Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes of the
Joint Meeting of the Anesthetic and Life Support Drugs and Drug Safety and Risk Management Advisory Committee

May 5, 2008
Holiday Inn, Gaithersburg
Two Montgomery Village Avenue, Gaithersburg, MD.

Anesthetic and Life Support Drugs Advisory Committee Members Present (voting)
Kanwaljeet J.S. Anand, M.D., Ph.D., John T. Farrar, M.D., Jeffrey R. Kirsch, M.D., Nancy A. Nussmeier, M.D., Donald S. Prough, M.D., Athena F. Zuppa, M.D.

Drug Safety and Risk Management Advisory Committee Members Present (voting)
Timothy Lesar, Pharm.D.

Anesthetic and Life Support Drugs Advisory Committee and Drug Safety and Risk Management Advisory Committee Consultants (voting):
Diane Aronson, B.S. (Acting Consumer Representative), Warren K. Bickel, Ph.D., Charles R. Cortinovis, M.D., Ruth S. Day, Ph.D., Thomas R. Fleming, Ph.D., Jacqueline S. Gardner, Ph.D., Thomas Kosten, M.D., Susan Krivacic (Patient Representative), Jane C. Maxwell, Ph.D., Lewis S. Nelson, M.D., Steven D. Passik, Ph.D., Leonard J. Paulozzi, M.D., M.P.H., Christine Sang, M.D., M.P.H., Sulpicio de Guzman Soriano, III, M.D., Frank Vocci, Ph.D., Sidney Wolfe, M.D. (Acting Consumer Representative), Michael Yesenko (Patient Representative)

Industry Representative (non-voting):
Bruce Burlington, M.D.
Charles McLeskey, M.D.

Anesthetic and Life Support Drugs Advisory Committee Members Absent:
David G. Nichols, M.D., M.B.A.

Drug Safety and Risk Management Advisory Committee Members Absent:
Terry C. Davis, Ph.D., Sander Greenland, Dr.P.H., Susan Heckbert, M.D., Ph.D., Richard Platt, M.D., M.Sc., Sean Hennessy, PharmD., Ph.D., and Judith M. Kramer, M.D., M.S.,

Guest Speakers:
Joe Gfroerer, Judy K. Ball, Ph.D., M.P.A., and Deborah Trunzo

FDA Participants:
Sandra Kweder, M.D., Curtis Rosebraugh, M.D., Bob Rappaport, M.D., Henry Francis, M.D., and Sharon Hertz, M.D.

Open Public Hearing Speakers:
Art VanZee, Larry Golbom, Beatrice Setnik, Micke Brown, Pete Jackson, and Ellen Jackson

Executive Secretary
Teresa A. Watkins

I certify that I attended the May 5, 2008 meeting of the Anesthetic and Life Support Drugs and Drug Safety and Risk Management Advisory Committee and that these minutes accurately reflect what transpired.

_____-s-_____	_____-s-_____
Teresa A. Watkins	John Farrar, M.D.
Executive Secretary, ALSDAC/DSaRM	Chair, ALSDAC

Minutes
Joint Meeting of the Anesthetic and Life Support Drugs Advisory Committee and Drug Safety and Risk Management Advisory Committee
May 5, 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. The meeting was called to order by John T. Farrar, M.D. (Chair, ALSDAC); the conflict of interest statement was read into the record by Teresa Watkins (Acting Designated Federal Official). There were approximately 350 persons in attendance. There were 6 speakers for the Open Public Hearing Session

Attendance:

Anesthetic and Life Support Drugs Advisory Committee Members Present (voting)
Kanwaljeet J.S. Anand, M.D., Ph.D., John T. Farrar, M.D., Jeffrey R. Kirsch, M.D., Nancy A. Nussmeier, M.D., Donald S. Prough, M.D., Athena F. Zuppa, M.D.

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Bruce Burlington, M.D.
Charles McLeskey, M.D.

Anesthetic and Life Support Drugs Advisory Committee Members Absent:
David G. Nichols, M.D., M.B.A.

Drug Safety and Risk Management Advisory Committee Members Absent:
Terry C. Davis, Ph.D., Sander Greenland, Dr.P.H., Susan Heckbert, M.D., Ph.D., Richard Platt, M.D., M.Sc., Sean Hennessy, PharmD., Ph.D., and Judith M. Kramer, M.D., M.S.,

Guest Speakers:
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Art VanZee, Larry Golbom, Beatrice Setnik, Micke Brown, Pete Jackson, and Ellen Jackson

Issue:
The committees discussed new drug application (NDA) 22-272, OXYCONTIN® (oxycodone hydrochloride controlled-release) Tablets, Purdue Pharma, L.P., 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 sustained-release characteristics of this formulation are purportedly less easily defeated than other formulations of OXYCONTIN.

The agenda proceeded as follows:

Call to Order Introduction of Committee	**John T. Farrar, M.D.** Acting Chair, ALSDAC
Conflict of Interest Statement	**Teresa Watkins, Pharm.D., R.Ph.** Acting Designated Federal Officer, ALSDAC/DSaRM
Opening Remarks	**Bob A. Rappaport, M.D.** Director, Division of Anesthesia, Analgesia, & Rheumatology Products CDER/FDA
Sponsor Presentations	
	J. David Haddox, D.D.S., M.D. Vice President, Risk Management and Health Policy Purdue Pharma, L.P.
	Jack E. Henningfield, Ph.D. Vice President, Research and Health Policy Pinney Associates

	Richard Mannion, BPharm., Ph.D. Senior Director, Pharmaceutics Purdue Pharma, L.P.
History of Oxycontin Labeling and Risk Management Program	**Mwango Kashoki, M.D.** Lead Medical Officer, Division of Anesthesia, Analgesia, & Rheumatology Products CDER/FDA
Utilization Trends	**LCDR Kendra Worthy, PharmD** U.S. Public Health Service Commissioned Corps Drug Utilization Analyst, Division of Epidemiology Office of Surveillance and Epidemiology (OSE), CDER/FDA
Prevalence and Patterns of Nonmedical Use of Oxycontin and Other Pain Relievers	**Joe Gfroerer** Director, Division of Population Surveys Office of Applied Studies, SAMHSA
Misuse/Abuse of Opioid Analgesics: Findings from The Drug Abuse Warning Network (DAWN)	**Judy K. Ball, Ph.D., M.P.A.** Acting Director, Division of Operations Office of Applied Studies, SAMHSA
Admissions to Substance Abuse Treatment for the Abuse of Opioid Analgesics: Findings from the Treatment Episode Data Set (TEDS)	**Deborah Trunzo** Team Leader, Drug and Alcohol Services Information System (DASIS) Office of Applied Sciences, SAMHSA
Questions for the SAMSHA presenters	
Summary of Drug Abuse Rates in the US	**Cathy Dormitzer, Ph.D., MPH** Division of Epidemiology Office of Surveillance and Epidemiology (OSE)

Overview of Reports of Manipulation of OxyContin Tablets

LCDR Kristina C. Arnwine, PharmD
U.S. Public Health Service
Commissioned Corps
Acting Team Leader
Division of Medication Error Prevention
Office of Surveillance and Epidemiology
(OSE)

Lunch

Open Public Hearing

Questions to the presenters

Discussion and Questions to the Committee
Questions for the Committee:

1. ***Discuss the adequacy of the tools we have to assess the impact of a novel opioid formulation on abuse, misuse and diversion of the product in the community. Do the available data suggest that this reformulation of OxyContin will likely reduce its abuse, misuse and diversion?***

   -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 it 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.
   -Some expressed concern with the variability in the amount of active drug that might be extracted using various extraction methods by individuals obtaining the drug for non-medical use. This could lead to an increase in overdose and mortality.
   -Some expressed that the rigor of the scientific data was insufficient and that more pre-marketing tests were necessary to adequately support the sponsor's claims that the drug is, in fact, more tamper resistant.
   -Others expressed that the testing methods within the protocol utilized by the sponsor need independent validation.
   -Others felt that more information is needed to address safety concerns relating to the injection of the gelatinous matrix that forms when aqueous media is added to the crushed tablet.

2. ***Currently, only the 10-mg, 20-mg, 30-mg and 40-mg strengths have been reformulated, although there are plans to reformulate the 60-mg and 80-mg strengths in the future. Could marketing and promotion of the lower, reformulated strength products as less abusable, prior to reformulation of the higher strength products, result in the misconception that the higher, non-reformulated strengths also provide a decreased risk of abuse? If so, are there ways to minimize this misconception? Given this concern, is this risk acceptable considering the potential benefit of the changes to the formulation for the lower strength products?***

   -All members of the committee felt that the higher strengths which have not yet been reformulated should not remain on the market if the reformulated lower strengths are approved.
   -Many suggested that the size, shape, and/or color of the reformulated tablets should differ significantly from the currently marketed non tamper-resistant formulations to avoid prescriber confusion.
   -Most members stated that the label should not be changed to allow the sponsor to make a claim of tamper-resistance without further evidence to support the claim.

3. ***Many of the cases of addiction, overdose and death associated with OxyContin abuse have been due to ingestion of the product without manipulation of the extended-release properties. Could inclusion of data on the physiochemical attributes of the new formulation into the product labeling 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? If so, is this risk 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.

4. ***If you concluded in Question 1 that the data suggest that this reformulation of OxyContin is likely to reduce its abuse, misuse and diversion, do you recommend inclusion of any of the data into the product labeling? If so, which specific data do you think 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.

5. ***If you do recommend any of these data be placed into the product label, are there risk minimization strategies that need to be put in place to support the appropriate use of this product, e.g., additional language in labeling (please specify), educational information that will describe proper use and the potential for misuse and abuse of the product, special educational requirements/training for prescribers, limitations on which patients should be treated with the product, formal agreements between prescribers and patients for proper use, registries for prescribers?***

   -Some felt that they did not have enough data to adequately respond to the question.
   -Others felt that risk minimization plans should be directed at the entire class of opioid pain relievers.
   -Many expressed that targeted education for prescribers, pharmacists, and nurses was needed to discourage over prescribing, but also to encourage support for appropriate prescribing.
   -Others suggested researching and applying aspects of existing risk minimization plans in place for other medications.
   -One suggested increased regulation of marketing procedures
   -One suggested restricting the indication to only severe chronic cancer and non-cancer pain.
   -One suggested developing separate oxycontin prescribing guidelines for chronic pain and for acute pain

   For a complete accounting, please refer to the transcript.

Adjourn approximately 5:15 p.m.