Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee Joint Meeting
June 8, 2016

Location: The FDA White Oak Campus, Building 31 Conference Center, The Great Room (Rm. 1503), 10903 New Hampshire Avenue, Silver Spring, Maryland.

Topic: The committees were asked to discuss new drug application (NDA) 207621, Oxycodone Hydrochloride and Naltrexone Hydrochloride Extended-Release Capsules, submitted by Pfizer, Inc., with the proposed indication of management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. The product is an extended-release formulation intended to have abuse-deterrent properties based on the presence of naltrexone, an opioid antagonist, in the formulation. The committees were asked to discuss whether the data submitted by the Applicant are sufficient to support labeling of the product with the properties expected to deter abuse.

These summary minutes for the June 8, 2016, joint meeting of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee of the Food and Drug Administration were approved on June 23, 2016.

I certify that I attended the June 8, 2016, joint meeting of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/	/s/
Stephanie L. Begansky, PharmD	Raeford Brown, MD
Designated Federal Officer, AADPAC	Acting Chairperson, AADPAC

Summary Minutes of the
Joint Meeting of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee
June 8, 2016

The following is the final report of the joint meeting of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee, held on June 8, 2016. A verbatim transcript will be available in approximately six weeks, sent to the Division of Analgesia, Anesthesia and Addiction Products and the Office of Safety and Epidemiology and posted on the FDA website at: http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/AnestheticAndAnalgesicDrugProductsAdvisoryCommittee/ucm486848.htm and http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/ucm486856.htm

All external requests for the meeting transcript should be submitted to the CDER Freedom of Information Office.

The Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research, met jointly on June 8, 2016, at the FDA White Oak Campus, 10903 New Hampshire Avenue, Building 31 Conference Center, the Great Room (Rm. 1503), Silver Spring, Maryland. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and Pfizer, Inc. The meeting was called to order by Raeford Brown, MD, FAAP (Acting Chairperson). The conflict of interest statement was read into the record by Stephanie Begansky, PharmD (Designated Federal Officer). There were approximately 100 people in attendance. There were 2 Open Public Hearing (OPH) speaker presentations.

Issue: The committees were asked to discuss new drug application (NDA) 207621, Oxycodone Hydrochloride and Naltrexone Hydrochloride Extended-Release Capsules, submitted by Pfizer, Inc., with the proposed indication of management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. The product is an extended-release formulation intended to have abuse-deterrent properties based on the presence of naltrexone, an opioid antagonist, in the formulation. The committees were asked to discuss whether the data submitted by the Applicant are sufficient to support labeling of the product with the properties expected to deter abuse.

Attendance:

Anesthetic and Analgesic Drug Products Advisory Committee Members Present (Voting): Raeford E. Brown, Jr., MD, FAAP (Acting Chairperson); Charles W. Emala Sr., MS, MD; Anita Gupta, DO, PharmD; Jennifer G. Higgins, PhD (Consumer Representative); Abigail B. Shoben, PhD

Anesthetic and Analgesic Drug Products Advisory Committee Members Not Present (Voting): Brian T. Bateman, MD, MSc; David S. Craig, PharmD; Jeffrey L. Galinkin, MD, FAAP; Rafael V. Miguel, MD

Anesthetic and Analgesic Drug Products Advisory Committee Member Present (Non-Voting): W. Joseph Herring, MD, PhD (Industry Representative)

Drug Safety and Risk Management Advisory Committee Members Present (Voting): Kelly Besco, PharmD, FISMP, CPPS;; Tobias Gerhard, PhD, RPh; Almut G. Winterstein, RPh, PhD, FISPE

Drug Safety and Risk Management Advisory Committee Members Not Present (Voting): Niteesh K. Choudhry, MD, PhD; Christopher H. Schmid, PhD; Andy S. Stergachis, PhD, RPh; Til Sturmer, MD, MPH, PhD; Linda Tyler, PharmD, FASHP

Drug Safety and Risk Management Advisory Committee Member Not Present (Non-Voting): Linda Scarazzini, MD (Industry Representative)

Temporary Members (Voting): Melinda Campopiano, MD; Alan D. Kaye, MD, PhD; Mary Ellen McCann, MD; Elaine Morrato, DrPH, MPH; Cynthia Chauhan (Patient Representative); Jeanmarie Perrone, MD, FACMT; Michael Sprintz, DO

FDA Participants (Non-Voting): Sharon Hertz, MD; Ellen Fields, MD, MPH; Judy Staffa, PhD, RPh

Designated Federal Officer (Non-Voting): Stephanie Begansky, PharmD

Open Public Hearing Speakers: Edwin R. Thompson (Pharmaceutical Manufacturing Research Services, Inc.); Sidney Wolfe (Public Citizen)

The agenda was as follows:

Call to Order and Introduction of Committee	**Raeford E. Brown, Jr., MD, FAAP** Acting Chairperson, AADPAC
Conflict of Interest Statement	**Stephanie L. Begansky, PharmD** Designated Federal Officer, AADPAC
FDA Introductory Remarks	**Ellen Fields, MD, MPH** Deputy Director Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) Office of Drug Evaluation II (ODE-II) Office of New Drugs (OND), CDER, FDA

Corrections to FDA In Vitro Abuse Deterrent Open Session Backgrounder	**Benjamin D. Stevens, PhD, MPH** CMC Drug Substance Reviewer Division of New Drug API, Branch II Office of New Drug Products (ONDP) Office of Pharmaceutical Quality (OPQ), CDER, FDA
APPLICANT PRESENTATIONS	**Pfizer, Inc.**
ALO-02 Abuse Deterrence Program Introduction	**Sean Donevan, PhD** Medical Affairs Lead Pfizer, Inc.
ALO-02 Clinical Pharmacology	**Bimal Malhotra, PhD** Clinical Pharmacology Lead Pfizer, Inc.
ALO-02 Efficacy and Safety	**Gernot Wolfram, MD** Global Clinical Lead Pfizer, Inc.
ALO-02 Abuse Deterrence Program In Vitro	**Sean Donevan, PhD**
ALO-02 Abuse Deterrence Program Human PK/PD	**Carl Roland, PharmD, MS** Clinical Development & Outcomes and Evidence Pfizer, Inc.
Conclusions	**Sean Donevan, PhD**
Clarifying Questions	
BREAK	
FDA PRESENTATIONS	
Drug Utilization Patterns for Oxycodone ER and Other ER/LA Opioid Analgesics 2011-2015	**Joann H. Lee, PharmD** Drug Utilization Data Analyst Division of Epidemiology II (DEPI-II) Office of Pharmacovigilance and Epidemiology Office of Surveillance and Epidemiology (OSE), CDER, FDA
Troxyca ER (oxycodone HCL and naltrexone HCL) Extended-Release Capsules for Oral Use Labeling Section 9: Drug Abuse	**Elizabeth Kilgore, MD** Medical Officer DAAAP, ODE-II, OND, CDER, FDA
Clarifying Questions	
LUNCH	

Open Public Hearing

Charge to the Committee — **Sharon Hertz, MD**
Director
DAAAP, ODE-II, OND, CDER, FDA

Questions to the Committee/Committee Discussion

BREAK

Questions to the Committee/Committee Discussion (cont.)

ADJOURNMENT

Questions to the Committee:

1. **DISCUSSION:** Please discuss whether there are sufficient data to support a finding that Troxyca ER (oxycodone hydrochloride and naltrexone hydrochloride extended-release capsules) has properties that can be expected to deter abuse, commenting on support for abuse-deterrent effects for each of the three possible routes of abuse:

    a. Oral
    b. Nasal
    c. Intravenous

    Committee Discussion: *The committee agreed there was sufficient data to support a finding that Troxyca ER fulfilled the criteria for abuse-deterrent characteristics for the oral, nasal and intravenous routes of administration. However, the committee acknowledged that the drug was capable of being manipulated in a relatively effortless fashion to become an oral drug of abuse and stated that they were unsure how robust the abuse-deterrent properties would be if the drug was introduced in the market. The committee recommended post-marketing studies be done on Troxyca ER, as well as more comprehensive qualifications for abuse-deterrence overall. Please see the transcript for details of the committee discussion.*

2. **VOTE:** Should Troxyca ER be approved for the proposed indication, management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate?

    Vote Result: Yes: 9 No: 6 Abstain: 0

    Committee Discussion: *The majority of the committee voted "Yes," agreeing that Troxyca ER should be approved for the proposed indication. Those members who voted "Yes" stated that they support approval because the drug met the current standards for approval of an extended-release product while showing clinical efficacy and safety data. Those members who voted "No" stated that the new Centers for Disease Control guidelines recommend against the use of opioids for chronic pain and the criteria for approving an extended-release*

opioid should be modified in accordance with the guidelines. Please see the transcript for details of the committee discussion.

3. **VOTE:** If approved, should Troxyca ER be labeled as an abuse-deterrent product by the oral route of abuse?

   Vote Result: Yes: 6 No: 9 Abstain: 0

   Committee Discussion: *The majority of the committee voted "No," stating that Troxyca ER should not be labeled as an abuse-deterrent product for the oral route of abuse. Those members who voted "No" were concerned with the extraction of oxycodone and separation from naltrexone in particular solvents. Those members who voted "Yes" stated that the benefits of having another product on the market outweighed the risks. Please see the transcript for details of the committee discussion.*

4. **VOTE:** If approved, should Troxyca ER be labeled as an abuse-deterrent product by the nasal route of abuse?

   Vote Result: Yes: 11 No: 4 Abstain: 0

   Committee Discussion: *The majority of the committee voted "Yes," stating that Troxyca ER should be labeled as an abuse-deterrent product for the nasal route of abuse. Those members who voted "Yes" agreed that there was sufficient data provided to show that the product would not separate when crushed. Those members who voted "No" were concerned with the potential of abuse and stated that the determination of an abuser should not be underestimated. Some members of the committee recommended the Agency set different standards for abuse-deterrence. Please see the transcript for details of the committee discussion.*

5. **VOTE:** If approved, should Troxyca ER be labeled as an abuse-deterrent product by the intravenous route of abuse?

   Vote Result: Yes: 9 No: 6 Abstain: 0

   Committee Discussion: *The majority of the committee voted "Yes," stating that Troxyca ER should be labeled as an abuse-deterrent product for the intravenous route of abuse. Those members who voted "Yes" agreed that the data was compelling and the drug would provide another option for patients. Those members who voted "No" suggested that the Agency clarify the meaning of abuse-deterrence. Please see the transcript for details of the committee discussion.*

The meeting was adjourned at approximately 4:00 p.m. on June 8, 2016.