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FENTORA ® Risk Minimization Actiqon Plan
(The SECURE Program)

3rd Quarterly Report

(April 1, 2007 through June 30, 2007)

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FENTORA ® Risk Minimization Actiqon Plan Quarterly Report

1 REGULATORY OVERVIEW

FENTORA was approved by the US FDA on 25-September -2006 for the treatment of breakthrough pain in opioid tolerant patients with cancer. It was approved with a risk minimization program, SECURE (Solutions through Education, Communication and Understanding Risk Minimization Excellence) in order to assure safe use of the product while mitigating risks perceived as being associated with its use.

The SECURE Program is focused on minimizing three perceived risks:

1. Use of FENTORA by opioid non-tolerant individuals;
2. Misuse, abuse and diversion of FENTORA ; and
3. Unintended (accidental) exposure to FENTORA .

In order to address these risks, Cephalon has identified three goals for the SECURE Program. These goals are expressed as outcomes of the FENTORA RiskMAP. Associated with each of these goals, there are specific and measurable program objectives that are described below.

Goal 1: FENTORA should be used only by opioid tolerant patients with cancer

Objectives associated with Goal 1:

1. Educate physicians that FENTORA should not be used in opioid non-tolerant patients
2. Educate patients that FENTORA should be used only by individuals with cancer who are opioid tolerant
3. Educate pharmacists, and other healthcare personnel of the importance of FENTORA being prescribed, distributed, and used only by opioid tolerant patients with cancer.

Goal 2: Abuse, misuse and diversion of FENTORA should not occur

Objectives associated with Goal 2:

1. Ensure adequate controls are instituted, and maintained to prevent the diversion of FENTORA from Cephalon's supply chain
2. Ensure adequate education, surveillance, and interventions are instituted and maintained to minimized diversion of FENTORA when the product is no longer within Cephalon's supply chain.
3. Reduce the potential abuse, misuse, and diversion of FENTORA by (a) providing education to healthcare personnel and to pertinent nationwide demographic communities; (b) performing ongoing surveillance of and reActiqon to geographical outbreaks of abuse, misuse, and diversion; and, (c) cooperating with and providing assistance to law enforcement in investigations of incidents of abuse or diversion.

Goal 3: Unintended (accidental) exposure to FENTORA should not occur

Objectives associated with Goal 3:

1. Reduce or eliminate accidental exposure through product packaging
2. Educate physicians, pharmacists, and patients about "safe product use" in efforts to reduce or eliminate accidental exposure
3. Reduce or eliminate accidental exposure during storage of FENTORA .

As part of the FENTORA RiskMAP, Cephalon committed to evaluate the tools implemented by the program on a quarterly basis in the effort of determining the success in meeting the three SECURE goals. The reporting period for this third quarterly report is from 1-April-2007 to 30-June-2007.

2 RESULTS

2.1 Background

In accordance with sections 4.1-4.7 of the RiskMAP, quarterly reports will include assessments of:

- Extent of use
- Indicators of off-label use and inappropriate prescribing (i.e., opioid-naïve), inclusive of patient longitudinal data
    - Notes:
        - summarization of all non-accidental pediatric exposures not associated with an ADR will be included here
        - off-label use and inappropriate prescribing results will be discussed separately in this report as they are discreet topics

- Summarization of reports involving all medication errors (actual and potential), regardless of patient outcome
- Summarization of all accidental exposures (in children and adults) including asymptomatic reports
- Summarization of all non-accidental pediatric exposures associated with an ADR (serious and non-serious)
- Summarization of ADRs involving opioid naïve patients
- Serious ADRs associated with suspected abuse, misuse or diversion
- Rates of suspected misuse, abuse, addiction or diversion reported
- Results of any investigation or surveys conducted, and
- Outcomes from any interventions, such as targeted educational interventions and antidiversion programs conducted

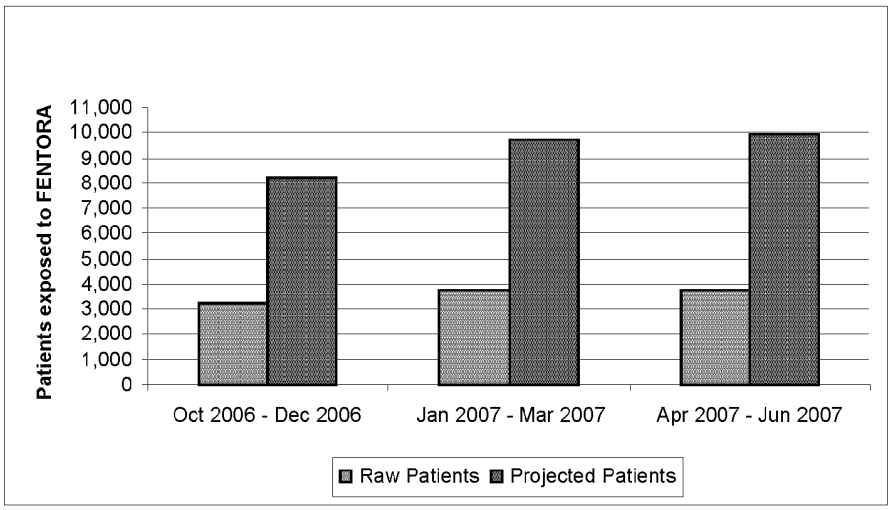
Because of the manner and frequency in which the surveys are being conducted as well as the lag time in receipt of data available from our surveillance initiatives, not every quarterly report will contain all of the aspects delineated above. For example, since the surveys are being conducted twice a year, results will not be included every quarter. Further specifics will be provided as it pertains to the specific surveillance component.

Results will be provided in sections 2.2-2.11of this report. Cephalon's interpretation of the results will be included in section 4.

2.2 Extent of Use

Patient exposure, as calculated from IMS data, is displayed in Figure 1 for the period of October 2006 through June 2007, where the raw patients equate to actual use and the projected are estimates.

Figure 1: Patient Exposure to FENTORA



2.3 Indicators of Off-Label Use (Patient Population)

Indicators of off-label use are evaluated both by syndicated third-party national audit data and by information provided to our Professional Services Medical Information (PMSI) department. As discussed with the FDA during the negotiations of the RiskMAP, syndicated third-party national audit data is initiated during the launch of the product; however, is not available for inclusion in this initial report. Spontaneous report data to evaluate the extent of FENTORA use in the labeled population was provided by Cephalon's Medical Services Department.

There were a total of 489 postmarketing reports received during the period, 01-April-2007 through 30-June-2007. The indication for treatment was unknown or not provided in approximately 9% (44/489) of the cases. Of the remaining 445 reports containing information regarding the indication for treatment with FENTORA , approximately 13% (60/445) involved patients with cancer. The remaining 385 reports (385/445;87%) involved patients with a non-cancer pain indication.

Cumulative summary of spontaneous reports: Since launch of FENTORA on 25-Sep-2006, Cephalon has received 1,344 reports. Of the 1,344 reports, there were 147 (10%;147/1344) reports in which the indication was unknown or not provided, leaving a total of 1,167 evaluable cases. Of the 1,167 cases, 161(14%;161/1167) involved patients treated for breakthrough cancer pain, and 1,036 (89%;1036/1167 involved patients with a non-cancer pain indication.

Syndicated Third-Party National Audit Data

Indicators of off-label use are evaluated by both syndicated third-party national audit data and by information provided to our Medical Services department. Spontaneous report data to evaluate the extent of FENTORA use in the labeled population was provided by Cephalon's Medical Services department.

Data obtained from syndicated third-party national audit data, specifically the IMS longitudinal prescription database (LRx) and the Electronic Medical Claims Switch database, during the period of October 2006 through June 2007, are presented in Table 1 LRx data are collected from retail pharmacies and prescription benefit managers (PBMs). The patient data are then matched with electronic medical claims for diagnosis information based on ICD9 diagnosis codes from physician offices and medical facilities. The patient matching process was HIPPA compliant. Limitations associated with this data are described in the data caveats below.

Table 1: IMS National Audit Data: Patient Population

	Oct 2006 - Dec 2006	Jan 2007 - Mar 2007	Apr 2007 - Jun 2007
Cancer	14.2%	15.9%	19.0%
Lower Back Pain	20.5%	21.8%	20.4%
Neuropathic Pain	12.6%	11.7%	11.7%
Arthritic disease	3.1%	2.9%	2.8%
All Other Pain*	27.8%	27.4%	27.1%
All Other Diagnoses**	21.9%	20.3%	19.0%

***All other pain includes**: migraine/headache, arthritic disease, sprains, fractures, abdominal pain, joint pain, etc.

****All other diagnosis**: includes all FENTORA patients that could not be mapped to one of the primary diagnosis. These patients may not have had any of the primary diagnosis or they may be associated with a primary diagnosis but the physician treating the patient may not be captured by the electronic medical switch (claims) data that supply the transActiqon data to the database.

2.4 Indicators of Inappropriate Prescribing (Opioid Tolerance)

Indicators of inappropriate prescribing are evaluated both by syndicated third-party national audit data and by information provided to our Professional Services Medical Information (PMSI) department. As discussed with the FDA during the negotiations of the RiskMAP, syndicated third-party national audit data is initiated during the launch of the product; however, is not available for inclusion in this initial report. Spontaneous report data to evaluate the extent of inappropriate prescribing of FENTORA use was provided by Cephalon's Medical Services Department.

Of the 489 reports received this quarter, approximately 22% (106/489) of the reports contained insufficient information needed to determine if the patient was opioid tolerant prior to receiving a prescription for FENTORA . Additionally, information regarding opioid tolerance was not obtained for 2 reports; thus there were 381 evaluable reports.

Of the remaining 381 reports, approximately 87% (332/381) involved patients who were opioid tolerant prior to starting FENTORA .

Approximately 13% of the reports (49/381) involved patients who were classified as opioid naïve.

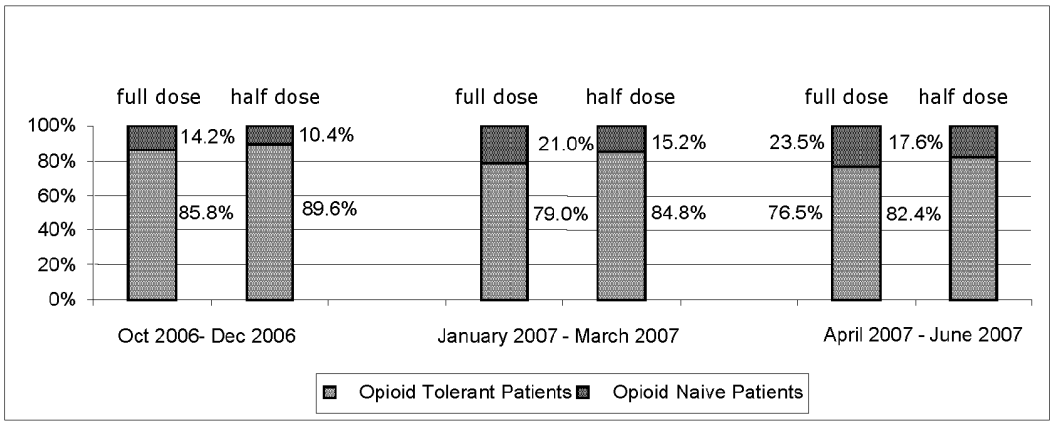
Cumulative summary of spontaneous reports: Since launch, Cephalon has received 1003 evaluable spontaneous reports containing sufficient information needed to determine opioid tolerance. Of these, approximately 87% (869/1003) reports involved patients who were opioid tolerant prior to starting FENTORA .

Syndicated Third-Party National Audit Data

Indicators of inappropriate prescribing are evaluated both by syndicated third-party national audit data and by information provided to our Medical Services department. Spontaneous report data to evaluate the extent of inappropriate prescribing of FENTORA use was provided by Cephalon's Medical Services Department.

For the time period 01-October-2006 through 31-December-2006, IMS Longitudinal Patient database estimated 2,252 FENTORA new patients. Of these new patients, 1,933 were opioid tolerant (85.8%). For the time period, 01-January-2007 through 31-March-2007, IMS estimated 1,726 FENTORA new patients and 1,363 of these patients were opioid tolerant (79%). For the time period, 01-April-2007 through 30-June-2007, IMS estimated 1,446 FENTORA new patients and of these patients 1,106 were opioid tolerant (76.5%). An ad-hoc analysis was conducted to evaluate those patients exposed to half of the required minimal opioid dose. These data are displayed in Figure 2. The classification algorithm to determine whether patients were opioid tolerant is located in Appendix I.

Figure 2: Percent of Patients Opiate Tolerant vs. Naive based on Patients taking Minimal Opioid Dose Required and Half Dose 90 days Prior to FENTORA



2.5 Summarization of Reports Involving All Medication Errors (actual and potential)

During this reporting period (01-April-2007 thru 30-June-2007), there were seven spontaneous reports of medication error received by Cephalon's Medical Services group. Thus since launch of FENTORA , there have been 10 spontaneous reports of medication error.

The seven cases are described below:

US020015

27-April-2007: A report received via Actiqve surveillance of the American Association of Poison Control Centers database regarding a 69-year-old male who received FENTORA (fentanyl buccal tablet), 100 mcg, via an incorrect dosing route on 25-June-2007. The event was judged as a nontoxic exposure with no clinical effects expected. Additional case details have been requested from the AAPCC.

Case Comment: No contact information for the patient or physician was provided. It was not possible to conduct further follow-up regarding this case.

US020016

27-April-2007: A reported received via Actiqve surveillance of the American Association of Poison Control Centers database, NCSBeta (case#2), regarding a female in her 60's, who received FENTORA (fentanyl buccal tablet), 100 mcg, via an incorrect dosing route on 08-Feburary-2007. The error did not result in any symptoms. Additional case details have been requested from the AAPCC.

Case Comment: No contact information for the patient or physician is provided. It is not possible to conduct further follow-up regarding this case.

US020033

01-May-2007: A report received from a female consumer who was prescribed FENTORA (fentanyl buccal tablet) for breakthrough cancer pain on 01-May-2007. The labeling instructions on the prescriptions stated "place one tablet under the tongue four times per day." It was not known if the physician prescribed the route of administration or if the instructions were erroneously placed on the label at the pharmacy.

Case Comment: The patient ended the call prior to obtaining physician and pharmacy information. Therefore, further follow-up is not reasonably possible to obtain.

US020133

15-May-2007: A report received from a female consumer who was prescribed FENTORA (fentanyl buccal tablet) for lower back pain. The patient's physician initially wrote a prescription for 400 mcg FENTORA when converting the patient from 400 mcg Actiq. However, the physician's nurse noted the error and informed the physician that the FENTORA conversion chart recommends starting patient at 100 mcg if being switched from Actiq. The patient was never given the prescription for 400 mcg FENTORA. The prescription was subsequently changed to FENTORA 100 mcg without incident.

Case Comment: The consumer declined to provide information regarding the prescribing physician. Before concluding the call, Cephalon's Medical Services Department provided information to the consumer regarding appropriate dosing as stated in the approved Package Insert for FENTORA .

US020247

06-June-2007: Limited information received from a registered nurse, via a sales representative, regarding a 34-year-old female who was prescribed FENTORA (fentanyl buccal tablet) therapy 400 mcg for an unspecified indication. On an unknown date, the patient died of a fatal overdose with FENTORA .

14-June-2007: Additional information received from the physician indicated that the patient had been previously taking two 800 mcg Actiq (oral transmucosal fentanyl citrate) as needed for severe headaches. She was not receiving any other opioids. At times, the patient also required additional Demerol (pethidine HCl) shots, 175 mg, at an urgent care clinic for headache relief. The physician stated that the patient had a high tolerance to opioids given the high doses of both Actiq and Demerol required to relieve her pain. On an unknown date in May-2007, the patient was switched from Actiq to FENTORA 400 mcg and the physician instructed her to use only one tablet. The physician wrote instructions on the prescription that the dose could be repeated once if no pain relief was obtained after 30 minutes.

The physician was told by the patient's husband that he thought the dispensed instructions stated that FENTORA could be taken every 30 minutes but the physician could not verify if true. The physician believed that the first dose was taken during the evening hours. The following morning, the patient awakened and was very groggy, but her husband stated that it was not unusual for her to be in that state when waking up so he was not concerned. The patient then went back to bed with a cold cloth to relieve her headache. Sometime later that morning, she was found dead by her father. It was then discovered that six FENTORA tablets were missing (2400 mcg total) and were presumed to have been consumed by the patient. The physician indicated that the patient may have been suicidal; however, she was speaking in terms of making plans for the future and at her last visit, she gave no indication of suicidal thoughts. It was not clear at the time of follow-up if the overdose was intentional or accidental. Both autopsy and toxicology results are pending.

Follow-Up information received 07-September-2007:

Autopsy and toxicology reports received indicated tha the patient was last seen alive by her husband on the morning of 17-May-2007. Shortly after noon that day, the patient was found unresponsive in bed by her father-in-law who been requested to check on the patient by her husband because she was complaining of migraine headaches. Emergency services were summoned and resuscitative efforts were begun. She was transported to a regional medical center where she was pronounced dead at 1:41pm. The patient's past medical history was significant for chronic migraine headaches and depression, but there was no previous history of suicidal ideation or attempts. No suicide note was recovered.

The autopsy revealed no significant gross or microscopic abnormality. Toxicology revealed blood fentanyl of 14.1 mcg/ml and urine fentanyl 133 ng/ml. Also found in the blood were ethanol 0.010 gm%, trazodone 0.20 mcg/ml, diazepam 0.42 mcg/ml, and nordiazepam 0.29 mcg/ml. The patient's death was ruled as an accidental fentanyl overdose.

- **Case Comment**: Subsequent to this report, Cephalon initiated a corporate review of all FENTORA safety messages, enhancing more details regarding patient selection and dosing and administration instructions. This information was incorporated into the drafting of Dear HCP letters (one to prescribers and one to other healthcare professionals). Lastly all promotional materials were reviewed and revised to reflect the incorporation of the updated information.

US020307

17-June-2007: A consumer report received regarding a 45-year-old female who initiated FENTORA (fentanyl buccal tablet) therapy, 200 mcg, on 17-June-2007, for the treatment of chronic pain. The patient accidentally ingested her first dose instead of "sucking on the tablet" as directed. Approximately three hours later, the patient had no ill effects. FENTORA therapy continued.

Additional information was received in follow-up with the patient who indicated that she had been instructed on the proper use of the FENTORA tablet and places it between the gum and cheek until dissolved. She also rotates the site with each use. The consumer reported that over the past two days, her gums have become bruised further described as red and tender. FENTORA continues with the event ongoing.

30-July-2007: Follow-up information received from the consumer indicated that she had been taking FENTORA at a dose of 200 mcg every eight hours and the event of bruising gums was resolving.

Case Comment: No further intervention was warranted for this case.

US020449

27-June-07: A consumer report received regarding a 44-year-old female who had been taking Actiq (oral transmucosal fentanyl citrate), 600 mcg lozenges, since 2005, for the treatment of chronic back pain and was accidentally dispensed FENTORA (fentanyl buccal tablet) 600 mcg on 26-June-2007. The patient reported that a prescription for Actiq was dropped off to her pharmacy on 01-June-2007 and was placed on hold until approximately three weeks later when she called the pharmacy to have it filled. On 26-June-2007, the prescription was picked up and on the prescription bag there was a note indicating that the contents included 17 branded Actiq and 13 generic OTFC. The generic substitute was actually FENTORA (fentanyl buccal tablet) 600 ug tablets. Just after midnight on 27-June-2007, the patent took a FENTORA tablet and experienced lightheadedness. The patient was concerned as she normally does not use an entire 600 mcg Actiq lozenge and when the entire 600 ug FENTORA tablet dissolved quickly, she called the local emergency room and was referred to the poison control center. The patient placed a call to the poison control center using the number provided on the Actiq box. She was advised to contact emergency services; however, the patient declined stating that she would awaken her mother.

The patient subsequently contacted Cephalon later on 27-June-2007 to learn more about FENTORA and to understand if FENTORA was a generic substitute for Actiq. The patient stated that her mother picked up the prescription for her and the pharmacy did not mention how the Actiq was substituted with another brand nor did the pharmacy contact her about it. There were no directions provided on how to use FENTORA . Additionally, the FENTORA tablets were placed in the Actiq box along with the Actiq lozenges with a note that "generic" were included. The lightheadedness subsided approximately 20 minutes later; and the patient admitted that she did not awaken her mother subsequent to the call placed to the poison center. The patient also reported that she experienced no pain relief from FENTORA .

Case Comment:

On 16-July-2007, a Cephalon Pain Care Specialist visited the pharmacy and spoke to the pharmacist who dispensed this prescription. The specialist discussed and reinforced the following information:

- FENTORA is **not** generic Actiq.
- FENTORA is more bioavailable than Actiq and that it is a totally different delivery system.
- Reviewed dosing differences, the indication, clinical trial results, dose strengths, impact on oral pH at application site, differences between tablet and Actiq lozenge, time to onset
- Instructions on proper administration, disposal of tablets

The pharmacist was receptive and thanked the representative for clearing up his previous misconceptions.

2.6 Summarization of All Accidental Exposures (in children and adults)

There were no spontaneous reports of accidental or inadvertent pediatric exposure reported during this reporting period.

Upon Actiqve surveillance of the TESS and DAWN Live! databases, no reports of accidental or inadvertent pediatric or adult exposure to FENTORA were identified.

However, there was one spontaneous report of accidental exposure involving an elderly adult female whose son was prescribed FENTORA . This case is further described below:

US020295:

14-June-2007: This report involved a 73 year old female with a history of Alzheimer's disease who was inadvertently exposed to FENTORA . The patient's son had been prescribed FENTORA , 600 mcg and 800 mcg dose strengths, for back pain. In December 2006, two FENTORA tablets (unknown dose strength) were removed from the original blister packaging and placed into an unlabeled container. The patient's mother mistakenly ingested 2 FENTORA tablets taken from the unlabeled container. Immediately after ingesting the FENTORA tablets, she became flushed and was sweating. Emergency Services were called and upon arrival noted that the patient's mother had six Lidoderm (lidocaine) patches on her skin. She was transported to the Emergency Room where she was treated with intravenous fluids for symptoms presumed to be related to a lidocaine overdose. It was reported that the emergency room physician was unaware that the patient had ingested FENTORA tablets. However, the patient responded quickly to treatment and was subsequently released to home approximately one hour later.

Case Comment: During the initial call, the consumer stated he had received information regarding proper storage and disposal of FENTORA . Attempts to contact the patient following the initial call were unsuccessful.

2.7 Summarization of All Non Accidental Pediatric Exposures Associated with an ADR (serious and non-serious)

In accordance with the post-marketing reporting requirements delineated in the RiskMAP, all non accidental pediatric exposures associated with an ADR would be submitted to the FDA as a 15-day alert. There were no cases of non-accidental pediatric exposure associated with an ADR during the reporting period.

2.8 Summarization of ADRs Involving Opioid Naïve Patients

There were 10 reports of adverse drug reActiqons involving opioid naïve patients during the reporting period; including one serious report of overdose that resulted in a fatal outcome. (This case is discussed in section 2.5.- US020247). The remaining nine reports were non-serious.

The reported events were coded to the following MedDRA (version 9.1) preferred terms: drug withdrawal syndrome, dry mouth, sweating (US019831); drug withdrawal syndrome, insomnia, drowsiness (US019924); agitation (US019939); application site pain, oesophageal pain (US019726); retching, vomiting (US020052); urticaria generalized, pruritus (US020071); amnesia, balance disorder (US020130); fatigue (US020139); application site vesicles (US020239) and overdose, drug dispensing error (US020247). See Table 2 below.

Table 2: Summary of Adverse Drug ReActiqons Involving Opioid Naïve Patients (Excludes accidental exposures, misuse, abuse and suicides) during the Reporting Period

Reporting period	Total Number of Reports in Opioid Naïve Patients	Number (%) of ADR Reports in Opioid Naïve Patients	Number of Reports in Opioid Naïve Patients Received without ADR	Total Number of AES Reports		AE Outcome*			
				Serious	Non-serious	Rec	Not Rec	Fatal	Unk
25-Sep-2006 thru 31-Dec-2006	39	5(5/39; 12.8%)	34 (34/39; 87%)	0	5	2	2	0	1
01-Jan-2007 thru 30-Mar-2007	46	5 (5/46; 10.9%)	41 (41/46; 89%)	0	5	2	2	0	1
01-Apr-2007 thru 30-Jun-07	49	10(10/49; 20.4%)	39 (39/49; 79.6%)	**1**	**9**	**4**	**5**	**1***	**0**
Cumulative Total	134	20(20/134; 15%)	114(114/134; 85%)	**1**	**19**	**8**	**9**	**1**	**2**

ADR Outcomes: Rec =recovered; Not Rec=Not recovered (includes resolving events), Unk=Unknown
* Case discussed in Section 2.5 – US020247

Since the launch of FENTORA , there have been 134 reports in opioid naïve patients. In the majority (86%) of cases, no ADRs were reported. Of the 19 reports with ADRs involving opioid naïve patients, nearly all of these events were non-serious. However, there has been one fatal outcome associated with use of FENTORA in an opioid naïve patient (US020247).See section 2.5 for case summary and subsequent Cephalon interventions

2.9 Rates of Suspected Misuse, Abuse, or Diversion

In Section 4.2 of the RiskMAP, Post-Marketing Reporting Systems, Cephalon committed to submitting 15-day alerts to the FDA for serious ADRS associated with suspected abuse, misuse or diversion. There were no serious ADRs associated with product misuse or suspected diversion received during the reporting period. There was 1 serious report of drug abuse (US020030); this case is described below:

US020030

01-May-2007: A report received from a physician, via a sales representative, regarding a 34-year-old female who initiated FENTORA (fentanyl buccal tablet) therapy, 800 mcg three to six times daily, on an unknown date, for an unspecified indication. On 14-April-2007, the patient overdosed by taking 1/3 of a box of 800 mcg FENTORA (approximately 10 tablets or 8000 mcg) all at once. She subsequently passed out and was taken to the Emergency Room (ER). The patient recovered and is currently seeking treatment for abuse. Subsequent to this event, the prescribing physician discharged her from his care.

Case Comment: Cephalon's Global Pharmacovigilance and Epidemiology department attempted to follow-up with the reporting physician. However, the physician declined to speak with them stating that he did not have any further information to report.

2.9.1 Reports from TESS and DAWN Live!

During the reporting period, there were no spontaneous reports of suspected misuse or abuse detected using TESS and DAWN Live!. There were no spontaneous reports of suspected misuse (non-medical use) involving FENTORA detected in DAWN Live!

Six reports involving exposures to FENTORA were identified in the American Association of Poison Center database for the period, 01-April through 30-June-2007. These exposures were reported to poison centers not included in the RADARS system study. The case information provided is limited; therefore, it is not possible to make a full assessment of the exposures listed. However, a copy of the case abstracts for these exposures will be requested from the AAPCC.

Table 3: Reports of Exposures to FENTORA Received from the American Association of Poison Control Centers (01-April through 30-June-2007)

Date of exposure	Poison Center Location	AAPCC Case Number	Cephalon Case Number	Age/ Gender	Reason for Exposure	Clinical Effect, if any	Comment	Outcome
08-May-07	Fresno/ Madera,CA	2593547	US021190	49/M	Intentional : Suspected suicidal	No info provided	Involved ingestion of two other unidentified substances	No effect
31-May-07	Palmetto, South Carolina	198632	US021191	40/F	Abuse	Drowsiness/ lethargy	None	Minor effect
17-June-07	RMPDC (Denver, Co)	173056200	US021192	45/F	Therapeutic error	No information provided	Insufficient information to assess	No effect
22-June-07	Tampa	1624319	US021193	52/F	Therapeutic error	No information provided	Circumstances not reported	
23-June-07	Oklahoma	825733	US021194	36/M	Intentional drug misuse/abuse	Drowsiness, lethargy, dyspnea	Involved ingestion of 3 other unindentified substances	Unknown
27-June-07	RMPDC	173740600	US021195	44/F	Therapeutic error	Other	Other clinical effect (not further defined)	Recovered

2.9.2 RADARS® Data and Analysis

During this reporting period, Cephalon received the first quarter 2007 RADARS® Report for all signal detection systems for FENTORA . This report includes data from the Drug Diversion, Key Informant, Methadone Treatment Program, Impaired Health Care Worker Studies and Poison Center Signal Detection system for the period, 01-January-2007 through 31-March-2007.

There were no signals reported in 3rd and 4th quarters 2006 or in 1st quarter 2007 by Drug Diversion, Key Informant, Poison Center, or Methadone Treatment Program. However, RADARS noted concerning URDD rates in two 3-digit zip codes from the Methadone Treatment Program.

The four signal detection systems (studies) are listed below with the corresponding data for first quarter 2007. Two denominators are used in the RADARS® System to describe the exposed or at risk population: population-based rates (per 100,000 population) and patient-based rates (per 1,000 URDD – number of patients prescribed a specific opioid analgesic). To date, signal thresholds have only been established for the population-based rates, not URDD.

Table 4: RADARS System Data for FENTORA : 1st Quarter, 2007 (31-December-2006 through 31-March-2007)

RADARS Study	Overall Rate Per 100,000 Population	Overall Rate Per 1,000 URDD*
Poison Center	0	0
Key Informant Network	0.001	0.3
Drug Diversion	0	0
Methadone Clinics	0.005	1.03

*URDD = Unique Recipient of Dispensed Drug

Drug Diversion Signal Detection System:

- A signal site is defined as any participating jurisdiction that registers 5 or more diversions, of any given drug, per hundred thousand population, during any quarter of the calendar year. Diversion rates are also calculated per unique recipients of dispensed drug (URDD).
- Of 306 sites participating in this study, 245 (80%) completed questionnaires, i.e., responded to requests for data during the period. No reports of suspected diversion were reported for FENTORA during 1st quarter 2007. No signals were detected for FENTORA .
- A RADARS review of the FENTORA trends as expressed in rate(s) per 100,000 populations revealed that the average FENTORA Drug Diversion population rate is decreasing over time, although data is needed for a minimum of three quarters with a positive rate to test significance.

Key Informant Network Signal Detection System

- The Key Informant Network System is a surveillance program designed to monitor prescription drug abuse in the United States.
- Of the 231 key informant sites, approximately 86% (198/231) reported data this period.
- A RADARS review of FENTORA trends as expressed in rate(s) per 100,000 populations revealed that the average FENTORA Key Informant population rate is decreasing over time, although data is needed for a minimum of three quarters with a positive rate to test significance.

Poison Control Center Study

- This study identifies exposure and information cases involving FENTORA and helps to determine rates of misuse, abuse, and diversion of FENTORA . A signal for the Poison Control Center Study is defined as 2 or more intentional exposures in any 3 digit zip code per 100,000 population during the reporting period. No FENTORA intentional exposures were reported in 1st quarter 2007.

  Data was available from all of the 42 sites participating in this study. There were no signals identified for FENTORA during the period.

  Supplemental data from the AAPCC

  As there are approximately 60 poison center sites in the U.S., data from the remaining poison centers is requested by Cephalon from the American Association of Poison Centers (AAPCC) directly.

  Data was received for the 17 poison centers not included in the RADARS Poison Control Center System. Six FENTORA exposures were reported from these centers. The cases are summarized in section 2.9.1.

Methadone Clinic Signal Detection System

This study is designed to assess opioid abuse among Methadone Treatment Program enrollees. A signal for this study is defined as an abuse rate of ≥ 2 per 100,000 population.

Of the 72 sites, 62 (86%) sites responded during the period. There were no signals identified for FENTORA by rate per 100,000 population. However, there were two 3-digit zip codes with an increase in the URDD rates during this period.

Rates in these two zip codes were concerning when evaluated based upon the potential drug (FENTORA) availability(measured by number of filled prescriptions for FENTORA) in the two geographic areas, Escondido, CA and Austin, Texas. The data indicate that the two zip codes appear to have relatively high rates of abuse. However, there is insufficient information available to draw a conclusion.

2.9.3 Internal Reports of Suspected Diversion Received by PSMI

There were three suspected diversion reports received during the reporting period, these cases are described below.

- A consumer called to report missing FENTORA tablets after receiving 4 boxes of 200 mcg and 4 boxes of 800 mcg (1month supply). The consumer checked all of the boxes before leaving the pharmacy and they all appeared to be sealed. She took them home, where she now keeps them locked in a safe that only she can access. However, when she pulled on the tab on the top of 1 of the boxes of 200 mcg FENTORA tablets, the whole top opened rather than the pull tab opening, as if it had either not been glued, or had been reglued. She then took out the blisters, and 4 of the blister cards were missing all 4 FENTORA tablets.

Company comment: This report was investigated by Cephalon's Manufacturing QA Department. The investigation conclusion noted that no determinate manufacturing cause was identified for this event. The results from the investigation suggest that this incident may have occurred outside Cephalon's scope and a that a third party may have removed the FENTORA tablets from the reported blister cards. All information gathered during the investigation confirmed that the lot was manufactured, tested, and released in accordance with cGMP requirements. Quality Assurance will continue to monitor and trend complaints of this nature and will take additional measures if deemed necessary.

- The second report was received from a Drug Enforcement Agency investigator requested information regarding FENTORA . He wanted to determine which fentanyl product he was dealing with. It was thought that someone has altered a brand-name fentanyl product that looks like a white tablet. Some of the tablets he thinks are FENTORA tablets. It appears they may have split a FENTORA tablet in half making the "C" appear as a "T" when the tablet is turned on its side. The investigation is ongoing, and the caller declined to provide any additional information.

Company comment: Two attempts were made to follow-up and request additional information from the DEA investigator by the Cephalon QA department. The investigator did not return these calls. No further information is available regarding this report.

- The third report was received from a consumer who reported that 16 FENTORA 200 mcg tablets were diverted. The source of the diversion is not known, the consumer stated that the FENTORA tablets are delivered to her pharmacy and secured there until she picks up the prescription , usually three to five days later. No further information has been received regarding this report.

2.10 15-Day Alert Reports

Cephalon submitted 8 initial 15-day alert reports under the RiskMAP for FENTORA during this reporting period. There were seven reports involving medication errors, including one report involving a fatal outcome (see section 2.5), one report of accidental exposure involving an adult female (see section 2.6), and one report of drug abuse in a patient treated with FENTORA; this case is discussed in section 2.9. There were no study related reports of death or serious ADRs associated with misuse or diversion during the reporting period.

2.11 Results of Any Investigation of Surveys

As discussed with the FDA during the negotiations of the RiskMAP, the patient, physician and pharmacy surveys are initiated after completion of the launch period to obtain the sample size information necessary to conduct the surveys in accordance with the methodology included in the approved RiskMAP (see sections 4.3.1-4.3.3 of RiskMAP).

The patient survey conducted by Walgreens, Inc. was initiated on 16-April-2007. This survey is intended to provide a mechanism for evaluating the effectiveness of patient educational tools utilized in the SECURE Program. The survey evaluates:

- Patient knowledge of the key risks associated with use of FENTORA
- Patient knowledge of the indication (regarding opioid tolerant cancer patients) associated with FENTORA
- Patient knowledge about the directions for use and safe storage of FENTORA , and
- Receipt of, and perceived utility of, the Medication Guide and other counseling tools for FENTORA

For the period, 16-April-2007 through 30-June-2007, Walgreens identified 1180 unique patients who filled prescriptions for FENTORA . Of the 1180 patients, completed surveys were received for 284 patients. The remaining patients either declined to participate in the survey, could not be contacted, or were ineligible for survey.

Responses to the survey questions were tabulated and then analyzed. A table listing the questions and responses to each question and a graph depicting the response to each question for trending purposes is included in Appendix III

Survey Findings:

Of the 284 patients who were contacted and initially surveyed, 237 patients indicated this was their first prescription for FENTORA .

Of the 237 patients who completed the 10 question survey,

- The majority 90% (213/237) of respondents indicated they received a Medication Guide with their prescription.
- Of the 213 respondents who received a medication guide, 73% (156/213) reported reading the Medication Guide and it was helpful in understanding how to use FENTORA correctly and safely.
- Approximately 45% (107/237) of the respondents indicated they were familiar with the medication called Actiq.
- The majority 90% (96/107) of respondents were aware that Actiq and FENTORA should not be substituted or used in place of each other and that someone using one of the medications should not use the other.
- The majority of the respondents (77%;183/237) were aware that FENTORA should be kept in its blister packaging until just before using.
- Approximately sixty percent of patients did not have children who lived in or visited their homes. Of the patients who reported that children lived in or visited their homes, almost all of the patients (97%; 92/95) were aware that FENTORA should be kept in a safe place out of reach of children.
- Approximately two-thirds of the 237 patients surveyed (66%; 158/237) were aware that FENTORA should be kept in a secure place to protect from theft.

Conclusions from data derived from 1st Survey cycle:

A review of the survey data derived from the first survey cycle indicates that the majority of patients interviewed received a medication guide with their prescription and that the respondents were aware of the key safety messages for FENTORA .

3 INTERVENTIONS AND OUTCOMES

This section provides the status of the prospective interventions that were delineated in Appendix A of the approved RiskMAP as well as the responsive interventions that Cephalon initiated during the reporting period. In each quarterly report, Table 5: will be updated to reflect the Actiqvity of a specific intervention for that particular period of time.

Tools 8, 17, and 21 (Introductory Letters to Healthcare Professionals, Introductory Letters to Drug Diversion Authorities, and Physician Education to Members of Professional Societies) were Actiqvities that occurred solely at launch and therefore have been removed from this table. Therefore, the table is not in consecutive numerical order.

Table 5: Prospective Intervertion

No.	Tool	Description	Goal(s)	Status
1	Blister	Launch and ongoing: Tablets will be supplied in double-foil blister which meet F1 requirements and which have passed tests for child resistance and senior friendliness. This tool is designed to minimize the risk of accidental exposure to FENTORA .	3	Ongoing
2	Blister label	Launch and ongoing: The blister label contains warning information that FENTORA should be kept of the reach of children and that is only for patients already taking opioids; it also contains instructions for use.	1,3	Ongoing
3	Carton label	Launch and ongoing: The labeling of the carton will contain warning information, be color coded by strength, and will contain a reminder checklist to prompt the pharmacist to counsel the patient about the 3 principal risks associated with use of FENTORA . The carton label also directs the patient and/or caregiver to read the Medication Guide for important warnings.	1,2,3	Ongoing

Table 5: Prospective Intervertion (continued)

No.	Tool	Description	Goal(s)	Status
4	Medication guide	Launch and ongoing: The FENTORA Medication Guide will emphasize the 3 principal risks associated with the use of FENTORA . Specifically it warns the patient of the potentially serious consequences, including death, that may occur when using FENTORA in opioid non-tolerant patients; it warns that the patient may become physically dependent on opioids and could become addicted to FENTORA ; and lastly it warns that FENTORA is to be kept out of the reach of children and that FENTORA contains medicine that could be harmful or fatal to someone who has not been prescribed the medicine. It will go directly to patients via packaging the carton and will be made available to all prescribers and FENTORA - stocking pharmacies (via 800#, product-specific website and Cephalon sales representatives) for education and dissemination to patients.	1,2,3	Labeling Supplement 1 was still under FDA review during this reporting period

Table 5: Prospective Intervertion (continued)

No.	Tool	Description	Goal(s)	Status
5	Package insert	Launch and ongoing: The package insert will contain a Boxed Warning about the life-threatening risks associated with the use of FENTORA in opioid non-tolerant patients; misuse, abuse and diversion; and accidental exposure to the medication.	1,2,3	Labeling Supplement 1 was still under FDA review during this reporting period.
6	Direct Risk communication by Cephalon field representatives	Launch and ongoing: Prescribers will be informed in person of the key messages and elements of the FENTORA RiskMAP, including the potentially life-threatening risk of use by an opioid non-tolerant individual, the high potential for FENTORA abuse as well as the risk of misuse and diversion, and the potentially life-threatening risk of accidental use of FENTORA in children or adults.	1,2,3	Ongoing dissemination by the field force.

Table 5: Prospective Intervertion (continued)

No.	Tool	Description	Goal(s)	Status
7	Direct Risk communication by Cephalon field representatives	Launch and ongoing: Pharmacists likely to dispense FENTORA will be informed in person of the key messages and elements of the FENTORA Risk MAP, including the potentially life-threatening risk of use by an opioid non-tolerant individual, the high potential for FENTORA abuse as well as the risk of misuse and diversion, and the potentially life-threatening risk of accidental use of FENTORA in children or adults.	1,2,3	Ongoing dissemination by the field force.
9	PharmAlert	Launch and as needed: Educational material that reinforces the 3 principal messages of the RiskMAP. Specifically these messages will address that FENTORA is to be used only by opioid-tolerant patients with cancer; a risk of misuse, abuse and diversion is associated with FENTORA ; and there is a risk of accidental exposure associated with the use of FENTORA . These will be distributed to 40,000 retail pharmacists.	1,2,3	Ongoing and assessing modifications to content and other capabilities for future PharmAlert distributions.

Table 5: Prospective Intervertion (continued)

No.	Tool	Description	Goal(s)	Status
10	Physician education directed to Pain Centers of Excellence	Launch and ongoing: Cephalon will contact each of the identified top 25 Pain Centers of Excellence to offer further educational opportunities to learn about FENTORA , including the 3 principal risks identified in the RiskMAP. Specifically risk of use by opioid non-tolerant individuals, the risks for misuse, abuse and diversion, and the risk of accidental exposure to FENTORA will be addressed. The educational platform for these offerings will include symposia and/or teleconferences.	1,2,3	There were no further educational offerings directed to these pain centers during this reporting period. However, additional platforms are scheduled for later in the year.
11	Pharmaceutical compendia	Launch and ongoing: Cephalon will provide FENTORA information, including the 3 principal risks identified in the RiskMAP, to several well-known compendia such as Physicians' Desk Reference (PDR), American Hospital Formulary Service (AHFS), and Drug Facts and Comparisons.	1,2,3	There was no Actiqvity with regard to compendia during the reporting period.

Table 5: Prospective Intervertion (continued)

No.	Tool	Description	Goal(s)	Status
12	Counseling messages	Launch and ongoing: Cephalon will provide risk information to First Data Bank and/or other major publishers of pharmacy counseling software to educate the majority of retail pharmacists on the 3 principal risks associated with use of FENTORA . Specifically these messages will address that FENTORA is to be used only by opioid-tolerant patients with cancer; a risk of misuse, abuse and diversion is associated with FENTORA ; and there is a risk of accidental exposure associated with the use of FENTORA .	1,2,3	There were no chanes affecting thc distribution of FENTORA during this period warranting notification to First Data Bank.

Table 5: Prospective Intervertion (continued)

No.	Tool	Description	Goal(s)	Status
13	Counseling aid	Launch and ongoing: In addition to the Mcdication Guidc, Cephalon will develop a counseling aid to be used by healthcare professionals when advising and educating patients about FENTORA . This aid will include information about the 3 principal risks associated with use of FENTORA . Specifically the aid will include information addressing that FENTORA is to be used only by opioid-tolerant patients with cancer: a risk of misuse, abuse and diversion is associated with FENTORA ; and there is a risk of accidental exposure associated with thc use of FENTORA .	1,2,3	Patient & healthcare profcssional 'Frequently Asked Questions' (FAQ) distributed by field force

Table 5: Prospective Intervertion (continued)

No.	Tool	Description	Goal(s)	Status
14	RiskMAP Speaker training	Launch and ongoing: Cephalon will formally train speakers on aspects of FENTORA consistent with the risk information in the package insert, including the key elements and messages of the RiskMAP. Cephalon will also provide speakers with information which they must present, that focus on the risks identified in the RiskMAP. Prior to speaking on behalf of Cephalon, these speakers will verify that they understand the 3 principal risks associated with the use of FENTORA . Evaluations provided will monitor whether speakers presented the required risk information.	1,2,3	A total of 100 speakers were trained on the FENTORA RiskMAP June 8-10 June 22-24

Table 5: Prospective Intervertion (continued)

No.	Tool	Description	Goal(s)	Status
15	RiskMAP Training for Cephalon field representatives	Launch and ongoing: In addition to product-specific training, Cephalon field representatives will receive - RiskMAP- specific training Upon completion of the training, field representatives will be tested on the training and will be required to verify their understanding of the information, including the information on the 3 principal risks identified in the RiskMAP.	1,2,3	No formal training of field reps occurred during this reporting period. However, a Sales Bulletin was distributed to the field force on April 23, 2007 pertaining to the RiskMAP.
16	Independent continuing medical education (CME)	Launch: Cephalon will support independent education on prescription drug misuse, abuse, and diversion targeted to physicians likely to prescribe FENTORA .	2	During the reporting period: 6 online monographs 3 online slide presentations 3 ESP electronic communications 3 exhibit booths 1 website
18	Product returns and disposal	Launch and ongoing: Cephalon will accept returns for disposal of unwanted FENTORA . This will be a tool to minimize the amount of excess product available.	2,3	No returns of product have been requested to-date.

Table 5: Prospective Intervertion (continued)

No.	Tool	Description	Goal(s)	Status
19	Physician and Pharmacist education	Ongoing (response to surveillance): Cephalon will implement medical education directed to 'geographic hot spots' that focus on preventing and/or minimizing misuse, abuse, and diversion of prescription drugs. The format of these programs will be tailored to the specific need (e.g., symposium, teleconferences, print materials, etc.)	2	There was no data received this quarter warranting such intervention.
20	Reports of diversion and abuse	Launch and ongoing: Cephalon will attempt to implement an Actiqve monitoring system (e.g., RADARS) at the time of the launch of FENTORA . Reports from the National Association of Drug Diversion Investigators (NADDI) will be Actiqvely monitored and screened for information on FENTORA .	2	Ongoing See Section 2.9.9 of report
22	Website	Launch and ongoing: This website will be a tool for healthcare professionals and for patients. It will educate both audiences about the 3 risks associated with FENTORA as identified in the SECURE Program.	1,2,3	Ongoing

3.1 Responsive Interventions

In response to the surveillance and monitoring Actiqvities employed in the RiskMAP, additional interventions were employed. Specifically, multiple instances of inquiries to the call center were received by Cephalon's Medical Services Department. In response, additional education and retraining was provided.

3.1.1 Abuse

There was one serious report of drug abuse (See section 2.9) reported during the period. Cephalon's GPE group attempted follow-up with the reporting physician; however, the physician declined to speak with them.

3.1.2 Suspected Diversions

For two of the three cases of suspected diversion reported during the period, interventions were employed or attempted (See section 2.9.3). In one of the cases an investigation by Cephalon's Manufacturing QA department was conducted and the findings noted that the diversion did not occur within Cephalon's supply chain. In the other case, Cephalon's QA department made multiple attempts to speak with the DEA investigator who provided the case to Cephalon; however, the DEA investigator did not return calls.

3.1.3 Medication Errors

Seven medication errors were reported during the period; 6 appear to be at the prescriber level and 1 was at the pharmacist level. Interventions were employed as a result of three of the reports.

One of the interventions included Cephalon's Medical Services Department re-enforcing appropriate dosage and administration instructions to a consumer who called in and reported a medication error. Another intervention included a Cephalon field representative following-up with a pharmacist who had in error dispensed FENTORA as a substitute for Actiq during the reporting period. The field rep reinforced that FENTORA is not a generic Actiq and that FENTORA must not be substituted for any other fentanyl products. Lastly, in response to a medication error that resulted in a fatal outcome, a series of interventions were employed including multiple Dear HCP letters, modifications to all labeling (package insert, Medication Guide, and carton labeling), and modifications to the RiskMAP. Cephalon is currently under discussions with the FDA with regard to the proposed labeling and RiskMAP changes.

4 SUMMARY

In summary, data obtained are increasing and allowing for greater review and assessment of components of the FENTORA RiskMAP. Patient survey data indicated that the Medication Guide is received and found helpful by 90% of survey respondents. This is useful information as Cephalon assesses modifications to their labeling and how they can increase patient awareness. There was one spontaneous report of accidental exposure involving an elderly adult during the reporting period; this incident resolved without an adverse outcome. Spontaneous reports of suspected diversion were seen and promptly addressed by employing in investigaton of the events in accordance with Cephalon's standard operating procedures. However, no data obtained from the RADARS early warning system detected any signals warranting interventions att his time. Seven medication errors were reported during this reporting period (for a cumulative total of 10) and promptly addressed. These reports continue to be closely monitored and additional interventions are being employed.

APPENDICES

APPENDIX I –ALGORITHM FOR PROCESSING OPIOID TOLERANCE FOR FENTORA PATIENTS

Opioid business rule*		
Generic	**Brand Name**	**Minimum Daily Dose**
Hydrocodone	Vicodin Lortab Norco Hycodan	60 mg
Levorphanol	Levo-Dromoran	4 mg
Hydromorphone	Dilaudid	8 mg
Codeine	Calcidrine	260 mg
Methadone	Dolophine	20 mg
Oxymorphone	Numorphan Opana®	20 mg
Oxycodone	OxyContin Roxicodone Oxyfast Percocet OxyIR	30 mg
Meperidine	Demerol, pethidine HCl	900 mg
Morphine	Kadian MSIR Roxanol MS Contin Avinza	60 mg
Fentanyl Patch	Duragesic	25 mcg/hr x 72 hrs
Tramadol	Ultram SR Ultram ODT Ultraset	200 mg
Propoxyphene	Darvon, Darvocet N50, N100, A500 Darvon Compound Darvon N Wygesic	200 mg

APPENDIX II –MAPPING OF FDA REQUIRED INFORMATION FROM RISKMAP TO FENTORA QUARTERLY REPORT

	Section 4.7 of FDA Approved RiskMAP	Location in Quarterly Report
1	Extent of use (denominator estimates)	Section 2.2
2	Indicators of off-label use, inappropriate prescribing (i.e., opioid-naïve), inclusive of patient longitudinal data (note: summarization of all non-accidental pediatric exposures not associated with an ADR will be included here)	Section 2.3 Section 2.4 Section 2.10
3	Summarizations of reports involving all medication errors, regardless of patient outcome	Section 2.5 Section 2.10
4	Summarization of all accidental exposures (in children and adults)	Section 2.6 Section 2.10
5	Summarization of all non-accidental pediatric exposures associated with an ADR (serious and non-serious)	Section 2.7 Section 2.10
6	Summarization of adverse events involving opioid naïve patients	Section 2.8
7	Rates of suspected misuse, abuse, addiction or diversion reported	Section 2.9
8	Results of any investigation or surveys conducted	Section 2.11
9	Outcomes from any interventions, such as targeted educational interventions and antidiversion programs conducted	Section 3 Section 4

APPENDIX III- FENTORA PATIENT SURVEY RESULTS

Question 1: Is this your first prescription of Fentora?

Tabulation of Responses for Quarter Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Totals	% of Respondents
Yes	237	83.5%	83.5%
No	47	16.5%	16.5%
Totals:	284	100.0%	100.0%

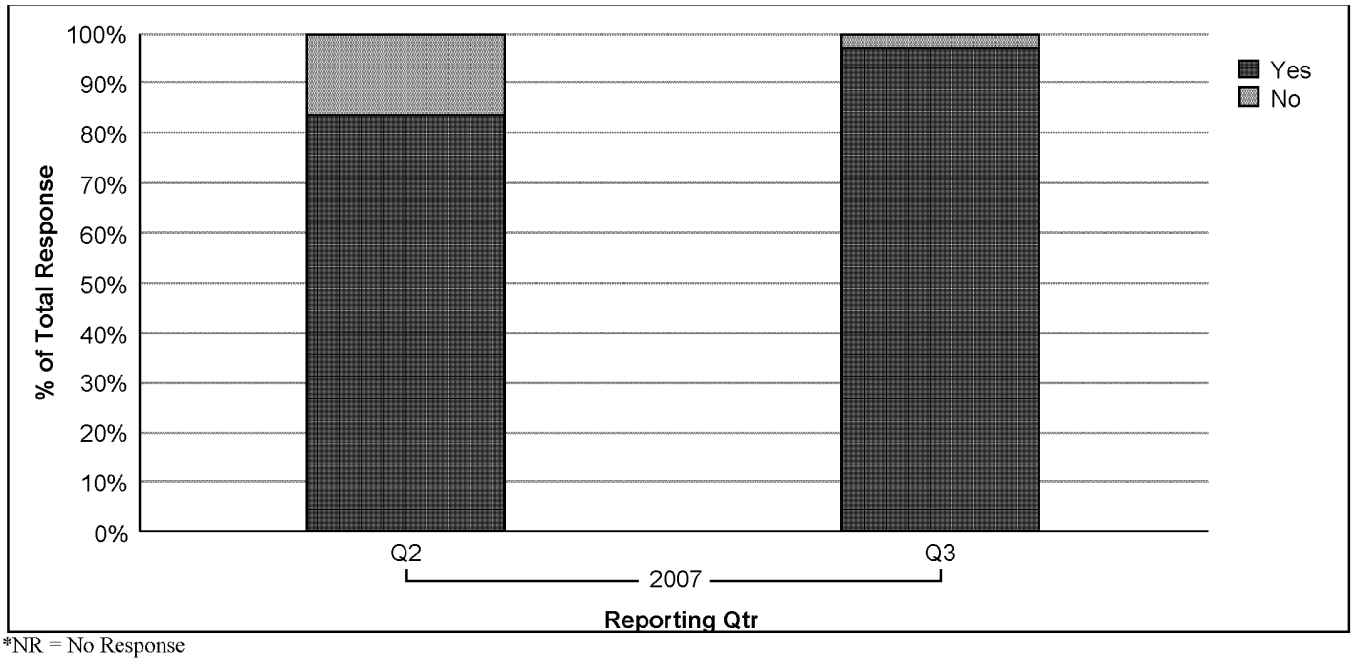
Year-to-Date Tabulation of Responses Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Totals	% of Respondents
Yes	237	83.5%	83.5%
No	47	16.5%	16.5%
Totals:	284	100.0%	100.0%

Cumulative Tabulation of Responses Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Totals	% of Respondents
Yes	237	83.5%	83.5%
No	47	16.5%	16.5%
Totals:	284	100.0%	100.0%

Cumulative Response by Quarter



*NR = No Response

Question 2: Did you receive a Medication Guide with your prescription of Fentora?

Tabulation of Responses for Quarter Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	213	89.9%	90.3%
No	21	8.9%	8.9%
Do not recall	2	0.8%	0.8%
NR	1	0.4%	0.0%
Totals:	237	100.0%	100.0%

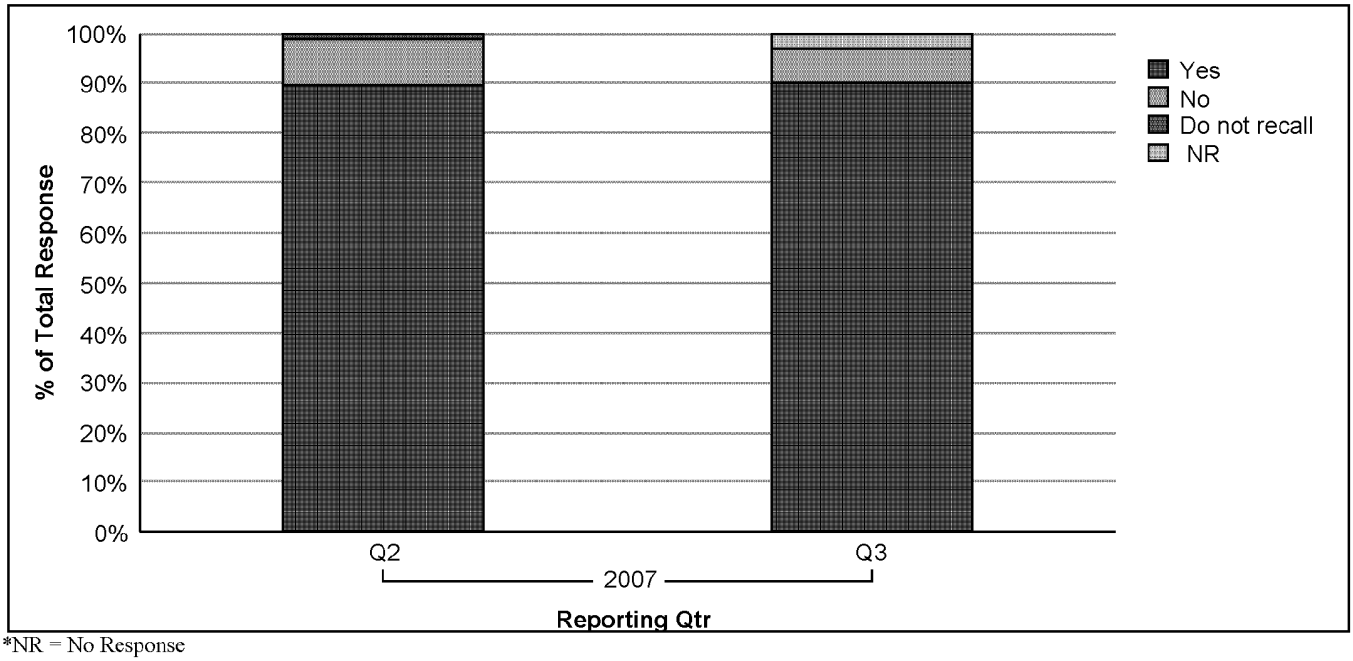
Year-to-Date Tabulation of Responses Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	213	89.9%	90.3%
No	21	8.9%	8.9%
Do not recall	2	0.8%	0.8%
NR	1	0.4%	0.0%
Totals:	237	100.0%	100.0%

Cumulative Tabulation of Responses Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	213	89.9%	90.3%
No	21	8.9%	8.9%
Do not recall	2	0.8%	0.8%
NR	1	0.4%	0.0%
Totals:	237	100.0%	100.0%

Cumulative Response by Quarter



*NR = No Response

Question 3: Have you read the Medication Guide?

Tabulation of Responses for Quarter Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Totals	% of Respondents
Yes	156	73.2%	73.2%
No	57	26.8%	26.8%
Totals:	**213**	**100.0%**	**100.0%**

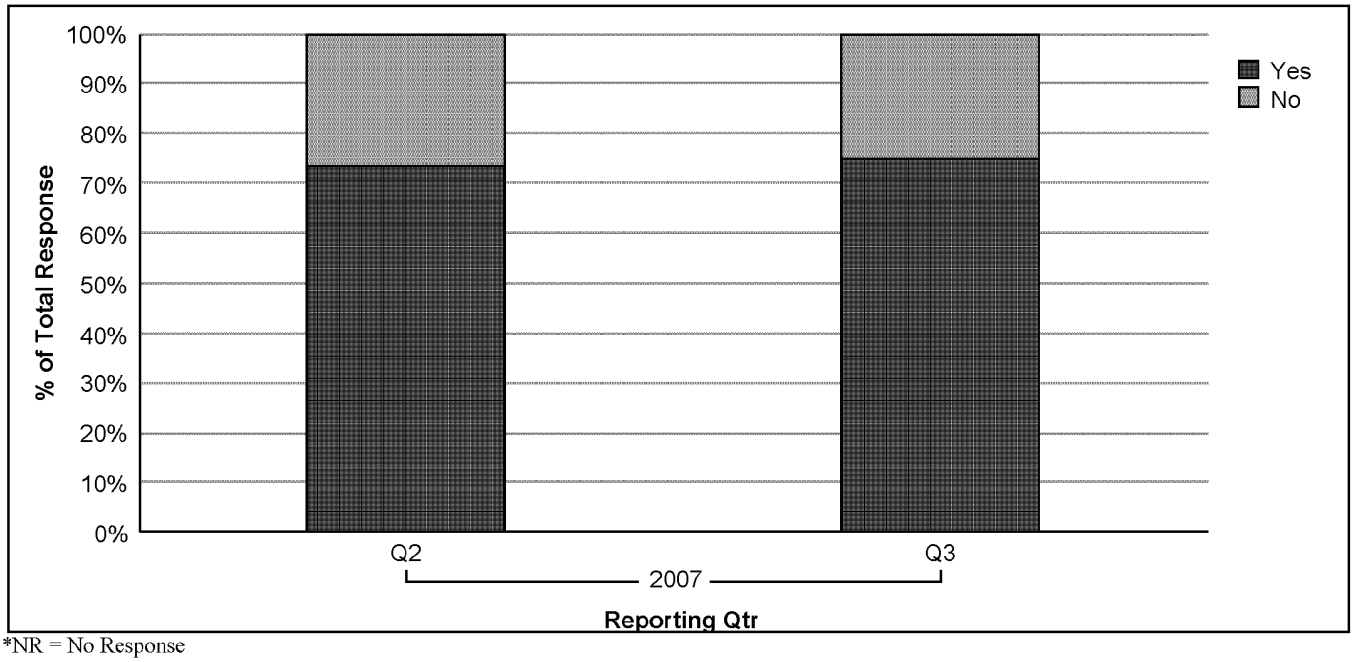
Year-to-Date Tabulation of Responses Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	156	73.2%	73.2%
No	57	26.8%	26.8%
Totals:	**213**	**100.0%**	**100.0%**

Cumulative Tabulation of Responses Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	156	73.2%	73.2%
No	57	26.8%	26.8%
Totals:	**213**	**100.0%**	**100.0%**

Cumulative Response by Quarter



*NR = No Response

Question 4: Did you find the Medication Guide helpful in understanding how to use FENTORA correctly and safely?

Tabulation of Responses for Quarter Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	146	93.6%	94.2%
No	9	5.8%	5.8%
NR	1	0.6%	0.0%
Totals:	156	100.0%	100.0%

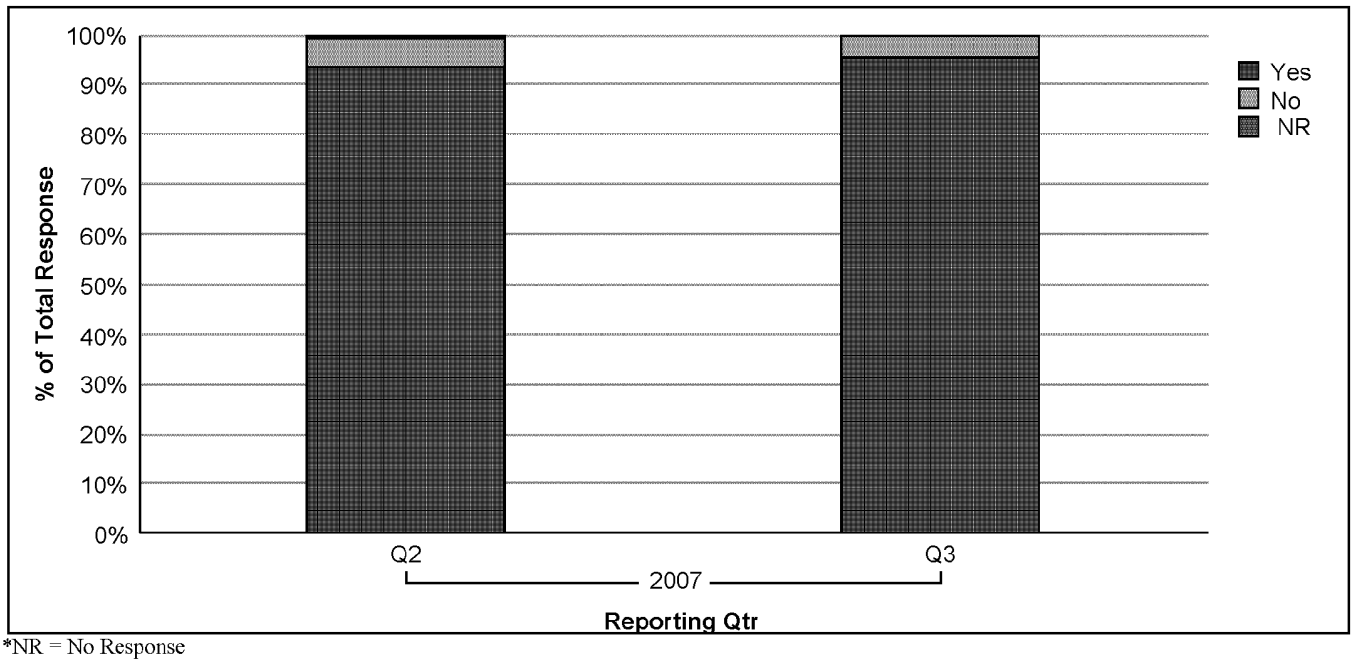
Year-to-Date Tabulation of Responses Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	146	93.6%	94.2%
No	9	5.8%	5.8%
NR	1	0.6%	0.0%
Totals:	156	100.0%	100.0%

Cumulative Tabulation of Responses Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	146	93.6%	94.2%
No	9	5.8%	5.8%
NR	1	0.6%	0.0%
Totals:	156	100.0%	100.0%

Cumulative Response by Quarter



*NR = No Response

Question 5: Are you familiar with another medicine called Actiq (if not on profile)?

Tabulation of Responses for Quarter Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	107	45.1%	45.1%
No	130	54.9%	54.9%
Totals:	**237**	**100.0%**	**100.0%**

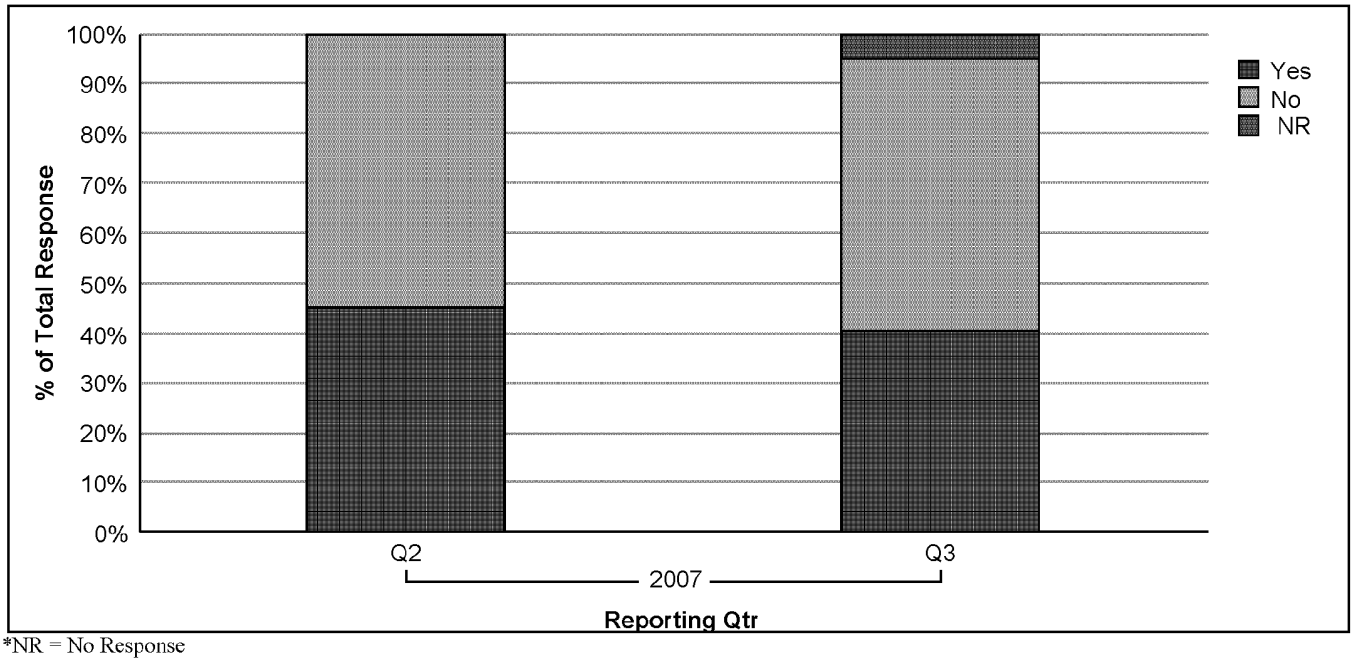
Year-to-Date Tabulation of Responses Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	107	45.1%	45.1%
No	130	54.9%	54.9%
Totals:	**237**	**100.0%**	**100.0%**

Cumulative Tabulation of Responses Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	107	45.1%	45.1%
No	130	54.9%	54.9%
Totals:	**237**	**100.0%**	**100.0%**

Cumulative Response by Quarter



*NR = No Response

Question 6: Both Fentora and Actiq contain a medicine called fentanyl. Are you aware that these two products should not be substituted or used in place of each other, and if you are using one of them you should not use the other?

Tabulation of Responses for Quarter Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	96	89.7%	89.7%
No	11	10.3%	10.3%
Totals:	**107**	**100.0%**	**100.0%**

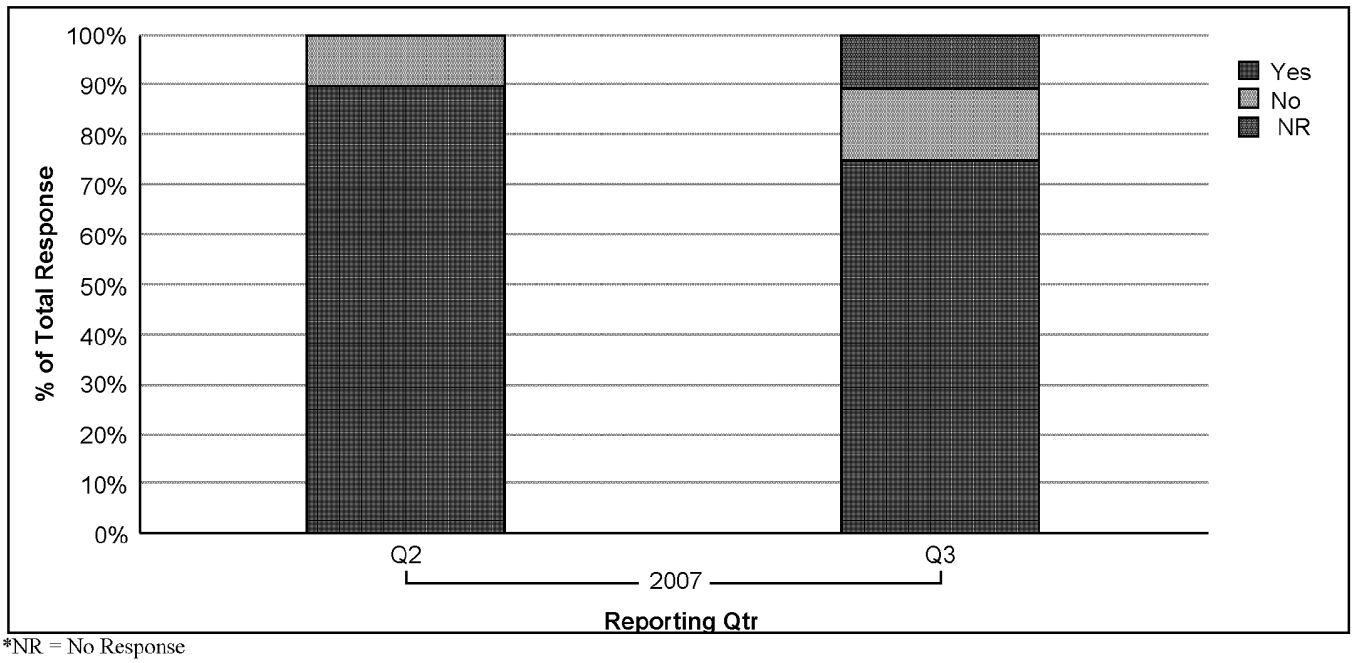
Year-to-Date Tabulation of Responses Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	96	89.7%	89.7%
No	11	10.3%	10.3%
Totals:	**107**	**100.0%**	**100.0%**

Cumulative Tabulation of Responses Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	96	89.7%	89.7%
No	11	10.3%	10.3%
Totals:	**107**	**100.0%**	**100.0%**

Cumulative Response by Quarter



*NR = No Response

Question 7: Are you aware that Fentora should be kept in its original (blister) packaging until just before using?

Tabulation of Responses for Quarter Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	183	77.2%	77.2%
No	54	22.8%	22.8%
Totals:	**237**	**100.0%**	**100.0%**

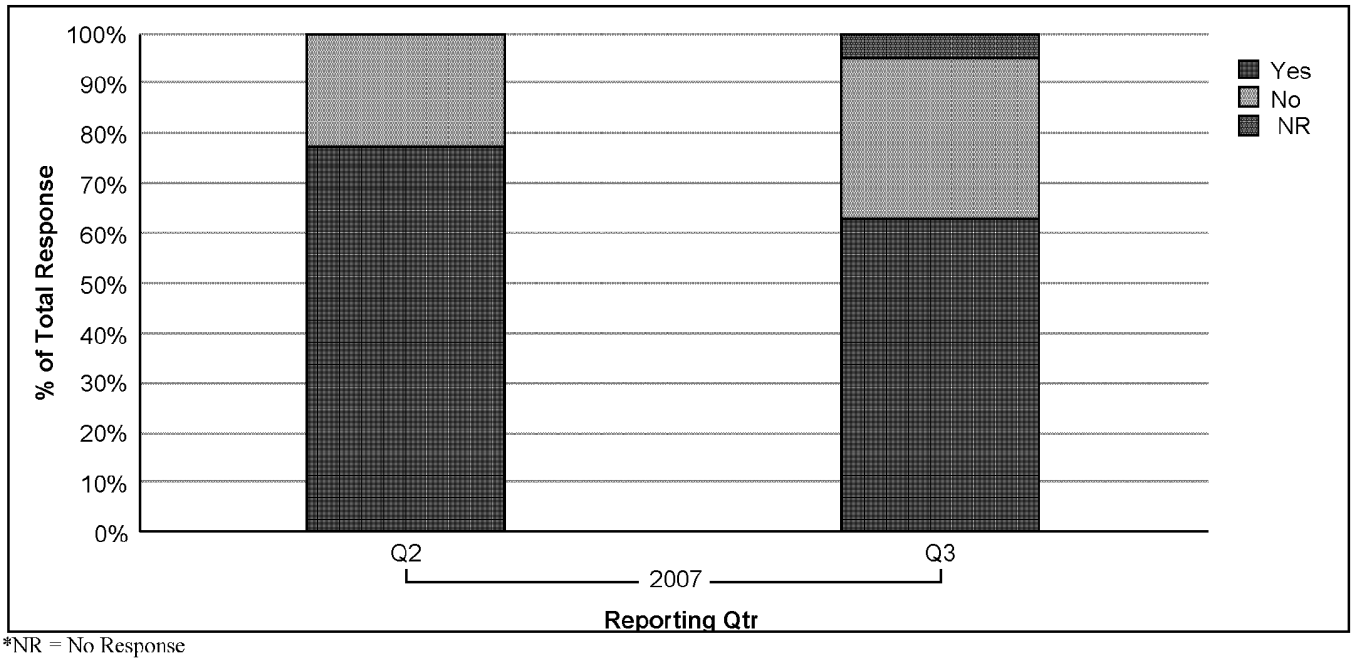
Year-to-Date Tabulation of Responses Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	183	77.2%	77.2%
No	54	22.8%	22.8%
Totals:	**237**	**100.0%**	**100.0%**

Cumulative Tabulation of Responses Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	183	77.2%	77.2%
No	54	22.8%	22.8%
Totals:	**237**	**100.0%**	**100.0%**

Cumulative Response by Quarter



*NR = No Response

Question 8: Do any children either live in or visit your home?

Tabulation of Responses for Quarter Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	95	40.1%	40.1%
No	142	59.9%	59.9%
Totals:	**237**	**100.0%**	**100.0%**

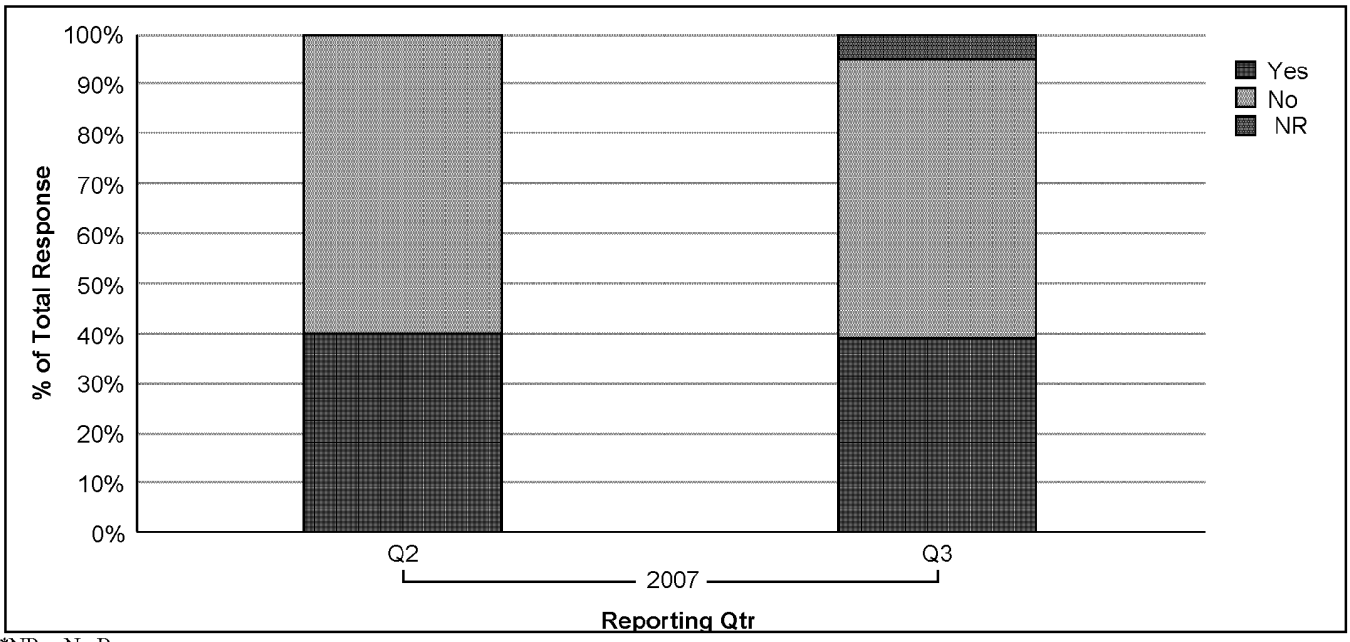
Year-to-Date Tabulation of Responses Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	95	40.1%	40.1%
No	142	59.9%	59.9%
Totals:	**237**	**100.0%**	**100.0%**

Cumulative Tabulation of Responses Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	95	40.1%	40.1%
No	142	59.9%	59.9%
Totals:	**237**	**100.0%**	**100.0%**

Cumulative Response by Quarter



*NR = No Response

Question 9: Are you aware that Fentora should be kept in a safe place out of reach of children?

Tabulation of Responses for Quarter Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	92	96.8%	97.9%
No	2	2.1%	2.1%
NR	1	1.1%	0.0%
Totals:	**95**	**100.0%**	**100.0%**

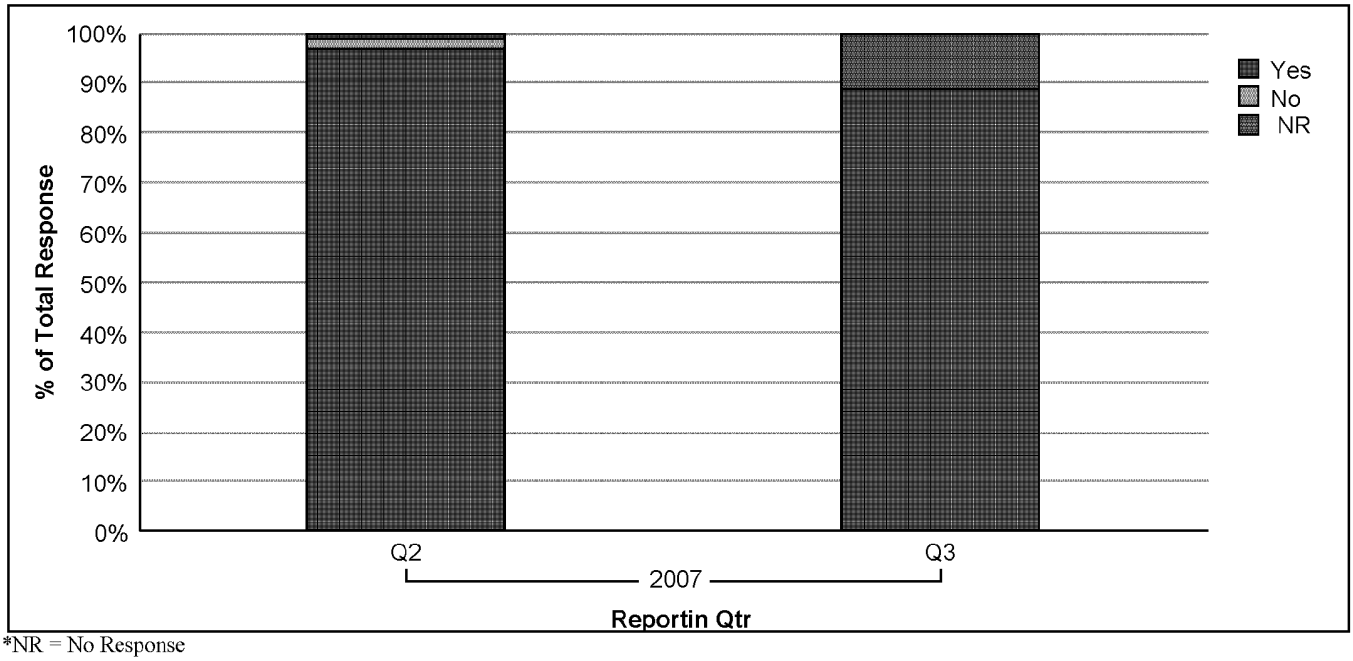
Year-to-Date Tabulation of Responses Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	92	96.8%	97.9%
No	2	2.1%	2.1%
NR	1	1.1%	0.0%
Totals:	**95**	**100.0%**	**100.0%**

Cumulative Tabulation of Responses Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	92	96.8%	97.9%
No	2	2.1%	2.1%
NR	1	1.1%	0.0%
Totals:	**95**	**100.0%**	**100.0%**

Cumulative Response by Quarter



*NR = No Response

Question 10: Are you aware that Fentora should be kept in a secure place to protect from theft?

Tabulation of Responses for Quarter Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	158	66.7%	66.9%
No	78	32.9%	33.1%
NR	1	0.4%	0.0%
Totals:	**237**	**100.0%**	**100.0%**

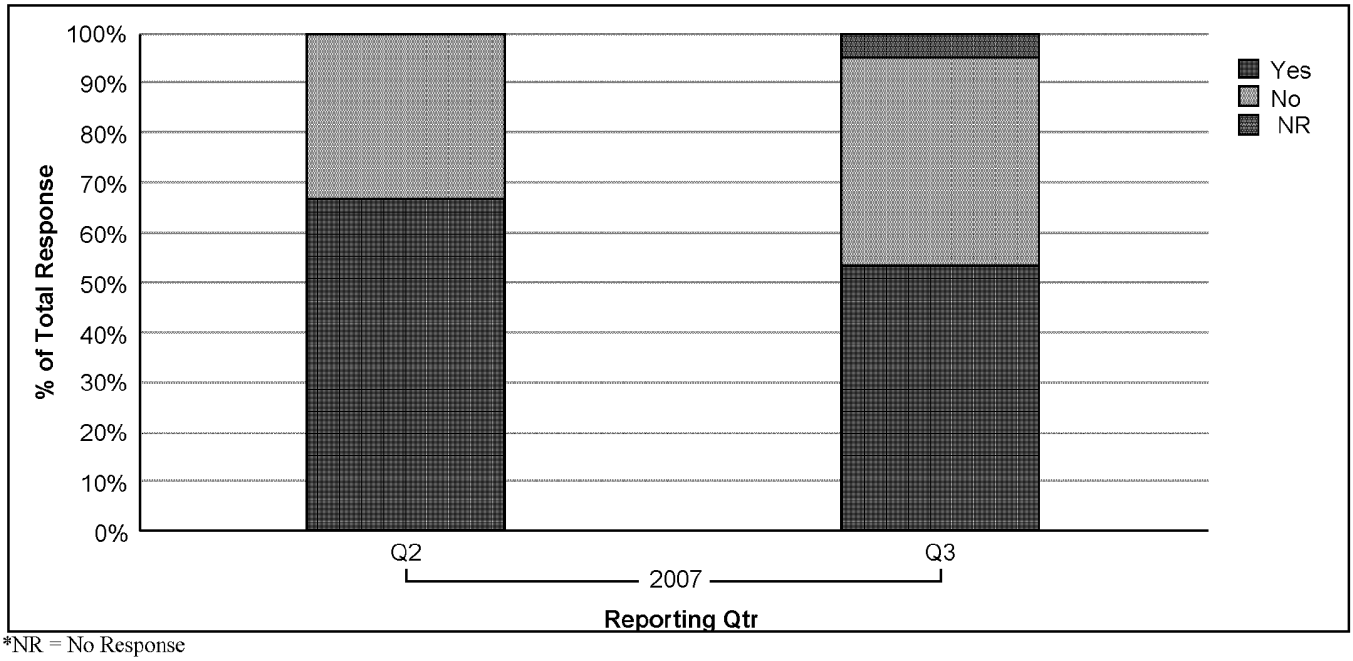
Year-to-Date Tabulation of Responses Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	158	66.7%	66.9%
No	78	32.9%	33.1%
NR	1	0.4%	0.0%
Totals:	**237**	**100.0%**	**100.0%**

Cumulative Tabulation of Responses Between Apr 1 2007 and Jun 30 2007

Response	Totals	% of Total	% of Respondents
Yes	158	66.7%	66.9%
No	78	32.9%	33.1%
NR	1	0.4%	0.0%
Totals:	**237**	**100.0%**	**100.0%**

Cumulative Response by Quarter



*NR = No Response

APPENDIX IV –RISKMAP ADVISORY BOARD EXECTUIVE SUMMARY

FENTORA® Risk Management Advisory Board
June 11-12, 2007
Normandy Farm Hotel & Conference Center
Blue Bell, PA

Meeting Minutes

BACKGROUND

The first in an ongoing series of FENTORA® Risk Management Advisory Boards (RiskMAP Ad Board) organized by the Cephalon Regulatory Affairs Department was convened on June 11-12, 2007 at the Normandy Farm Hotel & Conference Center in Blue Bell, PA.

Seven external advisors participated in the RiskMAP Ad Board, including Sid Schnoll, MD, PhD (Chairperson), Richard Dart, MD, PhD, Louis Morris, PhD, Steven Passik, PhD, Frank Sapienza, MS, Michael Weaver, MD, and James Zacny, PhD. External advisors were selected because of their expertise and interest in the topic of risk management, as well as the need for an interdisciplinary team approach in risk management, i.e. incorporating experts in basic science, clinical pharmacology, medicine, statistics, epidemiology, and informatics. *For complete advisor biographies, please see Addendum A.*

In addition to the external advisors, representatives from Cephalon Regulatory Affairs, Medical Services, Global Pharmacovigilance and Epidemiology, Clinical Research, Commercial and Legal departments were in attendance. *For a listing of all meeting attendees, please see Addendum B.*

OBJECTIVES

The main objective of the RiskMAP Ad Board was to obtain recommendations from risk management thought leaders to help mitigate risk associated with the use of FENTORA®. During the first day, Dr. Schnoll, Dr. Dart, and a number of Cephalon employees presented information to help the external advisors better understand FENTORA®, the current FENTORA® RiskMAP, and potential risks associated with the use of the product. On the second day, the meeting was reconvened to solicit specific advisor feedback on strengths, weaknesses, and potential gaps in the FENTORA® RiskMAP and to obtain recommendations for future direction and development. In addition, input was requested with regard to any modifications to the risk management program that may be warranted for an expanded indication for the use of FENTORA® beyond cancer pain. Recommendations for interventions to enhance benefits and reduce risks were requested. Also on the second day, Cephalon attendance was limited to assure the integrity of the independent advisory board. *For a complete meeting agenda, please see Addendum C.*

KEY LEARNINGS

Day 1 – Presentations

- Sid Schnoll, MD, PhD, presented an overview of the current understanding of the concept of risk management, including the FDA and EMEA definitions of risk management, and the March 2005 Prescription Drug User Fee Act (PDUFA III) which mandated development of risk management guidances. Dr. Schnoll stressed that these measures helped maximize public health benefit of a product, supported its appropriate use, reduced inappropriate use and diversion, and reduced product liability. He also described in detail FDA guidances for risk assessment and the development of risk minimization action plans (RiskMAPs), including their objectives, components, and examples of the categories of tools (targeted education and outreach, reminder systems, and performance-linked access systems). He also

explained various surveillance and monitoring techniques which help to identify and allow for investigation of potential signals that a RiskMAP is targeting. Examples of surveillance and monitoring tools mentioned include RADARS, NAVIPRO, CRS, Inc. monitoring, population-specific surveys, state and national surveys of drug use and misuse (DAWN, NSDUH), media monitoring, and internet monitoring.

- Richard Dart, MD, PhD, presented an overview of the Researched Abuse, Diversion, and Addiction-related Surveillance System (RADARS) which provides timely and geographic-specific data to the pharmaceutical industry, regulatory agencies, policymakers, and public health officials to aid in understanding trends in the abuse, misuse, and diversion of prescription drugs in the United States (US). The RADARS data offers multiple perspectives through the use of four unique signal detection systems that collect and provide data rapidly, with geographic specificity (three digit zip code level), address the rural nature of prescription opioid abuse, and include coverage/data of non-abuser victims. These four signal detection systems include poison centers, key informants, law enforcement, and opioid treatment centers. The goals of RADAR S is to identify sentinel events involving the misuse, abuse, and diversion of prescription drugs nationwide, measure rates of misuse, abuse, and diversion of prescription drugs, and to provide experienced and expert analysis and interpretation of the RADARS data. The RADARS data for Actiq was presented, as well as the preliminary data for FENTORA. The FENTORA data had only two quarters of data, but showed that FENTORA® trends in rates per 100,000 population for all four signal detection systems was not increasing significantly over time. , Dr. Dart, however, indicated that it takes a minimum of three quarters to really assess trends and that no hard conclusions could be made at this point in time.

- John Messina, PharmD, Senior Director of Clinical Research at Cephalon, presented a comprehensive overview of FENTORA and how it differs from Actiq. He began by describing fentanyl, a mu-opioid receptor, with FENTORA being a derivative of fentanyl which utilizes OraVescent® drug delivery technology. The advantage of the OraVescent® oral buccal delivery is that it generates release of carbon dioxide and is designed to enhance dissolution and absorption of fentanyl, which helps to minimize the first-pass effect. He also reviewed the pharmacokinetic properties of FENTORA and compared them to Actiq. Dr. Messina then explained the current indication for FENTORA; it is currently indicated only for the management of breakthrough pain in patients with cancer who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain. He then gave a thorough overview of the FENTORA Clinical Development Plan, including a pivotal study (099-14) which was a multicenter, randomized, double-blind, placebo-controlled, crossover trial of cancer patients using oral opioid equivalent to 60–1000 mg/d morphine or 50–300 mcg/h transdermal fentanyl to treat controlled persistent pain who were experiencing 1–4 breakthrough pain episodes per day. Lastly he reviewed ongoing trials with opioid tolerant patients with non-cancer-related breakthrough pain.

- Penny Levin, MS, Director of US Regulatory Affairs at Cephalon, presented a comprehensive overview of the current FENTORA Risk Minimization Action Plan (RiskMAP). She began by describing the purpose of a RiskMAP, including FDA's role in risk management of opioid analgesics. She reviewed potential RiskMAP components, including targeted education and outreach, reminder systems, restricted access, surveillance and monitoring, and interventions. Ms. Levin then detailed the methodology that Cephalon used to develop a comprehensive RiskMAP for FENTORA. This methodology included a historical review of Actiq's RiskMAP, the April 2005 pre-NDA meeting with the FDA requiring inclusion of a RiskMAP for FENTORA with the NDA submission, the organization of an internal cross-functional

team, led by Regulatory Affairs, which developed the FENTORA RiskMAP, and a review of other opioid requiring RiskMAPs. Cephalon identified three principal risks associated with FENTORA. These risks included use of FENTORA® by opioid non-tolerant individuals; misuse, abuse, and diversion of FENTORA®; and unintended (accidental) exposure to FENTORA®. Once risks were identified, Cephalon employed a failure mode effects analysis (FMEA) to identify points in a system that could results in a break or failure at any one or number of points in the system. It was identified that there were 6 points in this system where interventions would be necessitated; these were at the supply chain, point of prescribing, point of dispensing, consumer storage, patient consumer use, and disposal of product. Twenty-two interventions were aimed at the patient, prescriber, and pharmacist, in efforts to mitigate the above identified risks. Next she described ways in which the effectiveness of the RiskMAP would be measured, including surveillance systems, surveys, review of prescribing data, quarterly reporting to the FDA, and convening of a RiskMAP external Advisory Board on a bi-annual basis.. Quarterly reporting to the FDA would include response to questionnaires, prescription monitoring, serious Adverse Event (SAE) reporting, literature monitoring, and database monitoring (e.g., RADARS®, DAWN, TESS).

- Terrence Terifay, Director of Marketing-Pain Franchise at Cephalon, presented an overview of the current opioid market, including the competitive landscape, FENTORA performance, prescriber perceptions, FENTORA's Risk MAP data requirements and findings, and the definition of opioid tolerance as per the FENTORA package insert. Mr. Terifay showed that the Cephalon sales force focuses their efforts on a concentrated number of prescribers who treat patients with cancer and are highly skilled in the use of CII opioids. He also stressed that the majority of FENTORA® is prescribed by pain specialists. He also concluded that approximately 90% of FENTORA patients are considered opioid tolerant, per the market research data estimates.

- Martin Summers, Market Research Manager-Pain Franchise at Cephalon, presented the FENTORA team's market research methodology and preliminary market research data from a preliminary market utilization study. The objective of the FENTORA market utilization study was to track key patient-level metrics for FENTORA® including unique patient exposures, utilization by opioid tolerant versus opioid naïve patients, use by primary diagnosis, as well as average daily dosing data. The analysis utilizes two data sources, the IMS longitudinal prescription database (LRx) and the Electronic Medical Claims Switch database. According to Mr. Summers, the limitations of the data presented included that the LRx longitudinal prescription database includes retail data only, and that there is no data for medical facilities (such as hospitals), mail-order or long-term care prescriptions. According to Mr. Summers, the other caveat to the data that was presented is that the ability to directly link a FENTORA prescription to a diagnosis is limited. Mr. Summers also detailed future RiskMAP surveys for FENTORA prescribers and pharmacists.

- Kay McGhee, CRNP, MSN, Senior Manager, Global Pharmacovigilance and Epidemiology at Cephalon, presented an overview of the current pharmacovigilance RiskMAP activities at Cephalon. Her presentation detailed the pharmacovigilance components of the RiskMAP; regulatory reporting requirements at the individual case level and at the aggregate level (quarterly RiskMAP report), passive surveillance and analysis of aggregate data (opioid tolerance status, indication for use of FENTORA®, knowledge of safe handling and disposal requirements), active surveillance (surveys to assess effectiveness of patient education). Ms. McGhee stressed that Cephalon would submit expedited 15-day alerts to the FDA for serious adverse drug reactions (ADRs) associated with suspected abuse, misuse, or diversion, all

spontaneous and possibly related study reports of death, all accidental exposures, all non-accidental pediatric exposures associated with an ADR, and all actual and potential medication error reports. Sources for the reporting would include spontaneous reports received from Cephalon field personnel and communications from consumers or healthcare providers, as well as national databases, such as the American Association of Poison Control Centers, the Drug Abuse Warning Network (DAWN), and RADARS. For spontaneous reports, FENTORA use would be confirmed and a standard set of questions would be initiated, e.g. type of pain, what other opioids were taken, etc. Ms. McGhee described DAWN in detail, and also demonstrated the use of DAWN Live!, an online query system, which assists in tracking substance abuse that results in visits to hospital emergency departments and drug-related deaths. The system can also provide data on the non-medical use of FENTORA and can identify emerging drug abuse problems.

- Kay McGhee then presented an overview of the FENTORA RiskMAP quarterly report data. The quarterly report includes indicators of off-label use of FENTORA in the patient population, indicators of inappropriate prescribing (e.g. opioid non-tolerance), medication errors (actual and potential), all accidental exposures, all non-accidental exposures associated with an ADR, and rates of suspected misuse, abuse, or diversion. She provided information to the group that there was off-label use (non-cancer breakthrough pain 86% Q1-07), with a degree of inappropriate use (opioid naïve patients 15% Q1-07). Ms. McGhee also reported that to date for FENTORA there was one medication error report, no reports of accidental or inadvertent pediatric or adult exposure, and one report of non-accidental pediatric exposure associated with an ADR. In addition, no FENTORA reports have been identified in AAPCC exposure database or DAWN Live!, and two spontaneous reports of potential diversion reported by Cephalon's Medical Services.

- Penny Levin presented background on the FENTORA RiskMAP interventions, including prospective interventions (n=22) which are pre-defined tools designed to mitigate risks geared to patients, prescribers, and pharmacists. Ms. Levin also described responsive interventions which are conducted in response to data obtained through surveillance and monitoring.

- Lastly, Jay McKinley, Director, Contract Operations at Cephalon, gave a complete overview of Cephalon's commercial operations, FENTORA supply chain integrity, and RiskMAP activities. He detailed Commercial Operations' forward logistics (shipments), reverse logistics (returns), trade relations, pharmacy relations, contract operations, demand planning, data and analysis, and accounts receivable and credit processes. Mr. McKinley also described FENTORA packaging in some detail, especially their safety features (e.g. child-resistant blister cards). He also covered standard protocols for suspicious order activity, and ensuring safe shipping and storage of FENTORA, including Automation of Reports and Consolidated Orders System (ARCOS) reporting that ensures that all manufacturers and distributors report their annual inventories of controlled substances. Lastly he reviewed future protocols that Cephalon is planning, including product radiofrequency identification which will enable fast and accurate product tracking and tracing, and the advent of pedigree legislation which will require paper or electronic documentation of all files containing information regarding the distribution of prescription drugs.

Day 2 – Advisor Discussion and Feedback

Topics discussed by the advisors included:

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- The current FENTORA RiskMAP,
- Appropriate prescribing vs. off-label prescribing of FENTORA,
- Appropriate patient selection (opioid tolerant),
- Assessment of FENTORA abuse potential,
- Identification of safety signals and how to address once identified,
- Crisis management policies and procedures, and
- FENTORA supplemental NDA and potential enhancements to RiskMAP.

Current FENTORA Risk MAP

Overall, advisors expressed satisfaction with the FENTORA RiskMAP. . However, they did indicate since the approved indication is in patients with cancer and there is a significant level of prescribing occurring to patients without cancer, that Cephalon may want to consider a proactive discussion with the FDA on this topic. It was recommended that Cephalon continue review of adverse events and to monitor for any SAEs in this population. The data to-date indicate that the off-label prescribing does not correlate with SAEs.

Actions: Cephalon will review the prescribing errors, identify if there are any patterns or starts of trends, discuss potential modifications or solutions that could help remedy this situation, and approach to discussing with FDA.

Appropriate vs. Off-Label Prescribing of FENTORA

Appropriate Patient Selection (opioid tolerant)
There was a discussion around the definitions "opioid tolerant" and "opioid naïve." For current FENTORA studies, the look back period was 90 days. There was discussion whether the time period was adequate and whether it was able to accurately identify opioid tolerant patients.

The advisors agreed that true opioid naïve patients were the serious problem, and that concerted effort to find out more about the 12% that is totally opioid naïve was very important and that accurately categorizing patients was extremely important. Other options were discussed for helping prescribers properly identify opioid tolerant patients.

Actions: Cephalon will review their prescribing information and educational materials that are based on the prescribing to determine if enhancements regarding appropriate patient selection should first be made to the labeling and than subsequently through all educational and communicational vehicles.

Assessment of FENTORA Abuse Potential
Data shows that prescription drug abuse is a societal problem that is rampant in both rural and urban settings. One advisor mentioned that prescription drug abuse pervades when potential abusers can get their hands on what is "opportunistically" available in their environment. It was proposed that younger patients were more amenable to change. The advisors discussed some interesting questions regarding what percent of patients develop abuse being prescribed a drug for a reason versus what percent just want to abuse drugs. They

concluded that they are not really sure what percent is involved in each of these categories. It was also mentioned that there appears to be a plateau of prescription drug abuse, even though prescription levels are higher. This plateau trend is also evident in the National Survey of Drug Use and Health (NSDUH) data, where even opioid use appears to be leveling off. The point was also raised that DAWN data is skewed because the data is derived mostly from urban metropolitan areas.

The advisors reviewed the abuse and diversion data and acknowledged that levels of abuse seen with FENTORA to date are low and below signal thresholds. They appeared to be expecting higher numbers, but they also felt that it was early on in the sales cycle for the product.

Actions: Cephalon will continue to monitor the RADARS data; no further action warranted at this time.

Identification of Safety Signals and How to Address Once Identified
The advisors debated the concept of a safety signal and stressed that all companies are struggling with what is a signal, which signals should be acted upon and which should not. They agreed that there were available algorithms to help in the decision-making process. It was communicated that RADARS is changing to give more information about deaths, pediatric cases, etc.

There was also discussion regarding the value of internet web sites and blog sites in the monitoring of safety signals, the cautions associated with such information, and potential ways to systematically process and report adverse events revealed via the internet.

The advisors recommended for Cephalon to develop a process or processes that stipulate what to do when a safety concern is noted and or a signal is detected. Cephalon indicated they are working on such a process for diversion and need to expand such processes for all safety concerns. The Advisors requested review of the procedures before they are finalized.

The advisors indicated the most important aspect of follow-up was to implement procedures that consistently identify actionable signals, and then determine what procedure should be utilized to investigate that signal.

Actions: Cephalon will continue to participate in the RADARS quarterly meetings to ascertain their signal detection system and what interventions are under consideration and use such concepts, as appropriate, to assess what could be a signal with regard to AE/SAE data obtained internally.

Criminal Prescribing
The subject of criminal prescribing or obvious prescription for remuneration beyond appropriate treatment was discussed. Advisors recommended Cephalon assure their field reps are adequately trained on what to look for in criminal prescriber and than that the company has a process in place to cooperate with the DEA and/or other appropriate law enforcement.

No action warranted at this time.

Crisis Management Policies and Procedures

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The advisors stressed that it was crucial that crisis management planning should be evaluated and a written plan developed. How would Cephalon follow-up in an emergency situation?
We discussed whether Cephalon should create a prospective plan for potential emergency situations, which would include communications with the media, DEA, etc.

Actions: Cephalon will review their policies and procedures and determine if additional procedures are warranted for this topic.

Supplemental New Drug Application and Potential Enhancements to RiskMAP
The Cephalon Clinical Research Department explained that data from Study 3052 would be submitted with the Supplemental New Drug Application (sNDA) for FENTORA in breakthrough non-cancer pain. The advisors discussed the appropriateness of the current FENTORA RiskMAP once a broader label for all breakthrough pain is approved. In the case of a broader label, the advisors speculated that if FENTORA usage increased that there could be a corresponding increase in usage in non-tolerant patients. The Advisors also discussed the potential impact as increased usage in the market place may have on the risk of diversion.

Physician & Pharmacist Education
The advisors agreed that stronger healthcare practitioner education is warranted for all prescription pain medications, including FENTORA. They stressed that the FENTORA RiskMAP should instill the kind of education that helps to minimize risk as well as provide best practices as described in clinical trials.

Appropriate Prescribers for FENTORA
There was a brief discussion regarding the possibility that primary care physicians (PCPs) might be prescribers of FENTORA once the wider indication for the product is FDA approved. There was a brief discussion of what Cephalon could do to educate these physicians. One advisor stated however that because PCPs usually have a long history with their patients, and often spend more time with the patient, that this could be an advantage in better identifying which patients are at risk for abuse.

FENTORA Packaging
Packaging modifications were suggested as points for potential assessment to help mitigate risks of inadvertent exposure as well as to stress the important safety messages.

Actions: Cephalon will discuss their proposals with FDA in advance of SNDA submission and will incorporate FDA guidance into their proposed RiskMAP that will be included in the SNDA.

FUTURE MEETINGS
RiskMAP Ad Board Advisors will be receiving the RiskMAP quarterly reports and participate in Ad Board meeting twice a year. The next meeting for the RiskMAP advisors is scheduled for
December 2-4, 2007.