

## **Final Summary Minutes**

### **Joint Meeting of the Anesthetic and Life Support Drugs Advisory Committee and Drug Safety and Risk Management Advisory Committee November 13, 2008**

A verbatim transcript will be available in approximately four to six weeks, sent to the Division and posted on the FDA website at:

<http://www.fda.gov/ohrms/dockets/ac/cder08.html#AnestheticLifeSupport>

All external requests for the meeting transcripts should be submitted to the CDER, Freedom of Information office.

Prior to the meeting, the members and the invited consultants were provided the background material from the FDA and sponsor. The meeting was called to order by Jeffrey R. Kirsch, M.D. (Acting Chair, ALSDAC); the conflict of interest statement was read into the record by Kalyani Bhatt (Designated Federal Official). There were approximately 225 persons in attendance. There were 8 speakers for the Open Public Hearing Session.

#### **Attendance:**

##### **Anesthetic and Life Support Drugs Advisory Committee Members Present (voting)**

Jeffrey R. Kirsch, MD, Nancy Nussmeier, MD, Julia Pollock, MD, Athena F. Zuppa, MD, Daniel Zelterman, MD

##### **Drug Safety and Risk Management Advisory Committee Members Present (voting)**

Timothy Lesar, PharmD., Sean Hennessy, PharmD, PhD, Judith Kramer, MD, MS, Sidney Wolfe, MD, (Consumer Representative)

##### **Anesthetic and Life Support Drugs Advisory Committee and Drug Safety and Risk Management Advisory Committee Consultants (voting):**

Sorin Brull, MD, Richard Denisco, MD, Harriet de Wit, PhD, Robert Kerns, MD, Susan Krivacic (Patient Representative), Karl Lorenz, MD, Leonard Paulozzi, MD, M.P.H., Jack Rosenberg, MD, Sharon Walsh, PhD, Michael Yesenko (Patient Representative)

##### **Industry Representative for Anesthetic and Life Support Drugs Committee (non-voting):**

Bartholomew Tortella, MD, MTS, MBA

##### **Anesthetic and Life Support Drugs Advisory Committee Members Absent:**

Kanwaljeet Anand, J.J. MD, PhD, Jayant Deshpande, MD, John T. Farrar, MD, David G. Nichols, MD, MBA., Donald Prough, MD

##### **Drug Safety and Risk Management Advisory Committee Members Absent:**

Terry C. Davis, PhD., Sander Greenland, Dr., P.H., Susan Heckbert, MD, PhD, Bruce Burlington, M.D. (Industry Representative)

### **Open Public Hearing Speakers:**

Marti Hottenstein - Helping America Reduce Methadone Deaths

Mary Vargas - American Pain Foundation

Joanne Peterson - Learn to Cope

Ed Vanicky

Larry Goldbom - Prescription Addiction Radio

Lenore Duensing - American Academy of Pain Management

Marcie Bough - American Pharmacists Association

Scott Fishman - American Pain Foundation, American Academy of Pain Medicine

### **AGENDA**

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*The committees will discuss new drug application 22-324, REMOXY XRT (oxycodone hydrochloride controlled-release) Capsules, Pain Therapeutics Inc., and its safety for the proposed indication of management of moderate to severe pain when a continuous, around the-clock analgesic is needed for an extended period of time. The controlled-release characteristics of this formulation are purportedly less easily defeated than other formulations of controlled-release oxycodone.*

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Call to Order

Introduction of Committee

**Jeffrey R. Kirsch, M.D.**

Acting Chair, ALSDAC

Conflict of Interest Statement

**Kalyani Bhatt**

Designated Federal Officer,  
ALSDAC

Opening Remarks

**Bob A. Rappaport, M.D.**

Director, Division of Anesthesia,  
Analgesia, & Rheumatology Products  
CDER/FDA

History of Oxycontin Labeling and Risk  
Management Program

**Robert Shibuya, M.D.**

Lead Medical Officer,  
Division of Anesthesia, Analgesia, &  
Rheumatology Products, CDER/FDA

Sponsor Presentations

**Pain Therapeutics, Inc.**

Introduction

**Nadav Friedmann, Ph.D., M.D.**

Chief Operating and Medical Officer  
Pain Therapeutics Inc.

Remoxy In Vitro Testing

**Michael Zamloot**

Senior Vice President, Technical Operations  
Pain Therapeutics, Inc.

Remoxy In Vivo Testing	<b>Nadav Friedmann, Ph.D., M.D.</b>
Remoxy Risk Evaluation & Mitigation Strategy	<b>Eric Carter, Ph.D., M.D.</b> Chief Science Officer King Pharmaceuticals, Inc.
Remoxy In Vivo Abuse Resistance Studies	<b>Ping Ji, Ph.D.</b> Senior Clinical Pharmacologist Office of Clinical Pharmacology CDER/FDA
Outpatient Drug Utilization Trends for Oxycodone Products	<b>Laura Governale, Pharm.D., M.B.A.</b> Drug Utilization Analyst Team Leader Division of Epidemiology Office of Surveillance and Epidemiology (OSE), CDER/FDA
Prevalence and Patterns of Nonmedical Use of Oxycontin and Other Pain Relievers	<b>Joe Gfroerer</b> Director, Division of Population Surveys Office of Applied Studies, SAMHSA
Misuse/Abuse of Opioid Analgesics: Findings from The Drug Abuse Warning Network (DAWN)	<b>CAPT Kathy Poneleit</b> United States Public Health Service Director, Division of Facility Surveys Office of Applied Studies, SAMHSA
Admissions to Substance Abuse Treatment for the Abuse of Opioid Analgesics: Findings from the Treatment Episode Data Set (TEDS)	<b>Deborah Trunzo</b> Team Leader, Drug and Alcohol Services Information System (DASIS) Office of Applied Sciences, SAMHSA
Summary of Drug Abuse Rates in the US: Oxycodone	<b>Cathy Dormitzer, Ph.D., M.P.H.</b> Division of Epidemiology OSE/CDER/FDA
Overview of Reports of Manipulation of Controlled-release Oxycodone and Controlled-Release Morphine	<b>Richard Abate, R.Ph., M.S.</b> Safety Evaluator Division of Medication Error Prevention OSE/CDER/FDA
Open Public Hearing	

## Discussion and Questions to the Committee

***All questions were for Committee Discussion only; no votes were taken.***

1. a. Discuss the adequacy of the tools we have to assess the impact of a novel opioid formulation on the abuse, misuse and diversion of the product in the community.

*The agency stated that there are many tools available for evaluation of abuse in the community, including Drug Abuse Warning Network (DAWNS), The Treatment Episode Data Set (TEDS), National Survey on Drug Use & Health (NSDUH) Database, Florida Medical Examiners and State prescription monitoring. However, there is concern that these tools may not be robust enough to provide the committee with the information that they need to assess risk potential of new drugs expected to be tamper resistant.*

*The committee agreed that all of the available tools have limitations, which prevent the ability to use them to definitively assess the impact of new formulations on the communities at risk for abuse. The committee urged the agency to define minimum standards for assessment of tamper resistant qualities of any new application.*

- b. Discuss whether or not the available data suggest that this formulation will be less susceptible to abuse and misuse.

*The overall consensus of the committee is that the available data are not adequate to evaluate whether this reformulation of Oxycontin is likely to reduce its abuse, misuse, or diversion.*

*Some even suggested that new drug application 22-324, REMOXY XRT (oxycodone hydrochloride controlled-release) Capsules could lead to a false sense of security which in turn could lead to increased prescribing and in turn to increased abuse, misuse or diversion.*

2. Many of the cases of addiction, overdose and death associated with abuse of currently approved controlled-release oxycodone products have been due to ingestion of the product without manipulation of the controlled-release properties.
  - a. Discuss whether or not inclusion of data on the physicochemical attributes of this new formulation into the product labeling could potentially mislead prescribers or patients into thinking that this new formulation is less likely to be addictive, or unlikely to be abused or result in addiction or overdose.
  - b. If you believe that patients or prescribers could potentially be misled, discuss whether or not this risk is acceptable, considering the potential benefits of the changes to the formulation.

*Overall, the committee felt inclusion of the physiochemical attributes of the new formulation into the product labeling could potentially mislead prescribers or patients into*

*thinking that this new formulation of Oxycontin is less likely to be addictive or unlikely to be abused or result in addiction or overdose.*

*Overall, the committee did not feel the risk was acceptable.*

3. a. If, from Question 1, you believe that the data suggest that this formulation of controlled-release oxycodone is likely to reduce its abuse and misuse, discuss whether or not you recommend inclusion of any of the data in the product labeling.
- b. If you agree, please discuss which specific data should be incorporated into the labeling.

*The committee did not feel that the label should be permitted to make claims of tamper-resistance given the available data.*

*However, some suggested modifying the label to include safety concerns relating to the gel polymer.*

*The meeting adjourned at approximately 4:30 PM*