~~Program~~program to use your information is entirely voluntary, but necessary to take part in this survey.

Please be assured that your contact information and your individual responses will be kept strictly confidential. As noted above, however, information you provide will be combined with information and survey responses provided by others and shared or reported in anonymous form. By participating in the survey, you acknowledge and agree that such combined anonymous data may be used by the TIRF REMS Access ~~Program~~program and disclosed to the FDA. By participating, you also acknowledge that the FDA and/or IRB, may inspect the records related to this survey which may include your individual responses.

If you have questions about your rights as a research participant or related concerns, you may contact the IRB at 1-888-636-1062. Be sure to write down this telephone number; it will not be displayed again.

How to Learn More About This Survey

If you have questions about the survey, or have any problems with the survey, please contact the Survey Coordinating Center at 1-877-379-3297.

The information in this survey should not take the place of talking with your doctor or health care professional. If you have any questions about your condition or treatment or that of the person you care for, or if you would like more information about TIRF Medicines, talk to your doctor, pharmacist, or other health care professional.

Once you have answered a question and moved on, you cannot go back and change your answers.

Thank you for your participation in this survey.

[END ONLINE PREAMBLE 1]

[BEGIN PHONE PREAMBLE 1]

Before you begin, we would like to share some important information about this survey. The survey is being conducted by UBC on behalf of the Transmucosal Immediate Release Fentanyl (TIRF) Risk Evaluation and Mitigation Strategy (REMS) Access ~~Program (~~"program (TIRF REMS Access ~~Program"~~program or Program) sponsors of which include the makers of Abstral®, Actiq®, Fentora®, Lazanda®, Subsys® and the generic versions of any of these brands. These TIRF **(INTERVIEWER: Pronounce "TIRF," then spell out T-I-R-F)** Medicines~~,~~ are also known as rapid onset opioids **(INTERVIEWER: Please pause briefly)** ~~(~~and sometimes called ~~"~~"fast acting fentanyls~~") or TIRF Medicines.~~. Please note that references to the TIRF REMS Access ~~Program~~program in this introduction include the sponsors of the Program, as well as its retained agents or contractors, including UBC.

~~**(INTERVIEWER: Pronounce "TIRF," then spell out T-I-R-F).**~~

The information collected will help the makers of TIRF Medicines know if patients and their caregivers understand important information about taking these medicines. The survey will take about 20 minutes.

There are no known risks to you in taking this survey. You may refuse to take part or withdraw at any time without penalty or loss of benefits to which you are otherwise entitled. Your answers to the questions or your decision to take part in the survey will not affect your ability to receive or take TIRF Medicines.

Now I would like to tell you about how your contact information will be used.

The terms of the TIRF REMS Access ~~Program~~program Patient-Prescriber Agreement Form (PPAF) on file and the Patient Privacy Notice contained therein, provide that the TIRF REMS Access ~~Program~~program may receive, use, and share your health information, using a unique identifier instead of your name, in order to evaluate the proper use of TIRF Medicines and report to the Food and Drug Administration (FDA) about the effectiveness of the Program. Should you choose to participate in the survey, you agree that any information you provide during the course of the survey may be used or shared with the TIRF REMS Access ~~Program~~program according to these terms.

Your answers to the survey questions will be combined with answers given by other people taking the survey. All answers will be collected by UBC, compiled, and reported in anonymous form to the TIRF REMS Access ~~Program~~program and the FDA. Your name will not be used in any report. If you are eligible to take the survey, complete all the questions, and provide your contact information, you will receive a $50 gift card for your time.

Your name and address will be received only by UBC and will be used only to send you the gift card, a Thank You Letter, a product-specific Medication Guide, and a copy of the correct answers to key risk message questions, after you complete the survey.

Providing a telephone number is optional. Your telephone number will be used only if there are any questions about your answers.

Now I would like to tell you about how we protect your privacy.

We respect that the privacy of your personal information is important to you. You will not be contacted for marketing purposes based on your personal information or your answers to the survey. The TIRF REMS Access ~~Program~~program will not sell, transfer (except in connection with reporting to the FDA), or rent your information. Your privacy will be protected; however, research survey records may be inspected by the FDA and a company called Sterling Independent Services, Inc., which is the Institutional Review Board (IRB) that looks out for the interest of survey participants. Your choice to allow the TIRF REMS Access ~~Program~~program to use your information is entirely voluntary, but necessary to take part in this survey.

Please be assured that your contact information~~,~~ and your individual responses will be kept strictly confidential. As noted above, however, information you provide will be combined with information and survey responses provided by others and shared or reported in anonymous form. By participating in the survey, you acknowledge and agree that such combined anonymous data may be used by the TIRF REMS Access ~~Program~~program and disclosed to the FDA. By participating, you also acknowledge that the FDA and/or IRB~~,~~ may inspect the records related to this survey which may include your individual responses.

If you have questions about your rights as a research participant or related concerns, you may contact the IRB at 1-888-636-1062.

The information in this survey should not take the place of talking with your doctor or health care professional. If you have any questions about your condition or treatment or that of the person you care for, or if you would like more information about TIRF Medicines, talk to your doctor, pharmacist, or other health care professional.

Please feel free to ask me to repeat any questions or statements as we go through the survey.

Once you have answered a question and moved on, you cannot go back and change your answers.

Thank you for your participation in this survey.

[END PHONE PREAMBLE 1]

[BEGIN INCLUSION/EXCLUSION QUESTIONS]

1. Do you agree to take part in this survey?

   - ○ Yes
   - ○ No **[TERMINATE]**

2. Within the last 4 months (120 days), have you filled a prescription for yourself for a transmucosal immediate release fentanyl medicine (known as "TIRF medicines")? TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Subsys®, and the generic versions of any of these brands.

   - ○ Yes **[GO TO Q4]**
   - ○ No
   - ○ I don't know

3. Are you a caregiver for someone who has filled a prescription for a TIRF medicine within the last 4 months (120 days)? TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Subsys® and the generic versions of any of these brands.

   - ○ Yes
   - ○ No **[TERMINATE]**
   - ○ I don't know **[TERMINATE]**

4. **[PATIENT]** For which TIRF medicines have you filled a prescription in the last 4 months (120 days)? Please select all that apply.

[CAREGIVER] For which TIRF medicines has the person you care for filled a prescription in the last 4 months (120 days)? Please select all that apply.

- ☐ Abstral
- ☐ Actiq, including generic versions of Actiq
- ☐ Fentora
- ☐ Lazanda
- ☐ Subsys
- ☐ Other
- ☐ I don't know **[CLEAR ALL OTHER SELECTIONS]**

5. Have you ever taken part in a survey about a TIRF medicine before?

- ○ Yes **[TERMINATE]**
- ○ No
- ○ I don't know **[TERMINATE]**

6. Which of the following groups best describes your age?

- ○ Under 18 **[TERMINATE]**
- ○ 18 29
- ○ 30 39
- ○ 40 49
- ○ 50 59
- ○ 60 69
- ○ 70 or older
- ○ Prefer not to answer **[TERMINATE]**

7. **[CAREGIVER]** Which of the following groups best describes the patient's age?

- ○ Under 16
- ○ 16 29
- ○ 30 39
- ○ 40 49
- ○ 50 59
- ○ 60 69
- ○ 70 or older
- ○ Prefer not to answer **[TERMINATE]**

8. Have you or any of your immediate family members ever worked for any of the following companies or agencies? Please select all that apply.

- ☐ Actavis Laboratories FL, Inc. **[TERMINATE]**
- ☐ Anesta LLC **[TERMINATE]**
- ☐ BioDelivery Services International (BDSI) **[TERMINATE]**
- ☐ Cephalon, Inc. (a wholly-owned subsidiary of Teva Pharmaceutical Industries, Ltd.) **[TERMINATE]**
- ☐ Depomed, Inc. **[TERMINATE]**
- ☐ Galena Biopharma, Inc. **[TERMINATE]**
- ☐ Insys Therapeutics, Inc. **[TERMINATE]**
- ☐ Mallinckrodt Pharmaceuticals **[TERMINATE]**
- ☐ McKesson Specialty Care Solutions **[TERMINATE]**
- ☐ Mylan~~,~~ Inc. **[TERMINATE]**
- ☐ Par ~~Pharmaceutical~~Pharmaceuticals, Inc. **[TERMINATE]**
- ☐ RelayHealth**[TERMINATE]**
- ☐ Sentynl Therapeutics, Inc. **[TERMINATE]**
- ☐ Teva Pharmaceuticals, Ltd. **[TERMINATE]**
- ☐ United BioSource Corporation **[TERMINATE]**
- ☐ FDA (Food and Drug Administration) **[TERMINATE]**
- ☐ No **[IF SELECTED IN ADDITION TO OTHER RESPONSES, TERMINATE]**
- ☐ I don't know **[TERMINATE]**

[END INCLUSION/EXCLUSION QUESTIONS]

[BEGIN PREAMBLE 2 - DISPLAY ON SAME PAGE WITH NEXT QUESTION]

[BEGIN PATIENT] Please answer the following questions based on information about the TIRF medicine that was most recently prescribed for you. TIRF medicines include

Abstral®, Actiq®, Fentora®, Lazanda®, Subsys®, and the generic versions of these brands. Please think of the information that you read or that was provided to you by a doctor, nurse, or other healthcare professional. If you don't know the answers to any of the following questions please respond "I don't know" instead of guessing the correct responses.

[END PATIENT]

[BEGIN CAREGIVER] Please answer the following questions based on information about the TIRF medicine that was most recently prescribed for the patient. TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Subsys®, and the generic versions of these brands. Please think of the information that you read or that was provided to you or to the patient by a doctor, nurse, or other healthcare professional. If you don't know the answers to any of the following questions please respond "I don't know" instead of guessing the correct responses.

[END CAREGIVER]

[END PREAMBLE 2]

9. **[PATIENT]** Did ~~the~~a doctor, nurse, or other healthcare professional in the doctor's office ever talk to you about the risks and possible side effects of the TIRF medicine that was most recently prescribed for you? TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Subsys®, and the generic versions of these brands.

[CAREGIVER] Did ~~the~~a doctor, nurse, or other healthcare professional in the doctor's office ever talk to you about the risks and possible side effects of the TIRF medicine that was most recently prescribed to the patient? TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Subsys®, and the generic versions of these brands.

- ○ Yes
- ○ No
- ○ I don't know

10. **[PATIENT]** For which of the following conditions should you use a TIRF medicine? Please answer Yes, No, or I don't know for each statement.

[CAREGIVER] For which of the following conditions should the person you take care of use a TIRF medicine? Please answer Yes, No, or I don't know for each statement.

[RANDOMIZE LIST]	**Yes**	**No**	**I don't know**
10a. Headache or migraine pain	○	○	○
10b. Breakthrough pain from cancer	○	○	○
10c. Dental pain	○	○	○
10d. Pain after surgery	○	○	○
10e. Long-lasting pain not from cancer, like arthritis joint pain	○	○	○

11. Please answer True, False, or I don't know for the following statement:

TIRF medicines should only be taken by ~~cancer~~ patients who are opioid tolerant.

- ○ True
- ○ False
- ○ I don't know

12. Please answer True, False, or I don't know for each of the following statements.

[RANDOMIZE LIST]	**True**	**False**	**I don't know**
12a. Opioid tolerant means that a patient is already taking other opioid pain medicines around-the-clock and their body is used to these medicines.	○	○	○
12b. A patient must stop taking their TIRF medicine if they stop taking their around-the-clock opioid pain medicine.	○	○	○
12c. It is safe to switch to another medicine that contains fentanyl without talking to a healthcare provider first.	○	○	○
12d. A patient may give TIRF medicines to another person if	○	○	○

they have the same symptoms as the patient.

13. **[PATIENT]** Please answer True, False, or I don't know for each statement about the TIRF medicine that was most recently prescribed for you.

[CAREGIVER] Please answer True, False, or I don't know for each statement about the TIRF medicine that was most recently prescribed for the patient.

	[RANDOMIZE LIST]	**True**	**False**	**I don't know**
13a.	TIRF medicines should be stored in a safe place out of the reach of children.	○	○	○
13b.	It is OK for patients to take TIRF medicines for headache pain.	○	○	○
13c.	TIRF medicines should be taken exactly as prescribed by the doctor.	○	○	○
13d.	TIRF medicines can cause life-threatening breathing problems that can lead to death.	○	○	○

14. What should you do if an adult who has not been prescribed a TIRF medicine takes a TIRF medicine? (Please select one.)

[RANDOMIZE LIST]

- ○ Wait an hour and see if the person is OK.
- ○ Get emergency help right away.
- ○ Do nothing.
- ○ I don't know.

15. **[PATIENT]** Did ~~the~~a doctor, nurse, or other healthcare professional in the doctor's office ever tell you how to use the TIRF medicine that was most recently prescribed for you?

[CAREGIVER] Did ~~the~~a doctor, nurse, or other healthcare professional in the doctor's office ever tell you how to use the TIRF medicine that was most recently prescribed for the patient?

- Yes
- No
- I don't know

16. **[PATIENT]** Did ~~the~~a doctor, nurse, or other healthcare professional in the doctor's office ever tell you how to store or keep the TIRF medicine that was most recently prescribed for you?

[CAREGIVER] Did ~~the~~a doctor, nurse, or other healthcare professional in the doctor's office ever tell you how to store or keep the TIRF medicine that was most recently prescribed for the patient?

- Yes
- No
- I don't know

17. **[PATIENT]** Please answer True, False, or I don't know for each statement about the TIRF medicine that was most recently prescribed for you.

[CAREGIVER] Please answer True, False, or I don't know for each statement about the TIRF medicine that was most recently prescribed for the patient.

	[RANDOMIZE LIST]	**True**	**False**	**I don't know**
17a.	Selling or giving away TIRF medicines is against the law.	○	○	○
17b.	It is OK to take TIRF medicines for short-term pain that will go away in a few days.	○	○	○
17c.	TIRF medicines must be disposed of as described in the specific product's Medication Guide.	○	○	○
17d.	TIRF medicines are only available to patients through a pharmacy enrolled in a special program (called the TIRF REMS Access ~~Program~~program).	○	○	○
17e.	A TIRF medicine can cause an overdose and death in any child who takes it.	○	○	○

18. **[PATIENT]** Please answer True, False, or I don't know for each statement about the TIRF medicine that was most recently prescribed for you.

[CAREGIVER] Please answer True, False, or I don't know for each statement about the TIRF medicine that was most recently prescribed for the patient.

	[RANDOMIZE LIST]	**True**	**False**	**I don't know**
18a.	A side effect of TIRF medicines is the chance of abuse or addiction.	○	○	○
18b.	TIRF medicines can be misused by people who abuse prescription medicines or street drugs.	○	○	○
18c.	TIRF medicines should be kept in a safe place to prevent it from being stolen.	○	○	○

[BEGIN PREAMBLE 3 - DISPLAY ON SAME PAGE WITH NEXT QUESTION]

[BEGIN PATIENT] The next set of questions is about the Medication Guide for the TIRF medicine that was most recently prescribed for you.

[END PATIENT]

[BEGIN CAREGIVER] The next set of questions is about the Medication Guide for the TIRF medicine that was most recently prescribed for the patient.

[END CAREGIVER]

A Medication Guide is a paper handout that contains important information about the risks associated with the use of a TIRF medicine and how to use it safely. Medication Guides always include the title "Medication Guide" followed by the name of the medicine and its pronunciation. The Medication Guide usually has a section titled "What is the most important information I should know?" The Medication Guide is in a question-and-answer format and may be given to you by your pharmacist, doctor, or other healthcare professional.

[END PREAMBLE 3]

~~18.~~19 **[PATIENT]** Have you ever received a Medication Guide for the TIRF medicine that was prescribed for you?

[CAREGIVER] Have you or the patient ever received a Medication Guide for the TIRF medicine that was prescribed for the patient?

- ○ Yes
- ○ No -**[GO TO PREAMBLE 4]**
- ○ I don't know **[GO TO PREAMBLE 4]**

~~19.~~20 **[PATIENT]** Did you receive the Medication Guide from the doctor who prescribed the TIRF medicine or someone in the doctor's office?

[CAREGIVER] Did you or the patient receive the Medication Guide from the doctor who prescribed the TIRF medicine or someone in the doctor's office?

- ○ Yes
- ○ No -**[GO TO ~~Q21~~Q22]**
- ○ I don't know **[GO TO ~~Q21~~Q22]**

~~20.~~21 **[PATIENT]** When was the Medication Guide given to you? Please select all that apply.

[CAREGIVER] When was the Medication Guide given to you or the patient? Please select all that apply.

- ☐ At the first appointment with the doctor who prescribed the TIRF medicine
- ☐ At the last appointment with the doctor who prescribed the TIRF medicine
- ☐ I don't remember **[CLEAR ALL OTHER SELECTIONS]**

~~21.~~22 **[PATIENT]** Did you receive the Medication Guide for the TIRF medicine from the pharmacy?

[CAREGIVER] Did you or the patient receive the Medication Guide for the TIRF medicine from the pharmacy?

- Yes
- No -**[GO TO ~~Q23~~Q24]**
- I don't know **[GO TO ~~Q23~~Q24]**

~~22.~~23 **[PATIENT]** How frequently do you receive a Medication Guide for the TIRF medicine at the pharmacy?

[CAREGIVER] How frequently do you or the patient receive a Medication Guide for the TIRF medicine at the pharmacy?

- Only with the first filled prescription
- Each time a prescription is filled
- Other (please specify): **[FREE TEXT]**
- I don't know

~~23.~~24 Did you read the Medication Guide?

- Yes
- No **[GO TO ~~Q26~~Q27]**
- I don't know **[GO TO ~~Q26~~Q27]**

~~24.~~25 How much did you read?

- All of it
- Most of it
- Some of it
- I don't know

~~25.~~26. How much of the Medication Guide did you understand?

- ○ All of it
- ○ Most of it
- ○ Some of it
- ○ None of it
- ○ I don't know

~~26.~~27. Did someone offer to explain the Medication Guide to you?

- ○ Yes
- ○ No **[GO TO ~~Q30~~Q31]**
- ○ I don't know **[GO TO ~~Q30~~Q31]**

~~27.~~28. Who offered to explain the Medication Guide to you? Please select all that apply.

- □ The doctor or another healthcare professional in the doctor's office
- □ The pharmacist where the TIRF medicine prescription was filled
- □ Someone else **[IF SELECTED, SHOW THE FOLLOWING ON THE SAME PAGE:]**

  Specify the type of person but not his/her name:

  [FREE TEXT]

~~28.~~29. Did you accept the offer to have the Medication Guide explained to you?

- ○ Yes
- ○ No **[GO TO ~~Q30~~Q31]**
- ○ I don't know **[GO TO ~~Q30~~Q31]**

~~29.~~30. How much of the explanation did you understand?

- ○ All of it
- ○ Most of it
- ○ Some of it
- ○ None of it
- ○ I don't know

~~30.~~31. Did you or do you have any questions about the information in the Medication Guide?

- ○ Yes
- ○ No **[GO TO PREAMBLE 4]**
- ○ I don't know **[GO TO PREAMBLE 4]**

[IF QUESTION ~~30~~31 YES, DISPLAY ~~Q31~~Q32 ON SAME PAGE]

~~31.~~32. What are your questions? **[MULTILINE INPUT]**

[BEGIN PREAMBLE 4 – DISPLAY ON SAME PAGE AS NEXT QUESTION]

The next set of questions is about the Patient-Prescriber Agreement Form for TIRF medicines. As a reminder, TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Subsys®, and the generic versions of any of these brands. The Patient-Prescriber Agreement is a form that is signed by the doctor and the patient or their caregiver. This form may also be referred to as the Prescriber-Patient Agreement.

[END PREAMBLE 4]

~~32.~~33. Did the doctor or someone in the doctor's office explain the Patient-Prescriber Agreement Form to you?

- ○ Yes
- ○ No **[GO TO ~~Q34~~Q35]**
- ○ I don't know **[GO TO ~~Q34~~Q35]**

~~33.~~34. How much of the explanation did you understand?

- ○ All of it
- ○ Most of it
- ○ Some of it
- ○ None of it
- ○ I don't know

~~34.~~35. **[PATIENT]** Did you sign a Patient-Prescriber Agreement Form?

[CAREGIVER] Did you or the person you are caring for sign a Patient-Prescriber Agreement Form?

- ○ Yes
- ○ No **[GO TO ~~DEMOGRAPHICS~~ PREAMBLE 5]**
- ○ I don't know **[GO TO ~~DEMOGRAPHICS~~ PREAMBLE 5]**

~~35.~~36. Did the doctor or someone in the doctor's office give you a copy of the signed Patient-Prescriber Agreement Form?

- ○ Yes
- ○ No
- ○ I don't know

[BEGIN PREAMBLE 5 – DISPLAY ON SAME PAGE AS NEXT QUESTION]

[BEGIN PATIENT] Please answer the following questions based on the conversation you had with your doctor, nurse, or other healthcare professional in your doctor's office. If you don't know the answers to any of the following questions please respond "I don't know" instead of guessing the correct responses.

[END PATIENT]

[BEGIN CAREGIVER] Please answer the following questions based on the conversation you had with the patient's doctor, nurse, or other healthcare professional in the doctor's office. If you don't know the answers to any of the following questions please respond "I don't know" instead of guessing the correct responses.

[END CAREGIVER]

[END PREAMBLE 5]

37. **[PATIENT]** Did a doctor, nurse, or other healthcare professional in the doctor's office ever ask you about the presence of children in your home?

[CAREGIVER] Did a doctor, nurse, or other healthcare professional in the doctor's office ever ask you about the presence of children in the patient's home?

- ○ Yes
- ○ No
- ○ I don't know

38. **[PATIENT]** Did a doctor, nurse, or other healthcare professional in the doctor's office ever tell you not to share the TIRF medicines with anyone else?

[CAREGIVER] Did a doctor, nurse, or other healthcare professional in the doctor's office ever tell you and the patient not to share the TIRF medicines with anyone else ?

- ○ Yes
- ○ No
- ○ I don't know

39. **[PATIENT]** Did a doctor, nurse, or other healthcare professional in the doctor's office ever counsel you that accidental exposure to TIRF medicines by a child may be fatal ?

[CAREGIVER] Did a doctor, nurse, or other healthcare professional in the doctor's office ever counsel you and the patient that accidental exposure to TIRF medicines by a child may be fatal ?

- ○ Yes
- ○ No
- ○ I don't know

40. **[PATIENT]** Did a doctor, nurse, or other healthcare professional in the doctor's office ever tell you to keep TIRF medicines out of reach of children to prevent accidental exposure?

[CAREGIVER] Did a doctor, nurse, or other healthcare professional in the doctor's office ever tell you and the patient to keep TIRF medicines out of reach of children to prevent accidental exposure ?

- ○ Yes
- ○ No
- ○ I don't know

41. **[PATIENT]** Did a doctor, nurse, or other healthcare professional in the doctor's office ever tell you about proper disposal of any unused or partially used TIRF medicines?

[CAREGIVER] Did a doctor, nurse, or other healthcare professional in the doctor's office ever tell you and the patient about proper disposal of any unused or partially used TIRF medicine?

- ○ Yes
- ○ No
- ○ I don't know

[BEGIN DEMOGRAPHICS PREAMBLE - DISPLAY ON SAME PAGE AS NEXT QUESTION]

There are just a few more questions to help us combine your answers with other answers we have received.

[END DEMOGRAPHICS PREAMBLE]

~~36.~~42. What is your gender?

- ○ Male
- ○ Female
- ○ Prefer not to answer

~~37.~~43. What is the highest level of education you have completed?

- ○ Less than high school
- ○ Some high school
- ○ High school graduate/GED
- ○ Some college
- ○ ~~Some college~~/Associate's degree
- ○ Bachelor's degree
- ○ Master's degree
- ○ Professional or Doctoral degree
- ○ Prefer not to answer

~~38.~~44. What is the main language you speak at home?

- English
- French
- Spanish
- Portuguese
- Italian
- German
- Chinese
- Japanese
- Korean
- Other
- Prefer not to answer

~~39.~~45. Are you Hispanic or Latino?

- Yes
- No
- Prefer not to answer

~~40.~~46. For informational purposes only, which of the following U.S. census categories best describes your race?

- ○ American Indian or Alaska Native
- ○ Asian (origins of Far East, Southeast Asia or the Indian subcontinent)
- ○ Black or African American
- ○ Native Hawaiian or Other Pacific Islander
- ○ White
- ○ Two or more races
- ○ Other
- ○ Prefer not to answer

~~41.~~47. In which state do you live?

[DROP-DOWN LIST INPUT WITH STATES TABLE WITH "Prefer not to answer" AT END]

[PHONE - BEGIN ADVERSE EVENT/PRODUCT COMPLAINT – KEEP ON ONE PAGE]

(INTERVIEWER: Please record if respondent spontaneously reported an adverse event or product complaint during the course of this interview.)

- ○ Yes
- ○ No **[GO TO CLOSING 1]**

Enter Safety Adverse Event Verbatim

[MULTILINE INPUT]

(INTERVIEWER: Indicate to the respondent that someone may call back to ask more questions about the adverse event or product complaint that was reported.)

[END ADVERSE EVENT/PRODUCT COMPLAINT]

[BEGIN CLOSING 1 – KEEP ON ONE PAGE]

You are eligible to receive a $50 gift card for your time completing the survey. In order to receive the gift card, we need to collect your name and address so that we can mail it to you. If you do not provide your name and address you will not receive the gift card for your time taking the survey.

Do you agree to give us your name and mailing address so we can send your payment?

- ○ Yes
- ○ No **[GO TO CLOSING 2]**

FIRST NAME: [**FREE TEXT]**

LAST NAME: [**FREE TEXT]**

ADDRESS: **[MULTILINE INPUT]**

CITY: [**FREE TEXT]**

STATE: **[DROP-DOWN LIST INPUT WITH STATES TABLE]**

ZIP: **[MUST BE 5 DIGIT NUMERIC-ONLY CHARACTERS]**

[END CLOSING 1]

[BEGIN CLOSING 2 – KEEP ON ONE PAGE]

We would also like to ask for your telephone number. Providing your telephone number is optional and it will be used to contact you only if there are questions about your survey responses.

Do you want to provide your telephone number?

○ Yes

○ No **[GO TO CLOSING 3]**

Telephone: **[MUST BE 10-DIGIT NUMERIC-ONLY CHARACTERS]**

[END CLOSING 2]

[BEGIN CLOSING 3]

This is the end of the survey. If you have questions about the survey, please contact the Survey Coordinating Center at 1-877-379-3297. Thank you again for your help.

[END CLOSING 3]

[END SURVEY CONTENT]

APPENDIX B ~~SAMPLE Patient Letter of Invitation~~ Recruitment Letters

INVITATION LETTER

[CURR_DATE]
[PAT_FIRST_NAME] [PAT_LAST_NAME
] ~~[CURR_DATE]~~
[PAT_STREET_ADDR]
[PAT_CITY], [PAT_STATE] [PAT_ZIP]

Dear [PAT_FULL_NAME]:

~~Thank you for choosing [pharmacy partner or PBM name] for your prescription needs. The purpose of this letter is to inform you about a voluntary research survey being conducted by [COMPANY], the maker of [BRAND_GENERIC].~~
We are contacting you in connection with managing your participation in the Transmucosal Immediate Release Fentanyl (TIRF) Risk Evaluation and Mitigation Strategy (REMS) Access Program (TIRF REMS Access program or the Program). As you know, the TIRF REMS Access program is an FDA (Food and Drug Administration) required program designed to ensure appropriate use of TIRF medicines and to mitigate the risk of misuse, abuse, addiction, overdose and serious complications with the use of certain TIRF Medicines (Abstral®, Actiq®, Fentora®, Lazanda®, Subsys® and the generic versions of any of these brands). *References in this letter to the TIRF REMS Access program (Program) include the sponsors of the Program, as well as agents or contractors retained by the Program.*

As part of your participation in the TIRF REMS Access program, we would like to inform you of a voluntary research survey being conducted by the Program. The survey is part of an FDA requirement to find out if patients and/or their caregivers understand important safety information about ~~[BRAND]~~TIRF Medicines. Express Scripts and ~~other medicines like it. The first~~its subsidiary UBC have been retained by the Program to identify 300 people ~~who~~to complete this 20-minute survey~~ and provide their contact information~~. Eligible individuals who complete the survey will ~~receive~~be sent a $50 ~~[pharmacy partner or PBM name]~~ gift card ~~from [COMPANY]~~ to thank them for their time.

The terms of the TIRF REMS Access program Patient-Prescriber Agreement Form (PPAF) on file and the Patient Privacy Notice contained therein, provide that the TIRF REMS Access program may receive, use, and share your health information, using a unique identifier instead of your name, in order to evaluate the proper use of TIRF Medicines and report to the FDA about the effectiveness of the Program. Should you choose to participate in the survey, you agree that any information you provide during the course of the survey may be used by or shared with the TIRF REMS Access program according to these terms. You acknowledge, however, that should you choose to provide UBC with your name and contact information so that you may receive the $50 gift card for your time, UBC may use your name and contact

information for that purpose. Please be assured that your contact information and your individual responses will be kept strictly confidential. Any information you provide may, however, be combined with information and survey responses provided by others and shared or reported in anonymous form. By participating in the survey, you acknowledge and agree that such combined anonymous data may be used by the TIRF REMS Access program and disclosed to the FDA. By participating, you also acknowledge that the FDA as well as a company called Sterling Independent Services, Inc., which is the Institutional Review Board (IRB) that looks out for the interest of survey participants, may inspect the records related to this survey which may include your individual responses.

You may be eligible to take part in the survey if you have taken ~~[BRAND]~~a TIRF Medicine and are 18 years of age or older. If you are unable to take the survey yourself, a caregiver who is 18 or older may be eligible to take the survey for you. The survey asks questions about the type of information you received about ~~[BRAND]~~the TIRF Medicine you have taken and where and how you ~~get~~receive your medical information.

If you are interested in participating and to find out if you are eligible:

- Go online* to www~~.TIRFREMSsurvey.com~~.TIRFREMSsurvey.com any time or
- ~~Call 877-379-3297, 8 a.m. to 8 p.m. Eastern Time, Monday through Friday~~

~~Please have this letter with you at the time you take the survey. You will be asked to provide this code prior to starting the survey: **[CODE_ID]**.~~

- ~~***It is recommended***~~Call toll-free 1-877-379-3297, 8 a.m. to 8 p.m. Eastern Time, Monday through Friday

Please have this letter with you at the time you take the survey. You will be asked to provide this code prior to starting the survey: **[CODE_ID]**.

***Please note** that you **should** take the survey on a desktop or laptop computer. Taking the survey on mobile devices, such as smart phones, tablets, and e-notebooks, is not supported.*

~~(over, please)~~

You are not required to take part in this survey. If you choose to ~~take part, please be assured that your contact information and your individual responses will be kept strictly confidential. You~~ participate in the survey, you will not be ~~asked~~required to identify yourself ~~to participate in the survey.~~. However, if you wish to receive the $50 gift card from ~~[COMPANY],~~the TIRF REMS Access program, you must provide your name and contact information for delivery. ~~Your answers to the survey questions will be combined with answers given by others, and your name will not be used in any written report or publication.~~ Neither taking the survey nor your answers to the questions will affect your ability to receive or take ~~[BRAND].~~a TIRF Medicine.

~~Sincerely,~~

~~[Pharmacy partner or PBM name]~~

~~[COMPANY] funded the cost of the gift card, the cost of mailing this letter and paid a fee to [pharmacy partner or PBM name]. The research study is not being conducted by [pharmacy partner or PBM name]. No information that can identify you, your medication, or your health condition will be provided by [pharmacy partner or PBM name] to [COMPANY]. This letter provides information about a drug prescribed by your doctor and is not a recommendation by [pharmacy partner or PBM name] to use a particular drug for your condition. Call [pharmacy partner or PBM name] toll free at xxx-xxx-xxxx if you do not wish to continue receiving mailings about [BRAND] from [pharmacy partner or PBM name].~~

Sincerely,
The TIRF REMS Survey Team
1-877-379-3297
www.TIRFREMSsurvey.com

REMINDER LETTER

[CURR_DATE]

[PAT_FIRST_NAME] [PAT_LAST_NAME]
[PAT_STREET_ADDR]
[PAT_CITY], [PAT_STATE] [PAT_ZIP]

Dear [PAT_FULL_NAME]:

We recently sent you a letter in connection with managing your participation in the Transmucosal Immediate Release Fentanyl (TIRF) Risk Evaluation and Mitigation Strategy (REMS) Access program (TIRF REMS Access Program or the Program). As you know, the TIRF REMS Access program is an FDA (Food and Drug Administration) required program designed to ensure appropriate use of TIRF medicines and to mitigate the risk of misuse, abuse, addiction, overdose and serious complications with the use of certain TIRF Medicines (Abstral®, Actiq®, Fentora®, Lazanda®, Subsys® and the generic versions of any of these brands). *References in this letter to the TIRF REMS Access program or Program include the sponsors of the Program, as well as agents or contractors retained by the Program.*

As part of your participation in the TIRF REMS Access program, we would like to inform you of a voluntary research survey being conducted by the Program. The survey is part of an FDA requirement to find out if patients and/or their caregivers understand important safety information about TIRF Medicines. Express Scripts and its subsidiary UBC have been retained by the Program to identify 300 people to complete this 20-minute survey. Eligible individuals who complete the survey will be sent a $50 gift card to thank them for their time.

The terms of the TIRF REMS Access program Patient-Prescriber Agreement Form (PPAF) on file and the Patient Privacy Notice contained therein, provide that the TIRF REMS Access program may receive, use, and share your health information, using a unique identifier instead of your name, in order to evaluate the proper use of TIRF Medicines and report to the FDA about the effectiveness of the Program. Should you choose to participate in the survey, you agree that any information you provide during the course of the survey may be used by or shared with the TIRF REMS Access program according to these terms. You acknowledge, however, that should you choose to provide UBC with your name and contact information so that you may receive the $50 gift card for your time, UBC may use your name and contact information for that purpose. Please be assured that your contact information and your individual responses will be kept strictly confidential. Any information you provide may, however, be combined with information and survey responses provided by others and shared or reported in anonymous form. By participating in the survey, you acknowledge and agree that such combined anonymous data may be used by the TIRF REMS Access program and disclosed to the FDA. By participating, you also acknowledge that the FDA as well as a company called Sterling Independent Services, Inc., which is the Institutional Review Board

(IRB) that looks out for the interest of survey participants, may inspect the records related to this survey which may include your individual responses.

You may be eligible to take part in the survey if you have taken a TIRF Medicine and are 18 years of age or older. If you are unable to take the survey yourself, a caregiver who is 18 or older may be eligible to take the survey for you. The survey asks questions about the type of information you received about the TIRF Medicine you have taken and where and how you receive your medical information.

If you are interested in participating and to find out if you are eligible:

- Go online* to www.TIRFREMSsurvey.com any time or
- Call toll-free 1-877-379-3297, 8 a.m. to 8 p.m. Eastern Time, Monday through Friday

Please have this letter with you at the time you take the survey. You will be asked to provide this code prior to starting the survey: **[CODE_ID]**.

Please note that you should take the survey on a desktop or laptop computer. Taking the survey on mobile devices, such as smart phones, tablets, and e-notebooks, is not supported.

You are not required to take part in this survey. If you choose to participate in the survey, you will not be required to identify yourself. However, if you wish to receive the $50 gift card from TIRF REMS Access program, you must provide your name and contact information for delivery. Neither taking the survey nor your answers to the questions will affect your ability to receive or take a TIRF Medicine.

Sincerely,
The TIRF REMS Survey Team
1-877-379-3297
www.TIRFREMSsurvey.com

THANK YOU LETTER

[CURR_DATE]

[PAT_FIRST_NAME] [PAT_LAST_NAME]
[PAT_STREET_ADDR]
[PAT_CITY], [PAT_STATE] [PAT_ZIP]

Dear [PAT_FULL_NAME],

On behalf of the TIRF REMS Industry Group, we would like to thank you for taking the time to complete the TIRF Medicines Survey. Your participation helps us to meet the requirements from the FDA (Food and Drug Administration). To thank you for your time and participation, we have enclosed a $50 gift card.

Card Activation Instructions:
To prevent loss, the enclosed card is not activated. Prior to using your card, please call the TIRF Medicines Survey Team 1-877-379-3297 between 8:00 a.m. and 8:00 p.m. Eastern Time Monday through Friday to activate your card. Please have your card available when you make the call. Also, please read the enclosed Terms and Conditions document before using your gift card as well as the privacy policy that can be found at:
http://www.ctpayer.com/downloads/privacy_policy.pdf

Please note the enclosed gift card needs to be activated on or before **XX XXX XXXX**.

Additionally, for your information, we have enclosed the following two documents:

1. Medication Guide for [BRAND® (generic)]

2. The correct answers to survey questions about your medicine's key risks.

Sincerely,
The TIRF REMS Survey Team
1-877-379-3297

www.TIRFREMSsurvey.com

Enclosures: Gift Card with Terms and Conditions Document
Medication Guide for TIRF Medicines
Correct Answers to Important Survey Questions

APPENDIX C Correct Answer Document

Correct Responses to Select PATIENT Survey Questions about Important Safety Messages for Transmucosal Immediate Release Fentanyl (TIRF) medicines (TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Subsys®, and generic versions of any of these brands)

Q: Please answer True, False, or I don't know for each statement about the TIRF medicine that was most recently prescribed for you.

STATEMENT	DESIRED RESPONSE
TIRF medicines can cause life-threatening breathing problems that can lead to death.	**TRUE**
It is OK for patients to take TIRF medicines for headache pain.	**FALSE**
TIRF medicines should be taken exactly as prescribed by the doctor.	**TRUE**
It is OK to take TIRF medicines for short-term pain that will go away in a few days.	**FALSE**
Selling or giving away TIRF medicines is against the law.	**TRUE**
TIRF medicines should be stored in a safe place out of the reach of children.	**TRUE**
TIRF medicines must be disposed of as described in the specific product's Medication Guide.	**TRUE**
A TIRF medicine can cause an overdose and death in any child who takes it.	**TRUE**

Q: For which of the following conditions should you use a TIRF medicine? Please answer Yes, No, or I don't know for each statement.

STATEMENT	DESIRED RESPONSE
Headache or migraine pain	**NO**
Breakthrough pain from cancer	**YES**
Dental pain	**NO**
Pain after surgery	**NO**
Long-lasting pain not from cancer, like arthritis joint pain	**NO**

Q: What should you do if an adult who has not been prescribed a TIRF medicine takes a TIRF medicine? (Please select one.)

A: Get emergency help right away.

Q: Please answer True, False, or I don't know for each of the following statements:

STATEMENT	DESIRED RESPONSE
TIRF medicines should only be taken by patients who are opioid tolerant.	**TRUE**
Opioid tolerant means that a patient is already taking other opioid pain medicines around-the-clock and their body is used to these medicines.	**TRUE**
A patient must stop taking their TIRF medicine if they stop taking their around-the-clock opioid pain medicine.	**TRUE**
It is safe to switch to another medicine that contains fentanyl without talking to a healthcare provider first.	**FALSE**
A patient may give TIRF medicines to another person if they have the same symptoms as the patient.	**FALSE**
A side effect of TIRF medicines is the chance of abuse or addiction.	**TRUE**
TIRF medicines can be misused by people who abuse prescription medicines or street drugs.	**TRUE**
TIRF medicines should be kept in a safe place to prevent it from being stolen.	**TRUE**

If you have any questions about these survey responses, please discuss your questions with your healthcare provider and refer to the Medication Guide(s) for the TIRF medicine(s) that you take.

60-Month Pharmacist KAB Survey

Appendix A Pharmacist Questionnaire

Survey Legend

[PROGRAMMER] is used to indicate directions to the programmer and is set in bold, red, uppercase letters between square brackets.

(INTERVIEWER) is used to indicate directions to the telephone interviewer and is set in bold, blue, text between parentheses. This text appears when content is to be administered by telephone only (for example, spontaneous adverse event reporting).

[ONLINE] indicates a question is worded specifically for administering the survey online. **[PHONE]** indicates a question is worded specifically to be read by a telephone interviewer and differs from the online text.

[BEGIN SURVEY CONTENT] and **[END SURVEY CONTENT]** are used to indicate to the programmer the type of survey administration and the beginning and end of the survey or sections within the survey content, for example, **[BEGIN ADVERSE EVENT/PRODUCT COMPLAINT]** and **[END ADVERSE EVENT/PRODUCT COMPLAINT]**.

[TERMINATE] is displayed next to responses that should cause the survey to end. The following termination language will be programmed into the survey or read by the interviewer unless different language is specified with the question.

> *Thank you very much for your time today. Based on your answer, you are not eligible to take this survey. We appreciate your interest in the survey.*

[RANDOMIZE LIST] is inserted before questions to indicate to the programmer that the responses should be randomized. Responses such as "I don't know," "Prefer not to answer" or "None of the above" will always appear at the end of the randomized responses.

Response options for questions that allow multiple responses must be indicated with check boxes (□). At least one option must be selected for the question to be considered answered.

> If any response option requires text to be collected and does not need another question label, show **[FREE TEXT]** after the response option, if applicable.

Response options for questions that allow only one response must be indicated with radio buttons (○).

> If any response option requires text to be collected and does not need another question label, show **[FREE TEXT]** after the response option, if applicable.

[GO TO Qx] (skip logic) is inserted after a response to indicate to the programmer that the survey should skip to the indicated question (for example, **[GO TO Q17]** skips to question 17). If no skip logic is indicated the survey continues to the next question in the sequence.

Survey Legend

[FREE TEXT] indicates to the programmer that one line should be provided for data entry.

[MULTILINE INPUT] indicates to the programmer that multiple lines should be provided for data entry (for example, two address lines).

[DROP-DOWN LIST INPUT WITH STATES TABLE] indicates to the programmer that the response should be a drop-down list containing the states in the table below.

Alabama	Georgia	Massachusetts	New York	Tennessee
Alaska	Guam	Michigan	North Carolina	Texas
American Samoa	Hawaii	Minnesota	North Dakota	US Virgin Islands
Arizona	Idaho	Mississippi	Northern Mariana Islands	Utah
Arkansas	Illinois	Missouri	Ohio	Vermont
California	Indiana	Montana	Oklahoma	Virginia
Colorado	Iowa	Nebraska	Oregon	Washington
Connecticut	Kansas	Nevada	Pennsylvania	West Virginia
Delaware	Kentucky	New Hampshire	Puerto Rico	Wisconsin
District of Columbia	Louisiana	New Jersey	Rhode Island	Wyoming
Florida	Maine	New Mexico	South Carolina	
	Maryland		South Dakota	

The following is used to categorize survey populations into standard geographic regions but it is not displayed in the survey.

Geographic Distribution (based on address) [1]: Northeast, Midwest, South, and West regions

Northeast Region

- New England Division - ME, NH, VT, MA, RI, CT
- Middle Atlantic Division - NY, NJ, PA

Midwest Region

- East North Central Division - OH, IN, IL, MI, WI
- West North Central Division - MN, IA, MO, ND, SD, NE, KS

South Region

- South Atlantic Division - DE, MD, DC, VA, WV, NC, SC, GA, FL
- East South Central Division - KY, TN, AL, MS
  West South Central Division - AR, LA, OK, TX

Survey Legend

West

- Mountain Division - MT, ID, WY, CO, NM, AZ, UT, NV
- Pacific Division WA, OR, CA, AK, HI

The following US territories are categorized as Other: Puerto Rico, Northern Mariana Islands, US Virgin Islands, American Samoa, and Guam.

[1] U.S. Census Bureau, last revised Friday, 27-Jul-2001 12:59:43 EDT.

[BEGIN SURVEY CONTENT]

[BEGIN ONLINE PREAMBLE 1]

Before you begin, we would like to share some important information about this survey. The manufacturers of Transmucosal Immediate Release Fentanyl (TIRF) medicines are conducting this survey, as required by the FDA, to assess pharmacists' understanding of the safe use and dispensing of these medicines. These medicines are known as rapid onset opioids and referred to in this survey as "TIRF medicines." The TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Subsys®, and generic versions of any of these brands. The manufacturers of these medicines include Actavis Laboratories FL, Inc.; BioDelivery Sciences International, Inc. (BDSI); Cephalon, Inc. (a wholly-owned subsidiary of Teva Pharmaceutical Industries, Ltd.); Depomed, Inc.; ~~Galena Biopharma, Inc.;~~ Insys Therapeutics, Inc.; Mallinckrodt Pharmaceuticals; Mylan Inc.; Par Pharmaceuticals, Inc.; and ~~Par Pharmaceutical~~Sentynl Therapeutics, Inc. The survey will take 15-20 minutes.

There are no known risks to you in taking this survey. You may refuse to take part or withdraw at any time. Your answers to the questions or your decision to take part in the survey will not affect your ability to dispense TIRF medicines.

How We Use Your Information

Your answers to the survey questions will be combined with answers given by other pharmacists taking the survey. All answers will be put together and reported in anonymous form to the manufacturers of TIRF medicines. Your name will not be used in any report. If you are eligible to take the survey, complete all the questions, and provide your contact information, you will receive a $50 honorarium for your time and participation.

Your name and address will be used to send ~~you~~ the honorarium to you after you complete the survey. Your personal information will also be used if we have questions about your survey or if we are required to use your information to comply with a federal or state law or regulation.

Providing a telephone number is optional. Your telephone number will be used only if there are any questions about your survey responses.

How We Protect Your Privacy

We respect that the privacy of your personal information is important to you. You will not be contacted for marketing purposes based on your personal information or your answers to the survey. Neither the manufacturers of TIRF medicines nor their contractors will sell, transfer, or rent your information. Your answers will be kept strictly confidential. Your privacy will be protected; however, research survey records may be inspected by the FDA. Your choice to allow manufacturers of TIRF medicines to use your information is entirely voluntary but necessary to take part in this survey.

How to Learn More about This Survey

If you have questions about the survey, or problems with the survey, please contact the Survey Coordinating Center at 1-877-379-3297. Be sure to write down this telephone number; it will not be displayed again.

Taking the Survey

Once you have answered a question and moved on, you cannot go back and change your answers.

Thank you for your participation in this survey.

[END ONLINE PREAMBLE 1]

[BEGIN PHONE PREAMBLE 1]

Before you begin, we would like to share some important information about this survey. The manufacturers of Transmucosal Immediate Release Fentanyl (TIRF) medicines are conducting this survey, as required by the FDA, to assess pharmacists' understanding of the safe use and dispensing of these medicines. These medicines are known as rapid onset opioids and referred to in this survey as "TIRF medicines." **(INTERVIEWER: Say "TIRF" then spell out T-I-R-F)** The TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Subsys®, and generic versions of any of these brands. The manufacturers of these medicines include Actavis Laboratories FL, Inc.; BioDelivery Sciences International, Inc. (BDSI); Cephalon, Inc. (a wholly-owned subsidiary of Teva Pharmaceutical Industries, Ltd.); Depomed, Inc.; ~~Galena Biopharma, Inc.;~~ Insys Therapeutics, Inc.; Mallinckrodt Pharmaceuticals; Mylan Inc.; Par Pharmaceuticals, Inc.; and ~~Par Pharmaceutical~~Sentynl Therapeutics, Inc. The survey will take 15-20 minutes.

There are no known risks to you in taking this survey. You may refuse to take part or withdraw at any time. Your answers to the questions or your decision to take part in the survey will not affect your ability to dispense TIRF medicines.

Now I would like to read some information about how your contact information will be used.

Your answers to the survey questions will be combined with answers given by other pharmacists taking the survey. All answers will be put together and reported in anonymous form to the manufacturers of TIRF medicines. Your name will not be used in any report. If you are eligible to take the survey, complete all the questions, and provide your contact information, you will receive a $50 honorarium for your time and participation.

Your name and address will be used to send ~~you~~ the honorarium to you after you complete the survey. Your personal information will also be used if we have questions about your survey or if we are required to use your information to comply with a federal or state law or regulation.

Providing a telephone number is optional. Your telephone number will be used only if there are any questions about your survey responses.

Now I would like to tell you some information about how we protect your privacy.

We respect that the privacy of your personal information is important to you. You will not be contacted for marketing purposes based on your personal information or your answers to the survey. Neither the manufacturers of TIRF medicines nor their contractors will sell, transfer, or rent your information. Your answers will be kept strictly confidential. Your privacy will be protected; however, research survey records may be inspected by the FDA. Your choice to allow manufacturers of TIRF medicines to use your information is entirely voluntary but necessary to take part in this survey.

Now I will tell you how you can learn more about this survey. Please have a pen or pencil ready to write down a telephone number you can call should you have any questions about the survey. If you have questions about the survey, please ask me at any time. If you have questions at a later time, please contact the Survey Coordinating Center at 1-877-379-3297.

Please feel free to ask me to repeat any questions or statements as we go through the survey. Once you have answered a question and moved on, you cannot go back and change your answers. Thank you for your participation in this survey.

[END PHONE PREAMBLE 1]

[BEGIN INCLUSION/EXCLUSION QUESTIONS]

1. Your agreement to participate in this survey confirms mutual understanding in connection with completion of the survey and the fair market value of the payment to be rendered in connection with those services.

   Do you agree to participate in this survey?

   - ○ Yes
   - ○ No **[TERMINATE]**

2. Have you ever taken part in this survey about TIRF medicines before? TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Subsys®, and generic versions of any of these brands.

   - ○ Yes **[TERMINATE]**
   - ○ No
   - ○ I don't know **[TERMINATE]**

3. Do you work in a pharmacy that is enrolled in the TIRF REMS Access ~~Program~~program?

   - ○ Yes
   - ○ No **[TERMINATE]**
   - ○ I don't know **[TERMINATE]**

4. Have you or any of your immediate family members ever worked for any of the following companies or agencies? Please select all that apply.

   - □ Actavis Laboratories FL, Inc. **[TERMINATE]**
   - □ Anesta LLC **[TERMINATE]**
   - □ BioDelivery Sciences International, Inc. (BDSI) **[TERMINATE]**
   - □ Cephalon, Inc. (a wholly-owned subsidiary of Teva Pharmaceutical Industries, Ltd.) **[TERMINATE]**
   - □ Depomed, Inc. **[TERMINATE]**

- ☐ Galena Biopharma, Inc. **[TERMINATE]**
- ☐ Insys Therapeutics, Inc. **[TERMINATE]**
- ☐ Mallinckrodt Pharmaceuticals **[TERMINATE]**
- ☐ McKesson Specialty Care Solutions **[TERMINATE]**
- ☐ Mylan~~,~~ Inc. ~~-~~**[TERMINATE]**
- ☐ Par ~~Pharmaceutical~~Pharmaceuticals, Inc. **[TERMINATE]**
- ☐ RelayHealth **[TERMINATE]**
- ☐ Sentynl Therapeutics, Inc. **[TERMINATE]**
- ☐ Teva Pharmaceuticals, Ltd. **[TERMINATE]**
- ☐ United BioSource Corporation **[TERMINATE]**
- ☐ FDA **[TERMINATE]**
- ☐ None of these apply **[IF SELECTED IN ADDITION TO OTHER RESPONSES, TERMINATE]**
- ☐ I don't know **[TERMINATE]**
- ☐ Prefer not to answer **[TERMINATE]**

[END INCLUSION/EXCLUSION QUESTIONS]

5. Please select True, False, or I don't know for each of the following.

   According to the labeling for TIRF medicines, patients with cancer who are considered opioid-tolerant are those:

	[RANDOMIZE LIST]	**True**	**False**	**I don't know**
5a.	Who are taking around-the-clock opioid therapy for underlying, persistent cancer pain for one week or longer	○	○	○
5b.	Who are not currently taking opioid therapy, but have taken opioid therapy before	○	○	○
5c.	Who have no known contraindications to the drug fentanyl, but are not currently taking around-the-clock opioid therapy	○	○	○

6. Please answer True, False, or I don't know for each statement based on the labeling for TIRF medicines.

[RANDOMIZE LIST]	True	False	I don't know
6a. According to the product labeling, a cancer patient may start a TIRF medicine and an around-the-clock opioid at the same time.	○	○	○
6b. According to the product labeling, a cancer patient who has been on an around-the-clock opioid for 1 day may start taking a TIRF medicine for breakthrough pain.	○	○	○
6c. A patient must stop taking their TIRF medicine if they stop taking their around-the-clock opioid pain medicine.	○	○	○
6d. Use of a TIRF medicine with a CYP3A4 inhibitor may require dosage adjustment and monitoring of the patient for opioid toxicity as potentially fatal respiratory depression could occur.	○	○	○

7. Please answer True, False, or I don't know for each statement based on the labeling for TIRF medicines.

[RANDOMIZE LIST]	True	False	I don't know
7a. TIRF medicines are contraindicated in opioid non-tolerant patients because life-threatening respiratory depression could occur at any dose.	○	○	○
7b. Death has occurred in opioid non-tolerant patients treated with some fentanyl products.	○	○	○
7c. TIRF medicines may be used in opioid non-tolerant patients.	○	○	○
7d. Prescribers starting a patient on a TIRF medicine must begin with titration from the lowest dose available for that specific product, even if the patient has previously taken another TIRF medicine.	○	○	○
7e. It is important to monitor for signs of abuse and addiction in patients who take TIRF medicines.	○	○	○

8. Which of the following are risk factors for opioid abuse? Please answer Yes, No, or I don't know for each option.

	[RANDOMIZE LIST]	Yes	No	I don't know
8a.	A personal history of psychiatric illness	○	○	○
8b.	A personal history of past or current alcohol or drug abuse, or a family history of illicit drug use or alcohol abuse	○	○	○
8c.	A family history of asthma	○	○	○

9. Per the approved labeling for TIRF medicines, for which of the following indications can TIRF medicines be prescribed to opioid tolerant patients? Please answer Yes, No, or I don't know for each option.

	[RANDOMIZE LIST]	Yes	No	I don't know
9a.	Acute or postoperative pain	○	○	○
9b.	Headache or migraine pain	○	○	○
9c.	Dental pain	○	○	○
9d.	Breakthrough pain from cancer	○	○	○
9e.	Chronic non-cancer pain	○	○	○

10. Please answer True, False, or I don't know for each statement based on the labeling for TIRF medicines.

	[RANDOMIZE LIST]	True	False	I don't know
10a.	TIRF medicines can be abused in a manner similar to other opioid agonists.	○	○	○
10b.	TIRF medicines are interchangeable with each other regardless of route of administration.	○	○	○
10c.	The conversion of one TIRF medicine for another TIRF medicine may result in a fatal overdose because of differences in the pharmacokinetics of fentanyl absorption.	○	○	○
10d.	Dosing of TIRF medicines is not equivalent on a microgram-to-microgram basis.	○	○	○

11. Please select True, False, or I don't know for each of the following. According to the labeling for TIRF medicines, patients considered opioid-tolerant are those who are taking, for one week or longer, at least:

		True	False	I don't know
11a.	8 mg oral hydromorphone/day	○	○	○
11b.	60 mg oral morphine/day	○	○	○
11c.	30 mg oral oxycodone/day	○	○	○
11d.	25 mcg transdermal fentanyl/hour	○	○	○
11e.	25 mg oral oxymorphone/day	○	○	○
11f.	An equianalgesic dose of another oral opioid	○	○	○

12. Please answer True, False, or I don't know for the following statement about TIRF medicines:

TIRF medicines should only be taken by patients who are opioid tolerant.

- ○ True
- ○ False
- ○ I don't know

13. Which of the following risks are associated with the use of TIRF medicines? Please answer True, False, or I don't know for the following statements.

		True	False	I don't know
13a.	Misuse	○	○	○
13b.	Abuse	○	○	○
13c.	Addiction	○	○	○
13d.	Overdose	○	○	○
13e.	Hypothyroidism	○	○	○
13f.	Infection	○	○	○

~~12.~~14. How frequently do you perform the following activities when dispensing TIRF medicines? Please answer Always, Only with the first prescription, Sometimes, Never, or I don't know.

	[RANDOMIZE LIST]	Always	Only with the first prescription	Sometimes	Never	I don't know
~~12a.~~14a.	Ask patients (or their caregivers) about the presence of children in the home	○	○	○	○	○
~~12b.~~14b.	Instruct patients (or their caregivers) not to share TIRF medicines with anyone else	○	○	○	○	○
~~12c.~~14c.	Counsel patients (or their caregivers) that accidental exposure to TIRF medicines by a child may be fatal	○	○	○	○	○
~~12d.~~14d.	Instruct patients (or their caregivers) to keep TIRF medicines out of the reach of children to prevent accidental exposure	○	○	○	○	○
~~12e.~~14e.	Instruct patients (or their caregivers) about proper disposal of any unused or partially used TIRF medicines	○	○	○	○	○
~~12f.~~14f.	Give patients (or their caregivers) the Medication Guide for their TIRF medicine	○	○	○	○	○

~~13.~~15 How frequently do you perform the following activities when dispensing TIRF medicines? Please answer ~~True, False~~Always, Only with the first prescription, Sometimes, Never, or I don't know ~~for each statement about TIRF medicines~~.

	[RANDOMIZE LIST]	~~True~~Always	~~False~~Only with the first prescription	Sometimes	Never	I don't know
15a	Talk to the patient about the risks and possible side effects of the TIRF medicine that was most recently prescribed.	○	○	○	○	○
15b	Instruct the patient on how to use the TIRF medicine that was most recently prescribed.	○	○	○	○	○

15c	Instruct the patient on how to store or keep the TIRF medicine that was most recently prescribed.	○	○	○	○	○

16. Please answer True, False, or I don't know for each statement about TIRF medicines.

	[RANDOMIZE LIST]	True	False	I don't know
13a.16	TIRF medicines may be sold, loaned, or transferred to another pharmacy.	○	○	○
13b.16	All pharmacy staff that dispenses TIRF medicines must be educated on the requirements of the TIRF REMS Access ~~Program~~program.	○	○	○
13c.16	TIRF medicines with the same route of administration can be substituted with each other if the pharmacy is out of stock for one product.	○	○	○

14.17 **[INPATIENT PHARMACIST]** Does the inpatient pharmacy where you work have an established system, order sets, protocols and/or other measures to help ensure appropriate patient selection and compliance with the requirements of the TIRF REMS Access ~~Program~~program?

- ○ Yes
- ○ No
- ○ I don't know

15.18 **[OUTPATIENT PHARMACIST]** Does the outpatient or retail pharmacy where you work process all TIRF medicine prescriptions, regardless of method of payment, through the pharmacy management system?

- ○ Yes
- ○ No
- ○ I don't know

~~16.~~19. **[CSP OUTPATIENT PHARMACIST]** Does the pharmacy where you work process all TIRF medicine prescriptions, regardless of method of payment, through the TIRF REMS Access Call Center?

- ○ Yes
- ○ No
- ○ I don't know

~~17.~~20 **[INPATIENT PHARMACIST]** Please answer True, False, or I don't know for the following statement about TIRF medicines.

	True	False	I don't know
It is OK to dispense TIRF medicines from the inpatient pharmacy inventory to an outpatient for use at home.	○	○	○

[BEGIN PREAMBLE ~~3~~2]

The next set of questions is about the educational materials for TIRF medicines. As a reminder, the TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Subsys®, and generic versions of any of these brands.

[END PREAMBLE ~~3~~2]

~~18.~~21 Did you receive or do you have access to the Full Prescribing Information for the TIRF medicine(s) that you dispense?

- ○ Yes
- ○ No **[GO TO Q23~~2023~~]**
- ○ I don't know **[GO TO Q23~~2023~~]**

~~19.~~22 Did you read the Full Prescribing Information for the TIRF medicine(s) that you dispense?

- ○ Yes
- ○ No
- ○ I don't know

~~20.~~23 Did you receive or do you have access to the Medication Guide for the TIRF medicine(s) that you dispense?

- ○ Yes
- ○ No -**[GO TO Q25~~2225~~]**
- ○ I don't know **[GO TO Q25~~2225~~]**

~~21.~~24 Did you read the Medication Guide for the TIRF medicine(s) that you dispense?

- ○ Yes
- ○ No
- ○ I don't know

~~22.~~25 Did you or do you have any questions about the information in the Full Prescribing Information or Medication Guide?

- ○ Yes
- ○ No **[GO TO DEMOGRAPHICS PREAMBLE 1]**
- ○ I don't know **[GO TO DEMOGRAPHICS PREAMBLE 1]**

[IF QUESTION ~~22~~25 YES, DISPLAY QUESTION 26 ON SAME PAGE]

~~23.~~26 What are your questions? **[MULTILINE INPUT]**

[BEGIN DEMOGRAPHICS PREAMBLE 1 - DISPLAY ON SAME PAGE WITH NEXT QUESTION]

There are just a few more questions to help us combine your answers with other answers we have received.

[END DEMOGRAPHICS PREAMBLE 1]

~~24.~~27 Are you the Pharmacist in Charge for the TIRF REMS Access ~~Program~~program where you work?

- ○ Yes
- ○ No
- ○ I don't know

~~25.~~28 On average, how many times per month have you dispensed TIRF medicine within the last 6 months?

- ○ None **[Go to DEMOGRAPHICS PREAMBLE 2]**
- ○ 1 2 times per month
- ○ 3 5 times per month
- ○ More than 5 times per month
- ○ I don't remember

~~26.~~29 Please select the TIRF medicine(s) that you have dispensed within the last 6 months. Please select all that apply.

- ☐ Abstral®
- ☐ Actiq® or generic Actiq®
- ☐ Fentora®
- ☐ Lazanda®
- ☐ Subsys®

[BEGIN DEMOGRAPHICS PREAMBLE 2 - DISPLAY ON SAME PAGE WITH NEXT QUESTION]

These last few questions are for demographic purposes.

[END DEMOGRAPHICS PREAMBLE 2]

~~27.~~30 What is your gender?

- ○ Male
- ○ Female
- ○ Prefer not to answer

~~28.~~31 In total, how many years have you been a practicing pharmacist?

- ○ Less than 3 years
- ○ 3 5 years
- ○ 6 10 years
- ○ 11 15 years
- ○ More than 15 years
- ○ Prefer not to answer

~~29.~~32 In which state do you practice?

[DROP-DOWN LIST INPUT WITH STATES TABLE WITH "Prefer not to answer" AT END]

[PHONE - BEGIN ADVERSE EVENT/PRODUCT COMPLAINT – KEEP ON ONE PAGE]

(INTERVIEWER: Please record if respondent spontaneously reported an adverse event or product complaint during the course of this interview.)

- ○ Yes
- ○ No **[GO TO CLOSING 1]**

Enter Safety Adverse Event Verbatim

[MULTILINE INPUT]

(INTERVIEWER: Indicate to the respondent that someone may call back to ask more questions about the adverse event or product complaint that was reported.)

[END ADVERSE EVENT/PRODUCT COMPLAINT]

[BEGIN CLOSING 1 – KEEP ON ONE PAGE]

We would like to send you a $50 honorarium within the next few weeks to thank you for your time, but we need your name and address to do so. If you do not provide your name and address you will not receive the honorarium for your time and participation in the survey.

Do you agree to give us your name and mailing address so we can send you the

honorarium?

○ Yes

○ No **[GO TO CLOSING 2]**

FIRST NAME: **[FREE TEXT]**

LAST NAME: **[FREE TEXT]**

ADDRESS: **[MULTILINE INPUT]**

CITY: **[FREE TEXT]**

STATE: **[DROP-DOWN LIST INPUT WITH STATES TABLE]**

ZIP: **[MUST BE 5 NUMERIC-ONLY CHARACTERS]**

[END CLOSING 1]

[BEGIN CLOSING 2 – KEEP ON ONE PAGE]

We would also like to ask for your telephone number. Providing your telephone number is optional and it will be used to contact you only if there are questions about your survey responses.

Do you want to provide your telephone number?

○ Yes

○ No **[GO TO CLOSING 3]**

Telephone: **[MUST BE 10-DIGIT NUMERIC-ONLY CHARACTERS]**
[END CLOSING 2]

[BEGIN CLOSING 3]

That ends the survey. Thank you again for your help.

[END CLOSING 3]

-[END SURVEY CONTENT]

Appendix B SAMPLE Pharmacist Recruitment Materials

INVITATION LETTER

[
CURR_DATE]

[PHARMACY_NAME]

[PHARMACY _STREET_ADDR]
[PHARMACY_CITY], [PHARMACY _STATE] [PHARMACY _ZIP]

[PHARMACY_FAX_NUMBER]

Dear [PHARMACIST– IN CHARGE]

Your Pharmacypharmacy was selected to receive this letter, because of enrollment in the TIRF Transmucosal Immediate Release Fentanyl (TIRF) Risk Evaluation and Mitigation Strategy (REMS) Access Program.program and dispensing of TIRF medicines in the last 6 months. We are contacting you to inform you about a survey being conducted by the manufacturers of Transmucosal Immediate Release Fentanyl (TIRF) medicinesTIRF Medicines, as required by the Food and Drug Administration (FDA). The purpose of the survey is to assess pharmacists' understanding of the safe and appropriate use of these medicines. The TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Subsys®, and generic versions of any of these brands.

The FDA has requested that non-supervisory pharmacists participate in this survey; therefore, as part of this FDA request, we are asking for your help in distributing these surveys to non-supervisory pharmacists in your pharmacy. The survey will be open through [ENTER DATE] but could be extended if the desired number of completed surveys has not been collected. The survey should take about 20 minutes to complete.

You will find enclosed, [ENTER NUMBER] invitation letters to provide to [ENTER NUMBER] non-supervisory pharmacists.

The manufacturers of TIRF medicines include Actavis Laboratories FL, Inc.;., BioDelivery Sciences International, Inc. (BDSI);., Cephalon, Inc. (a wholly-owned subsidiary of Teva Pharmaceutical Industries, Ltd.);.), Depomed, Inc.; Galena Biopharma, Inc.;., Insys Therapeutics, Inc.;., Mallinckrodt Pharmaceuticals;, Mylan Inc., Par Pharmaceuticals, Inc.;., and Par PharmaceuticalSentynl Therapeutics, Inc. (collectively referred to as the "TIRF REMS Industry Group"). These manufacturers are looking for 300 non-supervisory pharmacists to complete the survey. Eligible pharmacists who complete the survey will be sent a $50 honorarium to thank them for their time. The survey will take 15-20 minutes.

Your answers will be kept strictly confidential and will be combined with the answers from other pharmacists who take this survey. Your name will not be used in the report of this survey and your contact information, if provided, will only be used to send you a $50 honorarium for your time to complete the survey.

~~You are under no obligation to participate in this survey. Only one pharmacist from each enrolled~~Your answers will be kept strictly confidential and will be combined with the answers from other pharmacists who take this survey. Your name will not be used in the report of this survey and your contact information, if provided, will only be used to send you a $50 honorarium for your time to complete the survey.

Your pharmacy ~~can~~is under no obligation to participate in this survey. If you ~~are~~or a staff pharmacist at your pharmacy is interested in participating and to find out if you are eligible:

- Go online* to www.TIRFREMSsurvey.com any time or
- Call 1-877-379-3297, 8 a.m. to 8 p.m. Eastern Time, Monday through Friday

Please have this letter with you at the time you take the survey. You will be asked to provide this code prior to starting the survey: **[CODE_ID]**. ~~*We recommend~~

***Please note** that you **should** take the survey on a desktop or laptop computer. Taking the survey on mobile devices, such as smart phones, tablets, and e-notebooks, is not supported.*

Neither taking the survey nor your answers to the questions will affect your ability to dispense any of the TIRF medicines identified above.

Sincerely,

The TIRF REMS Survey Team

1-877-379-3297

www.TIRFREMSsurvey.com

Dear Pharmacist,

The Food and Drug Administration (FDA) has requested that the sponsors of TIRF medicines conduct a survey to assess pharmacists' understanding of the safe and appropriate use of these medicines. The TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Subsys®, and generic versions of any of these brands. The FDA has requested that non-supervisory pharmacists, like yourself, participate in this survey.

The manufacturers of TIRF medicines include Actavis Laboratories FL Inc., BioDelivery Sciences International, Inc., Cephalon, Inc. (a wholly-owned subsidiary of Teva Pharmaceutical Industries, Ltd.), Depomed, Inc., Insys Therapeutics, Inc., Mallinckrodt Pharmaceuticals, Mylan Inc., Par Pharmaceuticals, Inc., and Sentynl Therapeutics, Inc. (collectively referred to as the "TIRF REMS Industry Group"). These manufacturers are looking for 300 non-supervisory pharmacists to complete the survey. Eligible pharmacists who complete the survey will be sent a $50 honorarium to thank them for their time. The survey will take 20 minutes to complete.

Your answers will be kept strictly confidential and will be combined with the answers from other pharmacists who take this survey. Your name will not be used in the report of this survey and your contact information, if provided, will only be used to send you a $50 honorarium for your time to complete the survey.

You are under no obligation to participate in this survey. If you are interested in participating and to find out if you are eligible:

- Go online* to www.TIRFREMSsurvey.com any time or
- Call 1-877-379-3297, 8 a.m. to 8 p.m. Eastern Time, Monday through Friday

Please have this letter with you at the time you take the survey. You will be asked to provide this code prior to starting the survey: **[CODE_ID]**.

Please note that you should take the survey on a desktop or laptop computer. Taking the survey on mobile devices, such as smart phones, tablets, and e-notebooks, is not supported.

Neither taking the survey nor your answers to the questions will affect your ability to dispense any of the TIRF medicines identified above.

Sincerely,

The TIRF REMS Survey Team

1-877-379-3297

www.TIRFREMSsurvey.com

THANK YOU LETTER

[CURR_DATE]

[PHARMACIST_FIRST_NAME] [[PHARMACIST_LAST NAME], [TITLE]
[PHARMACIST_STREET_ADDR]
[PHARMACIST_CITY], [PHARMACIST_STATE] [PHARMACIST_ZIP]

Dear [PHARMACIST_FULL_NAME],

On behalf of TIRF REMS Industry Group, we want to thank you for taking part in the TIRF REMS Survey. To express our appreciation for your valuable time, enclosed is a gift card for $50.

Card Activation Instructions:

To prevent loss, the enclosed card is not activated. Prior to using your card, please call the TIRF REMS Coordinating Center at 1-877-379-3297 between 8:00 a.m. and 8:00 p.m. Eastern Time, Monday through Friday, to activate your card. Please have your card available when you make the call. Also, please read the enclosed Terms and Conditions document before using your gift card as well as the privacy policy that can be found at: http://www.ctpayer.com/downloads/privacy_policy.pdf

Please note the enclosed card needs to be activated on or before: **xx xxx xxxx**

Additionally, for your information and to reinforce important safety messages about TIRF Medications, we have enclosed the following two documents:

1. A copy of the correct answers to the important survey questions about the TIRF REMS key risk message questions.
2. A copy of the Important Safety Information.

Additional information regarding TIRF REMS Access program can be found at www.TIRFREMSaccess.com.

Thank you for your time and consideration regarding this important safety information.

Sincerely,
The TIRF REMS Survey Team
1-877-379-3297
www.TIRFREMSsurvey.com

Enclosures: Gift Card and Terms and Conditions
Correct Answers to Important Survey Questions
TIRF Important Safety Information

Appendix C Correct Answer Document

Correct Responses to Select PHARMACIST Survey Questions about Important Safety Messages for Transmucosal Immediate Release Fentanyl (TIRF) medicines (TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Subsys®, and generic versions of any of these brands)

Q: Please select True, False, or I don't know for each of the following. According to the labeling for TIRF medicines, patients with cancer who are considered opioid-tolerant are those:

STATEMENT	DESIRED RESPONSE
Who are taking around-the-clock opioid therapy for underlying, persistent cancer pain for one week or longer	**TRUE**
Who are not currently taking opioid therapy, but have taken opioid therapy before	**FALSE**
Who have no known contraindications to the drug fentanyl, but are not currently taking around-the-clock opioid therapy	**FALSE**

Q: Please answer True, False, or I don't know for each statement based on the labeling for TIRF medicines.

STATEMENT	DESIRED RESPONSE
TIRF medicines are contraindicated in opioid non-tolerant patients because life-threatening respiratory depression could occur at any dose.	**TRUE**
Death has occurred in opioid non-tolerant patients treated with some fentanyl products.	**TRUE**
TIRF medicines may be used in opioid non-tolerant patients.	**FALSE**
Prescribers starting a patient on a TIRF medicine must begin with titration from the lowest dose available for that specific product, even if the patient has previously taken another TIRF medicine.	**TRUE**
According to the product labeling, a cancer patient may start a TIRF medicine and an around-the-clock opioid at the same time.	**FALSE**
According to the product labeling, a cancer patient who has been on an around-the-clock opioid for 1 day may start taking a TIRF medicine for breakthrough pain.	**FALSE**
A patient must stop taking their TIRF medicine if they stop taking their around-the-clock opioid pain medicine.	**TRUE**

Q: Please select True, False, or I don't know for each of the following. According to the labeling for TIRF medicines, patients considered opioid-tolerant are those who are taking, for one week or longer, at least:

STATEMENT	DESIRED RESPONSE
8 mg oral hydromorphone/day	**TRUE**
60 mg oral morphine/day	**TRUE**
30 mg oral oxycodone/day	**TRUE**
25 mcg transdermal fentanyl/hour	**TRUE**
25 mg oral oxymorphone/day	**TRUE**
An equianalgesic dose of another oral opioid	**TRUE**

Q: Per the approved labeling for TIRF medicines, for which of the following indications can TIRF medicines be prescribed to opioid tolerant patients? Please answer Yes, No, or I don't know for each option.

STATEMENT	DESIRED RESPONSE
Acute or postoperative pain	**NO**
Headache or migraine pain	**NO**
Dental pain	**NO**
Breakthrough pain from cancer	**YES**
Chronic non-cancer pain	**NO**

Q: Please answer True, False, or I don't know for each statement based on the labeling for TIRF medicines.

STATEMENT	DESIRED RESPONSE
It is important to monitor for signs of abuse and addiction in patients who take TIRF medicines.	**TRUE**
TIRF medicines can be abused in a manner similar to other opioid agonists.	**TRUE**
TIRF medicines are interchangeable with each other regardless of route of administration.	**FALSE**
The conversion of one TIRF medicine for another TIRF medicine may result in a fatal overdose because of differences in the pharmacokinetics of fentanyl absorption.	**TRUE**
Dosing of TIRF medicines is not equivalent on a microgram-to-microgram basis.	**TRUE**

Q: Please answer True, False, or I don't know for each statement about TIRF medicines.

STATEMENT	DESIRED RESPONSE
TIRF medicines with the same route of administration can be substituted with each other if the pharmacy is out of stock for one product.	**FALSE**
TIRF medicines should only be taken by patients who are opioid tolerant.	**TRUE**

Q: Which of the following are risk factors for opioid abuse? Please answer Yes, No, or I don't know for each option.

STATEMENT	DESIRED RESPONSE
A personal history of psychiatric illness	**YES**
A personal history of past or current alcohol or drug abuse, or a family history of illicit drug use or alcohol abuse	**YES**

Q: Which of the following risks are associated with the use of TIRF medicines? Please answer True, False, or I don't know for the following statements.

STATEMENT	DESIRED RESPONSE
Misuse	**TRUE**
Abuse	**TRUE**
Addiction	**TRUE**

Overdose	**TRUE**
Hypothyroidism	**FALSE**
Infection	**FALSE**

If you have questions or are unclear about any of these responses, please refer to the Full Prescribing Information, the Important Safety Information, and the Medication Guide for TIRF medicines.

60-Month Prescriber KAB Survey

Appendix A Prescriber Questionnaire

Survey Legend

[PROGRAMMER] is used to indicate directions to the programmer and is set in bold, red, uppercase letters between square brackets.

(INTERVIEWER) is used to indicate directions to the telephone interviewer and is set in bold, blue, text between parentheses. This text appears when content is to be administered by telephone only (for example, spontaneous adverse event reporting).

[ONLINE] indicates a question is worded specifically for administering the survey online.

[PHONE] indicates a question is worded specifically to be read by a telephone interviewer and differs from the online text.

[BEGIN SURVEY CONTENT] and **[END SURVEY CONTENT]** are used to indicate to the programmer the type of survey administration and the beginning and end of the survey or sections within the survey content, for example, **[BEGIN ADVERSE EVENT/PRODUCT COMPLAINT]** and **[END ADVERSE EVENT/PRODUCT COMPLAINT]**.

[TERMINATE] is displayed next to responses that should cause the survey to end. The following termination language will be programmed into the survey or read by the interviewer unless different language is specified with the question.

> *Thank you very much for your time today. Based on your answer, you are not eligible to take this survey. We appreciate your interest in the survey.*

[RANDOMIZE LIST] is inserted before questions to indicate to the programmer that the responses should be randomized. Responses such as "I don't know," "Prefer not to answer" or "None of the above" will always appear at the end of the randomized responses.

Response options for questions that allow multiple responses must be indicated with check boxes (□). At least one option must be selected for the question to be considered answered.

> If any response option requires text to be collected and does not need another question label, show **[FREE TEXT]** after the response option~~.~~, if applicable.

Response options for questions that allow only one response must be indicated with radio buttons (○).

> If any response option requires text to be collected and does not need another question label, show **[FREE TEXT]** after the response option, if applicable.

[FREE TEXT] indicates to the programmer that one line should be provided for data entry.

Survey Legend

[MULTILINE INPUT] indicates to the programmer that multiple lines should be provided for data entry (for example, two address lines).

[DROP-DOWN LIST INPUT WITH STATES TABLE] indicates to the programmer that the response should be a drop-down list containing the states and US territories in the table below.

Alabama	Georgia	Massachusetts	New York	Tennessee
Alaska	Guam	Michigan	North Carolina	Texas
American Samoa	Hawaii	Minnesota	North Dakota	US Virgin Islands
Arizona	Idaho	Mississippi	Northern Mariana Islands	Utah
Arkansas	Illinois	Missouri	Ohio	Vermont
California	Indiana	Montana	Oklahoma	Virginia
Colorado	Iowa	Nebraska	Oregon	Washington
Connecticut	Kansas	Nevada	Pennsylvania	West Virginia
Delaware	Kentucky	New Hampshire	Puerto Rico	Wisconsin
District of Columbia	Louisiana	New Jersey	Rhode Island	Wyoming
Florida	Maine	New Mexico	South Carolina	
	Maryland		South Dakota	

The following is used to categorize survey populations into standard geographic regions but it is not displayed in the survey.

Geographic Distribution (based on address) [1]: Northeast, Midwest, South, and West regions

Northeast Region

- New England Division - ME, NH, VT, MA, RI, CT
- Middle Atlantic Division - NY, NJ, PA

Midwest Region

- East North Central Division - OH, IN, IL, MI, WI
- West North Central Division - MN, IA, MO, ND, SD, NE, KS

South Region

Survey Legend

- South Atlantic Division - DE, MD, DC, VA, WV, NC, SC, GA, FL
- East South Central Division - KY, TN, AL, MS
- West South Central Division - AR, LA, OK, TX

West

- Mountain Division - MT, ID, WY, CO, NM, AZ, UT, NV
- Pacific Division WA, OR, CA, AK, HI

The following US territories are categorized as **Other**: Puerto Rico, Northern Mariana Islands, US Virgin Islands, American Samoa, and Guam.

[1] U.S. Census Bureau, last revised Friday, 27-Jul-2001 12:59:43 EDT.

[BEGIN SURVEY CONTENT]

[BEGIN ONLINE PREAMBLE 1]

Before you begin, we would like to share some important information about this survey. The manufacturers of Transmucosal Immediate Release Fentanyl (TIRF) medicines are conducting this survey, as required by the FDA, to assess prescribers' understanding of the safe use and prescribing of these medicines. These medicines are known as rapid onset opioids and referred to in this survey as "TIRF medicines." The TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Subsys®, and generic versions of any of these brands. The manufacturers of these medicines include Actavis Laboratories FL, Inc.; BioDelivery Sciences International, Inc. (BDSI); Cephalon, Inc. (a wholly-owned subsidiary of Teva Pharmaceutical Industries, Ltd.); Depomed, Inc.; ~~Galena Biopharma, Inc.;~~ Insys Therapeutics, Inc.; Mallinckrodt Pharmaceuticals; Mylan Inc.; Par Pharmaceuticals, Inc.; and ~~Par Pharmaceutical~~Sentynl Therapeutics, Inc. The survey will take approximately 20 minutes.

There are no known risks to you in taking this survey. You may refuse to take part or withdraw at any time. Your answers to the questions or your decision to take part in the survey will not affect your ability to prescribe TIRF medicines.

How We Use Your Information

Your answers to the survey questions will be combined with answers given by other healthcare professionals taking the survey. All answers will be put together and reported in anonymous form to the manufacturers of TIRF medicines. Your name will not be used in any report. If you are eligible to take the survey, complete all the questions, and provide your contact information, you will receive a $125 honorarium for your time and participation. This compensation represents the fair value for your services in connection with completion of the survey. The amount of the compensation was not determined in any manner that takes into account the volume or value of any referrals or business otherwise generated by you.

Your name and address will be used to send ~~you~~ the honorarium to you after you complete the survey. Your personal information will also be used if we have questions about your survey or if we are required to use your information to comply with a federal or state law or regulation, including without limitation, reporting payments made to physicians under the federal physician payment sunshine provisions. Physicians who practice in Vermont, Massachusetts, or Minnesota should be aware that they will not be permitted to receive payment for survey completion and may elect not to complete the survey.

Providing a telephone number is optional. Your telephone number will be used only if there are any questions about your survey responses.

How We Protect Your Privacy

We respect that the privacy of your personal information is important to you. You will not be contacted for marketing purposes based on your personal information or your answers to the survey. Neither the manufacturers of TIRF medicines nor their contractors will sell, transfer, or rent your information. Your answers will be kept strictly confidential. Your personal information will not be used in a manner inconsistent with this document. Your privacy will be protected; however, research survey records may be inspected by the FDA. Your choice to

allow manufacturers of TIRF medicines to use your information is entirely voluntary but necessary to take part in this survey.

How to Learn More about This Survey

If you have questions about the survey, or problems with the survey, please contact the Survey Coordinating Center at 1-877-379-3297. Be sure to write down this telephone number; it will not be displayed again.

Taking the Survey

Once you have answered a question and moved on, you cannot go back and change your answers.

Thank you for your participation in this survey.

[END ONLINE PREAMBLE 1]

[BEGIN PHONE PREAMBLE 1]

Before you begin, we would like to share some important information about this survey. The manufacturers of Transmucosal Immediate Release Fentanyl (TIRF) medicines are conducting this survey, as required by the FDA, to assess prescribers' understanding of the safe use and prescribing of these medicines. These medicines are known as rapid onset opioids and referred to in this survey as "TIRF medicines." **(INTERVIEWER: Say "TIRF" then spell out T-I-R-F)** The TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Subsys®, and generic versions of any of these brands. The manufacturers of these medicines include Actavis Laboratories FL, Inc.; BioDelivery Sciences International, Inc. (BDSI); Cephalon, Inc. (a wholly-owned subsidiary of Teva Pharmaceutical Industries, Ltd.); Depomed, Inc.; ~~Galena Biopharma, Inc.;~~ Insys Therapeutics, Inc.; Mallinckrodt Pharmaceuticals; Mylan Inc.; Par Pharmaceuticals, Inc.; and ~~Par Pharmaceutical~~Sentynl Therapeutics, Inc. The survey will take approximately 20 minutes.

There are no known risks to you in taking this survey. You may refuse to take part or withdraw at any time. Your answers to the questions or your decision to take part in the survey will not affect your ability to prescribe TIRF medicines.

Now I would like to read some information about how your contact information will be used.

Your answers to the survey questions will be combined with answers given by other healthcare professionals taking the survey. All answers will be put together and reported in anonymous form to the manufacturers of TIRF medicines. Your name will not be used in any report. If you are eligible to take the survey, complete all the questions, and provide your contact information, you will receive a $125 honorarium for your time and participation. This compensation represents the fair value for your services in connection with completion of the survey. The amount of the compensation was not determined in any manner that takes into account the volume or value of any referrals or business otherwise generated by you.

Your name and address will be used to send ~~you~~ the honorarium to you after you complete the survey. Your personal information will also be used if we have questions about your survey or if we are required to use your information to comply with a federal or state law or regulation, including without limitation, reporting payments made to physicians under the federal physician payment sunshine provisions. ~~-~~Physicians who practice in Vermont, Massachusetts, or Minnesota should be aware that they will not be permitted to receive payment for survey completion and may elect not to complete the survey.

Providing a telephone number is optional. Your telephone number will be used only if there are any questions about your survey responses.

Now I would like to tell you some information about how we protect your privacy.

We respect that the privacy of your personal information is important to you. You will not be contacted for marketing purposes based on your personal information or your answers to the survey. Neither the manufacturers of TIRF medicines nor their contractors will sell, transfer, or rent your information. Your answers will be kept strictly confidential. Your personal information will not be used in a manner inconsistent with this document. Your privacy will be protected; however, research survey records may be inspected by the FDA. Your choice to

allow manufacturers of TIRF medicines to use your information is entirely voluntary but necessary to take part in this survey.

Now I will tell you how you can learn more about this survey. Please have a pen or pencil ready to write down a telephone number you can call if you have any questions about the survey. If you have questions about the survey, please ask me at any time. If you have questions at a later time, please contact the Survey Coordinating Center at 1-877-379-3297. Please feel free to ask me to repeat any questions or statements as we go through the survey. Once you have answered a question and moved on, we cannot go back and change your answers. Thank you for your participation in this survey.

[END PHONE PREAMBLE 1]

[BEGIN INCLUSION/EXCLUSION QUESTIONS]

1. Your agreement to participate in this survey confirms mutual understanding in connection with completion of the survey and the fair market value of the payment to be rendered in connection with those services.

   Do you agree to participate in this survey?

   - o Yes
   - o No **[TERMINATE]**

2. Have you ever taken part in this survey about TIRF medicines before? TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Subsys®, and generic versions of any of these brands.

   - o Yes **[TERMINATE]**
   - o No
   - o I don't know **[TERMINATE]**

3. Are you enrolled in the TIRF REMS Access ~~Program~~program?

   - o Yes
   - o No **[TERMINATE]**
   - o I don't know **[TERMINATE]**

4. Have you or any of your immediate family members ever worked for any of the following companies or agencies? Please select all that apply.

- ☐ Actavis Laboratories FL, Inc. **[TERMINATE]**
- ☐ Anesta LLC **[TERMINATE]**
- ☐ BioDelivery Sciences International, Inc. (BDSI) **[TERMINATE]**
- ☐ Cephalon, Inc. (a wholly-owned subsidiary of Teva Pharmaceutical Industries, Ltd.) **[TERMINATE]**
- ☐ Depomed, Inc. **[TERMINATE]**
- ☐ Galena Biopharma, Inc. **[TERMINATE]**
- ☐ Insys Therapeutics, Inc. **[TERMINATE]**
- ☐ Mallinckrodt Pharmaceuticals **[TERMINATE]**
- ☐ McKesson Specialty Care Solutions **[TERMINATE]**
- ☐ Mylan~~,~~ Inc. **[TERMINATE]**
- ☐ Par ~~Pharmaceutical~~Pharmaceuticals, Inc. **[TERMINATE]**
- ☐ RelayHealth **[TERMINATE]**
- ☐ Sentynl Therapeutics, Inc. **[TERMINATE]**
- ☐ Teva Pharmaceuticals, Ltd. **[TERMINATE]**
- ☐ United BioSource Corporation **[TERMINATE]**
- ☐ FDA **[TERMINATE]**
- ☐ None of these apply **[IF SELECTED IN ADDITION TO OTHER RESPONSES, TERMINATE]**
- ☐ I don't know **[TERMINATE]**
- ☐ Prefer not to answer **[TERMINATE]**

[END INCLUSION/EXCLUSION QUESTIONS]

5. Please select True, False, or I don't know for each of the following.

   According to the labeling for TIRF medicines, patients with cancer who are considered opioid-tolerant are those:

	[RANDOMIZE LIST]	**True**	**False**	**I don't know**
5a.	Who are taking around-the-clock opioid therapy for underlying, persistent cancer pain for one week or longer	○	○	○
5b.	Who are not currently taking opioid therapy, but have taken opioid therapy before	○	○	○
5c.	Who have no known contraindications to the drug fentanyl, but are not currently taking around-the-clock opioid therapy	○	○	○

6. Please answer True, False, or I don't know for each statement based on the labeling for TIRF medicines.

	[RANDOMIZE LIST]	**True**	**False**	**I don't know**
6a.	According to the product labeling, a cancer patient may start a TIRF medicine and an around-the-clock opioid at the same time.	○	○	○
6b.	According to the product labeling, a cancer patient who has been on an around-the-clock opioid for 1 day may start taking a TIRF medicine for breakthrough pain.	○	○	○

7. Please answer True, False, or I don't know for each statement based on the labeling for TIRF medicines.

	[RANDOMIZE LIST]	True	False	I don't know
7a.	TIRF medicines are contraindicated in opioid non-tolerant patients because life-threatening respiratory depression could occur at any dose.	○	○	○
7b.	Death has occurred in opioid non-tolerant patients treated with some fentanyl products.	○	○	○
7c.	TIRF medicines may be used to treat opioid non-tolerant patients.	○	○	○
7d.	Prescribers starting a patient on a TIRF medicine must begin with titration from the lowest dose available for that specific product, even if the patient has previously taken another TIRF medicine.	○	○	○
7e.	It is important to monitor for signs of abuse and addiction in patients who take TIRF medicines.	○	○	○

8. Which of the following are risk factors for opioid abuse? Please answer Yes, No, or I don't know for each option.

	[RANDOMIZE LIST]	Yes	No	I don't know
8a.	A personal history of psychiatric illness	○	○	○
8b.	A personal history of past or current alcohol or drug abuse, or a family history of illicit drug use or alcohol abuse	○	○	○
8c.	A family history of asthma	○	○	○

9. ~~In your practice~~Per the approved labeling for TIRF medicines, for which of the following ~~indications do you prescribe~~indication(s) are TIRF medicines ~~to opioid tolerant patients~~approved? Please answer Yes, No, or I don't know for each option.

	[RANDOMIZE LIST]	**Yes**	**No**	**I don't know**
9a.	Acute or postoperative pain	○	○	○
9b.	Headache or migraine pain	○	○	○
9c.	Dental pain	○	○	○
9d.	Breakthrough pain from cancer	○	○	○
9e.	Chronic non-cancer pain	○	○	○

[IF 9E YES, DISPLAY Q10 and Q11 ON SUBSEQUENT PAGES]

10. For what type(s) of chronic non-cancer pain conditions do you prescribe a TIRF medicine to opioid tolerant patients?

[MULTILINE INPUT]

~~11.~~ ~~Why do you select a TIRF medicine to treat these chronic pain conditions in patients who are opioid tolerant?~~

~~**[MULTILINE INPUT]**~~

11. Why do you select a TIRF medicine to treat these chronic non-cancer pain conditions in patients who are opioid tolerant?

[MULTILINE INPUT]

12. Please answer True, False, or I don't know for each statement based on the labeling for TIRF medicines.

	[RANDOMIZE LIST]	**True**	**False**	**I don't know**
12a.	TIRF medicines can be abused in a manner similar to other opioid agonists.	○	○	○
12b.	TIRF medicines are interchangeable with each other	○	○	○

	regardless of route of administration.			
12c.	The conversion of one TIRF medicine for another TIRF medicine may result in a fatal overdose because of differences in the pharmacokinetics of fentanyl absorption.	○	○	○
12d.	Dosing of TIRF medicines is not equivalent on a microgram-to-microgram basis.	○	○	○

13. Please select True, False, or I don't know for each of the following. According to the labeling for TIRF medicines, patients considered opioid-tolerant are those who are taking, for one week or longer, at least:

		True	False	I don't know
13a.	8 mg oral hydromorphone/day	○	○	○
13b	60 mg oral morphine/day	○	○	○
13c.	30 mg oral oxycodone/day	○	○	○
13d	25 mcg transdermal fentanyl/hour	○	○	○
13e.	25 mg oral oxymorphone/day	○	○	○
13f.	An equianalgesic dose of another oral opioid	○	○	○

14. How frequently do you perform the following activities when prescribing TIRF medicines? Please answer Always, Only with the first prescription, Sometimes, Never, or I don't know.

	[RANDOMIZE LIST]	Always	Only with the first prescription	Sometimes	Never	I don't know
14a.	Ask patients (or their caregivers) about the presence of children in the home	○	○	○	○	○
14b.	Instruct patients (or their caregivers) not to share TIRF medicines with anyone else	○	○	○	○	○
14c.	Counsel patients (or their caregivers) that accidental exposure to TIRF medicines by a child may be fatal	○	○	○	○	○
14d.	Instruct patients (or their caregivers) to keep TIRF medicines out of the reach of children to prevent accidental exposure	○	○	○	○	○
14e.	Instruct patients (or their caregivers) about proper disposal of any unused or partially used TIRF medicines	○	○	○	○	○

14f. Give patients (or their caregivers) the Medication Guide for their TIRF medicine	○	○	○	○	○

15. The patients described are experiencing breakthrough pain. According to the labeling, a TIRF medicine is not appropriate for one of them. Which patient should not receive a TIRF medicine? Please select one option.

[RANDOMIZE LIST WITH I DON'T KNOW ALWAYS AT THE END]

- ○ Adult male with advanced lung cancer; underlying persistent cancer pain managed with 25 mcg/hour transdermal fentanyl patches for the past two months.
- ○ Adult female with localized breast cancer; just completed a mastectomy and reconstructive surgery; persistent cancer pain managed with 30 mg oral morphine daily for the past 6 weeks.
- ○ Adult male patient with advanced prostate cancer who, over the last 2 weeks, has been prescribed 100 mg oral morphine daily for pain due to bone metastasis.
- ○ Adult female with advanced sarcoma who has been taking a daily dose of 12 mg oral hydromorphone for the last 3 weeks.
- ○ I don't know

16. A patient is already taking a TIRF medicine but wants to change their medicine. His/her doctor decides to prescribe a different TIRF medicine (that is not a bioequivalent generic version of a branded product) in its place. According to the labeling, how should the prescriber proceed? Please select one option.

[RANDOMIZE LIST WITH I DON'T KNOW ALWAYS AT THE END]

- ○ The prescriber can safely convert to the equivalent dosage of the new TIRF medicine as it has the same effect as other TIRF medicines.
- ○ The prescriber must not convert to another TIRF medicine on a microgram-per-microgram basis because these medicines have different absorption properties and this could result in a fentanyl overdose.
- ○ Convert from the other TIRF medicine to the new TIRF medicine at half of the dose.
- ○ The prescriber should base the starting dose of the newly-prescribed TIRF medicine on the dose of the opioid medicine used for their underlying persistent cancer pain.

- ○ I don't know.

17. A patient is starting titration with a TIRF medicine. What dose must they start with? Please select one option.

[RANDOMIZE LIST WITH I DON'T KNOW ALWAYS AT THE END]

- ○ An appropriate dose based on the dose of the opioid medicine used for underlying persistent cancer pain.
- ○ The dose that the prescriber believes is appropriate based on their clinical experience.
- ○ The lowest available dose, unless individual product Full Prescribing Information provides product-specific guidance.
- ○ The median available dose.
- ○ I don't know.

18. A prescriber has started titrating a patient with the lowest dose of a TIRF medicine. However, after 30 minutes the breakthrough pain has not been sufficiently relieved. What should they advise the patient to do? Please pick the best option of the scenarios described.

[RANDOMIZE LIST WITH I DON'T KNOW ALWAYS AT THE END]

- ○ Take another (identical) dose of the TIRF medicine immediately.
- ○ Take a dose of an alternative rescue medicine.
- ○ Provide guidance based on the product-specific Medication Guide because the instructions are not the same for all TIRF medicines.
- ○ Double the dose and take immediately.
- ○ I don't know.

19. A patient is taking a TIRF medicine and the doctor would like to prescribe erythromycin, a CYP3A4 inhibitor. Please pick the best option of the scenarios described.

[RANDOMIZE LIST WITH I DON'T KNOW ALWAYS AT THE END]

- ○ The patient can't be prescribed erythromycin, because using it at the same time as a TIRF medicine could be fatal.
- ○ Use of a TIRF medicine with a CYP3A4 inhibitor may require a dosage adjustment; carefully monitor the patient for opioid toxicity, otherwise such use

may cause potentially fatal respiratory depression.

- ○ There is no possible drug interaction between CYP3A4 inhibitors and TIRF medicines.
- ○ The dose of the TIRF medicine must be reduced by one half if a CYP3A4 inhibitor is prescribed in the same patient.
- ○ I don't know.

20. Before initiating treatment with a TIRF medicine, prescribers must review the Medication Guide with the patient. Please select True, False, or I don't know for each of the following counseling statements.

	[RANDOMIZE LIST]	**True**	**False**	**I don't know**
20a.	TIRF medicines contain fentanyl in an amount that could be fatal to children of all ages, in individuals for whom they were not prescribed, and in those who are not opioid tolerant.	○	○	○
20b.	Inform patients that TIRF medicines must not be used for acute or postoperative pain, pain from injuries, headache/migraine, or any other short-term pain.	○	○	○
20c.	Instruct patients that they can continue to take their TIRF medicine, if they stop taking their around-the-clock opioid medicine.	○	○	○
20d.	Instruct patients to never share their TIRF medicine with anyone else, even if that person has the same symptoms.	○	○	○

21. Please answer True, False, or I don't know for the following statement about TIRF medicines:

TIRF medicines should only be taken by patients who are opioid tolerant.

- ○ True
- ○ False
- ○ I don't know

22. Which of the following risks are associated with the use of TIRF medicines? Please answer True, False, or I don't know for the following statements.

[RANDOMIZE LIST]	**True**	**False**	**I don't know**
22a. Misuse	○	○	○
22b. Abuse	○	○	○
22c. Addiction	○	○	○
22d. Overdose	○	○	○
22e. Hypothyroidism	○	○	○
22f. Infection	○	○	○

[BEGIN PREAMBLE 2 – DISPLAY ON SAME PAGE AS NEXT QUESTION]

The next set of questions is about the educational materials for TIRF medicines and the TIRF Patient-Prescriber Agreement. As a reminder, the TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Subsys® and generic versions of any of these brands.

[END PREAMBLE 2]

~~21.~~23 Did you receive or do you have access to the Full Prescribing Information for the TIRF medicine(s) that you prescribe?

- o Yes
- ~~o No **[GO TO Q23]**~~
- ~~o I don't know **[GO TO Q23]**~~
- o No **[GO TO Q25]**
- o I don't know **[GO TO Q25]**

~~22.~~24 Did you read the Full Prescribing Information for the TIRF medicine(s) that you prescribe?

- o Yes
- o No
- o I don't know

~~23.~~25 Did you receive or do you have access to the Medication Guide for the TIRF medicine(s) that you prescribe?

- o Yes
- o No **[GO TO Q27]**
- o I don't know **[GO TO Q27]**

- ~~o No **[GO TO Q25]**~~
- ~~o I don't know **[GO TO Q25]**~~

~~24.~~26 Did you read the Medication Guide for the TIRF medicine(s) that you prescribe?

- Yes
- No
- I don't know

~~25.~~27 Did you or do you have any questions about the information in the Full Prescribing Information or Medication Guide?

- Yes
- ~~No **[GO TO Q27]**~~
- ~~I don't know **[GO TO Q27]**~~
- No **[GO TO Q29]**
- I don't know **[GO TO Q29]**

[IF QUESTION ~~26~~27 YES, DISPLAY QUESTION 28 ON SAME PAGE]

~~26. What are your questions? **[MULTILINE INPUT]**~~

28. What are your questions?

[MULTILINE INPUT]

~~27.~~29 Do you review the Patient-Prescriber Agreement Form with each of your patients for whom you prescribe TIRF medicines or their caregiver?

- Yes
- No **[GO TO ~~DEMOGRAPHICS PREAMBLE 1~~QUESTION 32]**
- I don't know **[GO TO ~~DEMOGRAPHICS PREAMBLE 1~~QUESTION 32]**

~~28.~~30 Do you and the patient or their caregiver sign the Patient-Prescriber Agreement Form for TIRF medicines after you have reviewed it with him/her?

- ○ Yes
- ○ No
- ○ I don't know

~~29.~~31 Do you give a copy of the Patient-Prescriber Agreement Form for TIRF medicines to the patient or their caregiver?

- ○ Yes
- ○ No
- ○ I don't know

32. How frequently do you perform the following activities when prescribing TIRF medicines? Please answer Always, Only with the first prescription, Sometimes, Never, or I don't know.

	[RANDOMIZE LIST]	**Always**	**Only with the first prescription**	**Sometimes**	**Never**	**I don't know**
32a.	Talk to the patient about the risks and possible side effects of the TIRF medicine that was most recently prescribed.	○	○	○	○	○
32b.	Instruct the patient on how to use the TIRF medicine that was most recently prescribed.	○	○	○	○	○
32c.	Instruct the patient on how to store or keep the TIRF medicine that was most recently prescribed.	○	○	○	○	○

[BEGIN DEMOGRAPHICS PREAMBLE 1 - DISPLAY ON SAME PAGE WITH NEXT QUESTION]

There are just a few more questions to help us combine your answers with other answers we have received.

[END DEMOGRAPHICS PREAMBLE 1]

~~30.~~33 On average, how many times per month have you prescribed the TIRF medicines within the last 6 months?

- o None **[GO TO DEMOGRAPHICS PREAMBLE 2]**
- o 1 2 times per month
- o 3 5 times per month
- o More than 5 times per month
- o I don't remember

~~31.~~34 Please select the TIRF medicines that you have prescribed within the last 6 months. Please select all that apply.

- ☐ Abstral®
- ☐ Actiq® or generic Actiq®
- ☐ Fentora®
- ☐ Lazanda®
- ☐ Subsys®

[BEGIN DEMOGRAPHICS PREAMBLE 2 - DISPLAY ON SAME PAGE WITH NEXT QUESTION]

These last few questions are for demographic purposes.

[END DEMOGRAPHICS PREAMBLE 2]

~~32.~~35 What is your gender?

- o Male
- o Female
- o Prefer not to answer

~~33.~~36 What is your medical degree?

- o MD
- o DO
- o Nurse Practitioner
- o Physician Assistant
- o Prefer not to answer

~~34.~~37 In total, how many years have you been practicing medicine, since completing your education?

- o Less than 3 years
- o 3 5 years
- o 6 10 years
- o 11 15 years
- o More than 15 years
- o Prefer not to answer

~~35.~~38 Do you practice in a closed healthcare system, such as: (b) (4) VA, DoD, or NIH?

- Yes
- No

~~36.~~39 In which state do you practice?

[DROP-DOWN LIST INPUT WITH STATES TABLE WITH "Prefer not to answer" at END]

~~37.~~40 What is your medical specialty?

- Oncology
- Primary care
- Pain management
- Other (please specify): **[FREE TEXT]**
- No designated specialty

[PHONE - BEGIN ADVERSE EVENT/PRODUCT COMPLAINT – KEEP ON ONE PAGE]

(INTERVIEWER: Please record if respondent spontaneously reported an adverse event or product complaint during the course of this interview.)

- Yes
- No **[GO TO CLOSING 1]**

Enter Safety Adverse Event Verbatim

[MULTILINE INPUT]

(INTERVIEWER: Indicate to the respondent that someone may call back to ask more questions about the adverse event or product complaint that was reported.)

[END ADVERSE EVENT/PRODUCT COMPLAINT]

[BEGIN CLOSING 1 – KEEP ON ONE PAGE]

We would like to send you a $125 honorarium within the next few weeks to thank you for your time, but we need your name and address to do so. If you do not provide your name and address you will not receive the honorarium for your time and participation in the survey. As a reminder, physicians who practice in Vermont, Massachusetts, or Minnesota should be aware that they will not be permitted to receive payment for survey completion.

Do you agree to give us your name and mailing address so we can send you the honorarium?

- ○ Yes
- ○ No **[GO TO CLOSING 2]**

FIRST NAME: **[FREE TEXT]**

LAST NAME: **[FREE TEXT]**

ADDRESS: **[MULTILINE INPUT]**

CITY: **[FREE TEXT]**

STATE: **[DROP-DOWN LIST INPUT WITH STATES TABLE]**

ZIP: **[MUST BE 5 NUMERIC CHARACTERS ONLY]**

[END CLOSING 1]

[BEGIN CLOSING 2 – KEEP ON ONE PAGE]

We would also like to ask for your telephone number. Providing your telephone number is optional and it will be used to contact you only if there are questions about your survey responses.

Do you want to provide your telephone number?

○ Yes

○ No **[GO TO CLOSING 3]**

Telephone: **[MUST BE 10-DIGIT NUMERIC-ONLY CHARACTERS]**

[END CLOSING 2]

[BEGIN CLOSING 3]

That ends the survey. Thank you again for your help.

[END CLOSING 3]

[END SURVEY CONTENT]

Appendix B ~~SAMPLE~~ Prescriber ~~Invitation Letter~~Recruitment Materials

INVITATION LETTER

[CURR DATE]~~———~~

[PRESCRIBER~~_~~ FIRST NAME]

~~[~~[PRESCRIBER LAST NAME], [TITLE]
[PRESCRIBER STREET ADDR]

~~[~~
[PRESCRIBER CITY], [PRESCRIBER STATE] [PRESCRIBER ZIP]

Dear [PRESCRIBER~~_~~ FULL NAME~~];~~],

You were selected to receive this letter because you have enrolled in the TIRF REMS Access ~~Program~~program and have prescribed a TIRF medicine in the last 6 months. We are contacting you to invite you to participate in a survey being conducted by the manufacturers of Transmucosal Immediate Release Fentanyl (TIRF) medicines, as required by the Food and Drug Administration (FDA). The purpose of the survey is to assess prescribers' understanding of the safe and appropriate use of these medicines. The TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Subsys®, and generic versions of any of these brands.

The manufacturers of TIRF medicines ~~(collectively referred to as the "TIRF REMS Industry Group")~~ include Actavis Laboratories FL~~,~~ Inc.~~;~~., BioDelivery Sciences International, Inc.~~ (BDSI);~~., Cephalon, Inc. (a wholly-owned subsidiary of Teva Pharmaceutical Industries, Ltd.~~);~~.), Depomed, Inc.~~; Galena Biopharma, Inc.;~~., Insys Therapeutics, Inc.~~;~~., Mallinckrodt Pharmaceuticals~~;~~, Mylan Inc., Par Pharmaceuticals, Inc., and ~~Par Pharmaceutical~~Sentynl Therapeutics, Inc.~~.~~., (collectively referred to as the "TIRF REMS Industry Group"). These manufacturers are looking for 300 prescribers to complete the survey. Eligible prescribers who complete the survey will be sent a $125 honorarium to thank them for their time. The survey will take 15-20 minutes.

You are not obligated to take part in this survey. If you are interested in participating and to find out if you are eligible:

- Go online* to www.TIRFREMSsurvey.com any time, or
- Call 1-877-379-3297, 8 a.m. to 8 p.m. Eastern Time, Monday through Friday

Please have this letter with you at the time you take the survey. You will be asked to provide this code prior to starting the survey: **[CODE ID]**.

Please note that you should take the survey on a desktop or laptop computer. Taking the survey on mobile devices, such as smart phones, tablets, and e-notebooks, is not supported.

Your answers will be kept strictly confidential and will be combined with the answers from other prescribers who take this survey. Your name will not be used in the report of this survey and your contact information will only be used to send you a $125 honorarium for the time you took to complete the survey and, if required, to comply with a federal or state law or regulation, including without limitation, reporting payments made to physicians under the federal physician payment sunshine provisions. ~~Prescribers~~Physicians who practice in Vermont, Massachusetts, or Minnesota should be

aware that they will not be permitted to receive payment for survey completion and may elect not to complete the survey.

~~You are under no obligation to participate in this survey. If you are interested in participating, go to **www.TIRFREMSsurvey.com** anytime or call **1-877-379-3297,** 8AM to 8PM Eastern Time Monday through Friday. You will be asked to give this unique code prior to starting the survey: **[CODE_ID]**.~~

~~* We recommend that you take the survey on a desktop or laptop computer. Taking the survey on mobile devices, such as smart phones, tablets, and e-notebooks, is not supported.~~

~~Please have this letter with you at the time you take the survey.~~ ~~Thank you in advance for your help with this important effort.~~

Sincerely,

The TIRF REMS Survey Team

1-877-379-3297

www.TIRFREMSsurvey.com

REMINDER LETTER

[CURR_DATE]

[PRESCRIBER_FIRST_NAME] [PRESCRIBER_LAST NAME], [TITLE]
[PRESCRIBER_STREET_ADDR]
[PRESCRIBER_CITY], [PRESCRIBER_STATE] [PRESCRIBER_ZIP]

Dear [PRESCRIBER_FULL_NAME],

Recently you were sent a letter, inviting you to participate in a survey being conducted by the manufacturers of Transmucosal Immediate Release Fentanyl (TIRF) medicines, as required by the Food and Drug Administration (FDA). The purpose of the survey is to assess prescribers' understanding of the safe and appropriate use of these medicines. The TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Subsys®, and generic versions of any of these brands.

The manufacturers of TIRF medicines include Actavis Laboratories FL Inc., BioDelivery Sciences International, Inc., Cephalon, Inc. (a wholly-owned subsidiary of Teva Pharmaceutical Industries, Ltd.), Depomed, Inc., Insys Therapeutics, Inc., Mallinckrodt Pharmaceuticals, Mylan Inc., Par Pharmaceuticals, Inc., and Sentynl Therapeutics, Inc., (collectively referred to as the "TIRF REMS Industry Group"). These manufacturers are looking for 300 prescribers to complete the survey. Eligible prescribers who complete the survey will be sent a $125 honorarium to thank them for their time. The survey will take 15-20 minutes.

You are not obligated to take part in this survey. If you are interested in participating and to find out if you are eligible:

- Go online* to www.TIRFREMSsurvey.com any time, or
- Call 1-877-379-3297, 8 a.m. to 8 p.m. Eastern Time, Monday through Friday

Please have this letter with you at the time you take the survey. You will be asked to give this code prior to starting the survey: **[CODE_ID]**.

Please note that you should take the survey on a desktop or laptop computer. Taking the survey on mobile devices, such as smart phones, tablets, and e-notebooks, is not supported.

Your answers will be kept strictly confidential and will be combined with the answers from other prescribers who take this survey. Your name will not be used in the report of this survey and your contact information will only be used to send you a $125 honorarium for the time you took to complete the survey and, if required, to comply with a federal or state law or regulation, including without limitation, reporting payments made to physicians under the federal physician payment sunshine provisions. Physicians who practice in Vermont, Massachusetts, or Minnesota should be aware that they will not be permitted to receive payment for survey completion and may elect not to complete the survey.

Sincerely,

The TIRF REMS Survey Team

1-877-379-3297

www.TIRFREMSsurvey.com

THANK YOU LETTER – HONORARIUM PAYMENT

[CURR_DATE]

[PRESCRIBER_FIRST_NAME] [PRESCRIBER_LAST NAME], [TITLE]
[PRESCRIBER_STREET_ADDR]
[PRESCRIBER_CITY], [PRESCRIBER_STATE] [PRESCRIBER_ZIP]

Dear [PRESCRIBER_FULL_NAME],

On behalf of the TIRF REMS Industry Group, we want to thank you for taking part in the TIRF REMS Survey. To express our appreciation for your valuable time, enclosed is a gift card for $125.

Card Activation Instructions:

To prevent loss, the enclosed card is not activated. Prior to using your card, please call the TIRF REMS Coordinating Center at 1-877-379-3297 between 8:00 a.m. and 8:00 p.m. Eastern Time, Monday through Friday, to activate your card. Please have your card available when you make the call. Also, please read the enclosed Terms and Conditions document before using your gift card as well as the privacy policy that can be found at: http://www.ctpayer.com/downloads/privacy_policy.pdf.

Please note the enclosed card needs to be activated on or before: **xx xxx xxxx**

Additionally, for your information and to reinforce important safety messages about TIRF medicines, we have enclosed the following two documents:

1. A copy of the correct answers to the important survey questions about the TIRF REMS key risk message questions.
2. A copy of the Important Safety Information.

Additional information regarding TIRF REMS Access program can be found at www.TIRFREMSaccess.com.

Thank you for your time and consideration regarding this important safety information.

Sincerely,

The TIRF REMS Survey Team

1-877-379-3297

www.TIRFREMSsurvey.com

Enclosures: Gift Card and Terms and Conditions
Correct Answers to Important Survey Questions
TIRF Important Safety Information

THANK YOU LETTER – NO HONORARIUM PAYMENT

[CURR_DATE]

[PRESCRIBER_FIRST_NAME] [PRESCRIBER_LAST NAME], [TITLE]
[PRESCRIBER_STREET_ADDR]
[PRESCRIBER_CITY], [PRESCRIBER_STATE] [PRESCRIBER_ZIP]

Dear [PRESCRIBER_FULL_NAME],

On behalf of the TIRF REMS Industry Group, we want to thank you for taking part in the TIRF REMS Survey.

For your information and to reinforce important safety messages about TIRF medicines, we have enclosed two documents:

1. A copy of the correct answers to the important survey questions about the TIRF REMS key risk message questions.
2. A copy of the Important Safety Information.

Additional information regarding TIRF REMS Access program can be found at www.TIRFREMSaccess.com.

Thank you for your time and consideration regarding this important safety information.

Sincerely,

The TIRF REMS Survey Team
1-877-379-3297
www.TIRFREMSsurvey.com

Enclosures: Correct Answers to Important Survey Questions

TIRF Important Safety Information

Appendix C Correct Answer Document

Correct Responses to Select PRESCRIBER Survey Questions about Important Safety Messages for Transmucosal Immediate Release Fentanyl (TIRF) medicines (TIRF medicines include Abstral®, Actiq®, Fentora®, Lazanda®, Subsys®, and generic versions of any of these brands)

Q: Please select True, False, or I don't know for each of the following. According to the labeling for TIRF medicines, patients with cancer who are considered opioid-tolerant are those:

STATEMENT	DESIRED RESPONSE
Who are taking around-the-clock opioid therapy for underlying, persistent cancer pain for one week or longer	TRUE
Who are not currently taking opioid therapy, but have taken opioid therapy before	FALSE
Who have no known contraindications to the drug fentanyl, but are not currently taking around-the-clock opioid therapy	FALSE

Q: Please answer True, False, or I don't know for each statement based on the labeling for TIRF medicines.

STATEMENT	DESIRED RESPONSE
TIRF medicines are contraindicated in opioid non-tolerant patients because life-threatening respiratory depression could occur at any dose.	TRUE
Death has occurred in opioid non-tolerant patients treated with some fentanyl products.	TRUE
TIRF medicines may be used to treat opioid non-tolerant patients.	FALSE
Prescribers starting a patient on a TIRF medicine must begin with titration from the lowest dose available for that specific product, even if the patient has previously taken another TIRF medicine.	TRUE
According to the product labeling, a cancer patient may start a TIRF medicine and an around-the-clock opioid at the same time.	FALSE
According to the product labeling, a cancer patient who has been on an around-the-clock opioid for 1 day may start taking a	FALSE

TIRF medicine for breakthrough pain.	

Q: Please select True, False, or I don't know for each of the following. According to the labeling for TIRF medicines, patients considered opioid-tolerant are those who are taking, for one week or longer, at least:

STATEMENT	DESIRED RESPONSE
8 mg oral hydromorphone/day	**TRUE**
60 mg oral morphine/day	**TRUE**
30 mg oral oxycodone/day	**TRUE**
25 mcg transdermal fentanyl/hour	**TRUE**
25 mg oral oxymorphone/day	**TRUE**
An equianalgesic dose of another oral opioid	**TRUE**

Q: Per the approved labeling for TIRF medicines, for which of the following indication(s) are TIRF medicines approved? Please answer Yes, No, or I don't know for each option.

STATEMENT	DESIRED RESPONSE
Acute or postoperative pain	**NO**
Headache or migraine pain	**NO**
Dental pain	**NO**
Breakthrough pain from cancer	**YES**
Chronic non-cancer pain	**NO**

Q: The patients described are experiencing breakthrough pain. According to the labeling, a TIRF medicine is not appropriate for one of them. Which patient should not receive a TIRF medicine? Please select one option.

A: Adult female with localized breast cancer; just completed a mastectomy and reconstructive surgery; persistent cancer pain managed with 30 mg oral morphine daily for the past 6 weeks.

Q. Before initiating treatment with a TIRF medicine, prescribers must review the Medication Guide with the patient. Please select True, False, or I don't know for each of the following counseling statements.

STATEMENT	DESIRED RESPONSE
Inform patients that TIRF medicines must not be used for acute or postoperative pain, pain from injuries, headache/migraine, or any other short-term pain.	**TRUE**
Instruct patients that they can continue to take their TIRF medicine, if they stop taking their around-the-clock opioid medicine.	**FALSE**

Q: Please answer True, False, or I don't know for each statement based on the labeling for TIRF medicines.

STATEMENT	DESIRED RESPONSE
It is important to monitor for signs of abuse and addiction in patients who take TIRF medicines.	**TRUE**
TIRF medicines can be abused in a manner similar to other opioid agonists.	**TRUE**
Dosing of TIRF medicines is not equivalent on a microgram-to-microgram basis.	**TRUE**
TIRF medicines are interchangeable with each other regardless of route of administration.	**FALSE**
The conversion of one TIRF medicine for another TIRF medicine may result in a fatal overdose because of differences in the pharmacokinetics of fentanyl absorption.	**TRUE**

Q: Which of the following are risk factors for opioid abuse? Please answer Yes, No, or I don't know for each option.

STATEMENT	DESIRED RESPONSE
A personal history of psychiatric illness	**YES**
A personal history of past or current alcohol or drug abuse, or a family history of illicit drug use or alcohol abuse	**YES**

Q: A patient is already taking a TIRF medicine but wants to change their medicine. His/her doctor decides to prescribe a different TIRF medicine (that is not a bioequivalent generic version of a branded product) in its place. According to the labeling, how should the prescriber proceed? Please select one option.

A: The prescriber must not convert to another TIRF medicine on a microgram-per-microgram basis because these medicines have different absorption properties and this could result in a fentanyl overdose.

Q: Please answer True, False, or I don't know for the following statement about TIRF medicines:

STATEMENT	DESIRED RESPONSE
TIRF medicines should only be taken by patients who are opioid tolerant.	**TRUE**

Q: Which of the following risks are associated with the use of TIRF medicines? Please answer True, False, or I don't know for the following statements.

STATEMENT	DESIRED RESPONSE
Misuse	**TRUE**
Abuse	**TRUE**
Addiction	**TRUE**
Overdose	**TRUE**
Hypothyroidism	**FALSE**
Infection	**FALSE**

If you have questions or are unclear about any of these responses, please refer to the Full Prescribing Information, the Important Safety Information, and the Medication Guide for TIRF medicines.

Appendix B Survey Tables

Listing 1.1 and Listing 2.1 includes individual responses to Question 10 (*For what type(s) of chronic pain conditions do you prescribe a TIRF medicine to opioid tolerant patients?*), and Question 11 (*Why do you select a TIRF medicine to treat these chronic pain conditions in patients who are opioid tolerant?*), respectively. Aggregate data for Question 10 is provided in Table 14 and aggregate data for Question 11 is provided in Table 15. The verbatim responses are provided unedited as submitted by the prescriber.