From: Marchione, Carol </O=CEPHALON/OU=US01 ADMINISTRATIVE GROUP/CN=RECIPIENTS /CN=CMARCHIO>
To: Del Ricci, Francine
Sent: 6/7/2004 3:32:21 PM
Subject: FW: FDA Contact Report- FDA Raises Concerns about Actiq Off-Label Use and Diversion
Attachments: working document.doc

-----Original Message-----
From: Marchione, Carol
Sent: Friday, June 04, 2004 7:45 AM
To: Blake, Paul; Berg, Edward; Craig, Roy; Brookes, Lynne; Pyfer, Andy; Beckhardt, Stacey; Civil, Richard; Bader, Robert; McGhee, Kay
Cc: 420 (Regulatory Affairs); Roche, Robert; Osborn, John; Grupp, Robert
Subject: FDA Contact Report- FDA Raises Concerns about Actiq Off-Label Use and Diversion

Attached is a telephone contact report detailing a phone call that I received yesterday from Bob Rappaport, Director of the Division of Anesthetic, Critical Care and Addiction Drug Products. He expressed to me that high levels of FDA are very concerned about information that they have analyzed that reflect staggering off-label use and increasing reports of diversion, misuse and unintended pediatric use of Actiq. He is requesting that Cephalon representative come to FDA within the next couple of months to discuss. He asked for a meeting package prior to this.

Since many of us are off-site today at an RMP meeting, I will call a meeting early next week to discuss next steps. Carol

PLAINTIFFS TRIAL EXHIBIT
P-19060_00001

Regulatory Telephone Contact Report

To:	Paul Blake, Ed Berg, Roy Craig, Michael Richardson, Lynne Brookes, Andy Pyfer, Stacey Beckhardt, Rich Civil, Bob Bader, Kay McGhee,
cc:	42000, Bob Roche, John Osborn
From:	**Carol Marchione**

Subject

Drug: Actiq (OTFC)
Country: **USA**
Application #: **NDA 20-747**
Indication: Breakthrough Cancer Pain

Contact/Title: **Dr. Robert Rappaport, Director of Anesthetic, Critical Care and Addiction Drug Products and, Kim Compton, FDA Project Manager**
Date: **June 3, 2004**

Discussion

Dr. Rappaport stated that FDA is very concerned about reports of diversion and misuse of Actiq. He said that there have been discussions at very high levels of the Agency regarding several issues involving the use of our product. I explained that recent published articles have come to the attention of our company regarding the diversion of the product that virtually stem from a single incident of diversion that occurred in the beginning of the year in the Philadelphia area. This incident was picked up by a local newspaper and has been echoed recently by other publications but did not reflect a recurring event. I stated that Cephalon was aware of a total of 40 reports since the launch of the product that we put in the category of diversion but that most of these reports were notifications that law enforcement agencies or other contacts heard of diversionary activities but that most were unsubstantiated. Cephalon was going to contact FDA approximately 2 or 3 weeks ago regarding these publications, as we contacted DEA, but that due to Kim's vacation and mine, there was no occasion to discuss this.

Dr. Rappaport stated that the Agency's concern stems from analysis and reports that have come to FDA's attention from review of their sources. He stated that rather than discussing specific details, the Agency would like to meet with our company. One of the intentions of the risk management program was to limit the use of the product to the indication and the reports that they are receiving regarding off-label use have them extremely concerned. Their sources reflect that many of the elements that the RMP intended to control, such as off-label use especially, but also pediatric exposures, diversion and abuse, are increasing. Theses analyses are causing a real concern at high levels in the Agency. I asked if he could provide the source of the analyses and he stated that an example is the limited use of the Welcome Kit to 20%. I stated that we were aware of the data from our survey that reflect approximately a 23% distribution of the kit but that this percent, albeit not stellar, was understandable if one considers that approximately 32% of the people surveyed had children in the home. He stated just because people do not have children living with them does not mean that children would not enter the home. Dr. Rappaport stated that he did not want the company's interpretation used to support practices that the Agency finds alarming but he wants to review the actual data. He reiterated that the off-label use of the product is staggering.

He stated that he was very much involved with the drafting of our RMP and that he knows this document very well and the Agency is very concerned that the situation that occurred with Oxycontin may happen

again. He further stated that the RMP was designed to limit the use of the product to the indicated use and this does not seem to be working.

Dr. Rappaport stated that he would like our company to come in for a meeting in a month or two to provide a review of the data on misuse, diversion, off-label use, deaths, pediatric exposure, addiction and abuse. I asked if he would like a package prior to the meeting with our data and he responded that this would be helpful. He stated that it would be an inverse to a meeting package that the company normally provides in the context that FDA would have the questions when we meet rather than the company providing questions. I told him that I understood and that I would be in touch with Kim in the next day or two to set up the meeting.

I concluded that our company is also concerned about the proper use of our product in the market and that we are actively evaluating all incidents associated with diversion and misuse. We look forward to working with the Agency to address their concerns and to avoid a situation that occurred with Oxycontin. Dr. Rappaport thanked me and said he wants to work with us in this regard.