Food and Drug Administration
Center for Drug Evaluation and Research

Final Summary Minutes of the Joint Meeting of Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee November 14, 2018

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

Topic: The committees discussed new drug application (NDA) 209774, for an immediate-release oral tablet formulation of oxycodone, which is intended to resist common methods of physical or chemical manipulation and to deter intravenous and intranasal abuse, submitted by SpecGx LLC, for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. The committees were also asked to determine whether the Applicant adequately demonstrated that the abuse-deterrent properties of the proposed product are sufficient to include this information in the product label, and whether the product should be approved.

These summary minutes for the November 14, 2018 joint meeting of the Anesthetic and Analgesic Drug Products Advisory Committee (AADPAC) and the Drug Safety and Risk Management (DSaRM) Advisory Committee of the Food and Drug Administration were approved on January 24, 2019.

I certify that I attended the November 14, 2018 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/**
Moon Hee V. Choi, PharmD	Brian Bateman, MD, MSc
Designated Federal Officer, AADPAC	Acting Chairperson, AADPAC

Final Summary Minutes of the Joint Meeting of the
Anesthetic and Analgesic Drug Products Advisory Committee and the
Drug Safety and Risk Management Advisory Committee
November 14, 2018

The Anesthetic and Analgesic Drug Products Advisory Committee (AADPAC) and the Drug Safety and Risk Management Advisory Committee (DSaRM) of the Food and Drug Administration, Center for Drug Evaluation and Research met on November 14, 2018, at the FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503), 10903 New Hampshire Avenue, Silver Spring, Maryland. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and SpecGx LLC. The meeting was called to order by Brian Bateman, MD, MSc (Acting Chairperson). The conflict of interest statement was read into the record by Moon Hee Choi, PharmD (Designated Federal Officer). There were approximately 90 people in attendance. There were 10 Open Public Hearing (OPH) speaker presentations.

A verbatim transcript will be available, in most instances, at approximately ten to twelve weeks following the meeting date.

Agenda: The committees discussed new drug application (NDA) 209774, for an immediate-release oral tablet formulation of oxycodone, which is intended to resist common methods of physical or chemical manipulation and to deter intravenous and intranasal abuse, submitted by SpecGx LLC, for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. The committees were also asked to determine whether the Applicant adequately demonstrated that the abuse-deterrent properties of the proposed product are sufficient to include this information in the product label, and whether the product should be approved.

Attendance:
Anesthetic and Analgesic Drug Products Advisory Committee Members Present (Voting): Brian T. Bateman, MD, MSc (Acting Chairperson); Basavana G. Goudra, MD, FRCA, FCARSCI; Mary Ellen McCann, MD, MPH; Abigail B. Shoben, PhD; Lonnie Zeltzer, MD

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

Anesthetic and Analgesic Drug Products Advisory Committee Members Not Present (Voting): Raeford E. Brown, Jr., MD, FAAP; Ronald S. Litman, DO, ML; Kevin L. Zacharoff, MD, FACIP, FACPE, FAAP

Drug Safety and Risk Management Advisory Committee Members Present (Voting): Sonia Hernandez-Diaz, MD, MPH, DrPH**;** Steven B. Meisel, PharmD, CPPS; Suzanne B. Robotti

Drug Safety and Risk Management Advisory Committee Members Not Present (Voting): Kelly Besco, PharmD, FISMP, CPPS**;** Denise M. Boudreau, PhD, RPh**;** Marie R. Griffin, MD, MPH; Laurel A. Habel, MPH, PhD**;** Martin Kulldorff, PhD**;** Anne-Michelle Ruha, MD, FACMT; Soko Setoguchi, MD, DrPH**;** Terri L. Warholak, PhD, RPh, CPHQ, FAPhA

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

Temporary Members (Voting): Cynthia L. Arfken, PhD; Michael Fischer, MD, MS; Traci C. Green, PhD, MSc; Jennifer Higgins, PhD (Acting Consumer Representative); Brandon D.L. Marshall, PhD; Joseph P. O'Brien, MBA (Patient Representative); Jeanmarie Perrone, MD, FACMT; Thomas Prisinzano, PhD; Jon E. Zibbell, PhD

FDA Participants (Non-Voting): Sharon Hertz, MD; Jennifer L. Nadel, MD; Judy Staffa, PhD, RPh; Tamra Meyer, PhD, MPH; Dominic Chiapperino, PhD

Designated Federal Officer (Non-Voting): Moon Hee V. Choi, PharmD

Open Public Hearing Speakers: Sidney M. Wolfe, MD (Public Citizen's Health Research Group); Stacy Litz; Edwin R. Thompson (Pharmaceutical Manufacturing Research Services, Inc.); Charlie Cichon (National Association of Drug Diversion Investigators); Barrye Price (Community Anti-Drug Coalitions of America); Stephen C. Mullenix, BPharm, RPh on behalf of Dan Cohen (Abuse Deterrent Coalition); Fred Wells Brason II (Project Lazarus); Stephen C. Mullenix, BPharm, RPh (National Council for Prescription Drug Programs); Dave Zook (Collaborative for Effective Prescription Opioid Policies); Joshua Lewis

The agenda was as follows:

Call to Order and Introduction of Committee	**Brian Bateman, MD** Acting Chairperson, AADPAC
Conflict of Interest Statement	**Moon Hee V. Choi, PharmD** Designated Federal Officer, AADPAC
FDA Opening Remarks	**Sharon Hertz, MD** Director, Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) Office of Drug Evaluation II (ODE-II) Office of New Drugs (OND), CDER, FDA
APPLICANT PRESENTATIONS	**SpecGx LLC**
Introductions	**Martha Sclicher, PhD** Vice President, R&D Mallinckrodt Pharmaceuticals

APPLICANT PRESENTATIONS (CONT.)

Public Health Need for Abuse-Deterrent IR Opioid Analgesics	**Richard Dart, MD, PhD** Director Rocky Mountain Poison & Drug Center Professor of Emergency Medicine University of Colorado School of Medicine Executive Director, RADARS® System
Category 1 *In Vitro* Studies	**Edward Cone, PhD** Principal Scientist Drug Delivery and Abuse Deterrent Drug Products Pinney Associates
Nonclinical Excipient Safety Studies	**Mike Orr, PhD, DABT** President/CEO Orr Nonclinical Consulting, LLC
Intranasal Human Abuse Potential Study	**Sandra Comer, PhD** Professor of Neurobiology (in Psychiatry) Division on Substance Use Disorders Columbia University
Clinical Perspective	**Jeff Gudin, MD** Director Pain Management and Palliative Care Englewood Hospital and Medical Center
Clarifying Questions	

BREAK

FDA PRESENTATIONS

MNK-812 Introduction and Overview	**Jennifer L. Nadel, MD** Medical Officer DAAAP, ODE-II, OND, CDER, FDA
In Vitro Category I Abuse-Deterrent Studies of MNK-812	**Valerie Amspacher, PharmD** Chemistry, Manufacturing and Controls Reviewer Division of New Drug Products II Office of New Drug Products (ONDP) Office of Pharmaceutical Quality, CDER, FDA
Nonclinical Safety Assessment of MNK-812 Excipients	**R. Daniel Mellon, PhD** Pharmacology Toxicology Supervisor DAAAP, ODE-II, OND, CDER, FDA

FDA PRESENTATIONS (CONT.)

Examination of Intranasal Human Abuse Potential Study MNK48121013	**James M. Tolliver, PhD** Pharmacologist Controlled Substance Staff Office of the Center Director CDER, FDA
Review of Recent Epidemiologic Data on Use, Misuse and Abuse of Oxycodone	**Tamra Meyer, PhD, MPH** Team Lead, Prescription Drug Abuse Team Division of Epidemiology II Office of Pharmacovigilance and Epidemiology Office of Surveillance and Epidemiology CDER, FDA
MNK-812 Clinical Summary of Abuse Deterrence	**Jennifer L. Nadel, MD**
Clarifying Questions	

LUNCH

OPEN PUBLIC HEARING

Charge to the Committee	**Sharon Hertz, MD**
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 oxycodone hydrochloride immediate-release tablets (MNK-812) has properties that can be expected to deter abuse, commenting on support for abuse-deterrent effects for each of the following routes of abuse:

    a. Nasal
    b. Intravenous

***Committee Discussion**: Overall, a majority of the committee members agreed that there were sufficient data to support a finding that oxycodone hydrochloride immediate-release tablets (MNK-812) has properties that can be expected to deter intranasal abuse. Some committee members disagreed that the data were sufficient to determine if the oxycodone hydrochloride immediate-release tablets (MNK-812) would be effective in dissuading physically-dependent abusers. Other committee members expressed concern that the formulation would result in individuals who abuse opioids transitioning to the intravenous route of abuse if they were unsuccessful with abuse by the nasal route.*

The majority of the committees agreed that there was insufficient evidence to show effectiveness in deterring intravenous abuse. Several committee members expressed concern that dosage form could be manipulated using large volumes of solvent, which could potentially lead to increased intravenous drug abuse. Please see the transcript for details of the committees' discussion.

2. **DISCUSSION:** The Applicant is requesting approval of oxycodone hydrochloride immediate-release tablets (MNK-812) as an analgesic with properties expected to deter abuse by the intravenous and intranasal routes. Discuss whether you have any concerns regarding the impact of this oxycodone hydrochloride immediate-release product (MNK-812) on public health. Take into consideration its potential effect on the abuse of opioids, including oxycodone, as well as potential consequences of administration of this product by unintended routes.

***Committee Discussion**: Some committee members expressed concerns that oxycodone hydrochloride immediate-release ADF products may provide a false sense of safety among prescribers that could lead to over-prescribing. Other members emphasized the gap in data about the effectiveness of ADF products and stressed the importance of getting data from studies that evaluate both the effectiveness of ADFs and their impact on opioid prescribing patterns. In terms of the impact on public health, some committee members expressed concern that some ADF products could increase the risk of sharing paraphernalia for injection and transmitting bloodborne disease similar to other opioids that are abused via the intravenous route. Some committee members wanted the oral route of abuse to be addressed. Please see the transcript for details of the committees' discussion.*

3. **VOTE:** If approved, should oxycodone hydrochloride immediate-release tablets (MNK-812) be labeled as an abuse-deterrent product by the nasal route of abuse?

Vote Result: Yes: 12 No: 5 Abstain: 0

***Committee Discussion**: The majority of the committees agreed that if approved, oxycodone hydrochloride immediate-release tablets (MNK-812) should be labeled as an abuse-deterrent product by the nasal route of abuse. Some committee members who voted "Yes" noted that the clinical trial data demonstrated an abuse-deterrent effect, but that it was only demonstrated in the very narrow study population. The committee members who voted "No" stated that any aversive effects demonstrated in the study were very short-lived and there was*

insufficient evidence that the abuse-deterrent effect would be effective in a real-world setting. Please see the transcript for details of the committees' discussion.

4. **VOTE:** If approved, should oxycodone hydrochloride immediate-release tablets (MNK-812) be labeled as an abuse-deterrent product by the intravenous route of abuse?

   Vote Result: Yes: 7 No: 10 Abstain: 0

   ***Committee Discussion**: The majority of the committees did not agree that oxycodone hydrochloride immediate-release tablets (MNK-812) should be labeled as an abuse-deterrent product by the intravenous route of abuse, if approved. Some of these committee members agreed that there was a lack of data to support this labeling. Other committee members expressed concerns with possible long-term safety effects of injecting excipients intended for oral administration and the potential for transmission of infectious diseases with the intravenous route of abuse. The committee members who voted "Yes" agreed that this formulation of oxycodone hydrochloride immediate-release tablets (MNK-812) presents more of a barrier compared to oxycodone immediate-release tablets not formulated to have abuse-deterrent properties (e.g., Roxicodone). Please see the transcript for details of the committees' discussion.*

5. **VOTE:** Should oxycodone hydrochloride immediate-release tablets (MNK-812) be approved for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate?

   Vote Result: Yes: 10 No: 7 Abstain: 0

   ***Committee Discussion**: The majority of the committees agreed that oxycodone hydrochloride immediate-release tablets (MNK-812) should be approved for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Some of the committee members who supported approval based their decisions on the demonstration of bioequivalence to the comparator oxycodone hydrochloride immediate-release product and concluded that oxycodone hydrochloride immediate-release tablets (MNK-812) represents an abuse-deterrent option relative to existing non-ADF immediate-release oxycodone formulations. The committee members who voted "No" concluded that oxycodone hydrochloride immediate-release tablets (MNK-812) would provide minimal benefit over risk and expressed concern that it may provide a false sense of security to prescribers. Please see the transcript for details of the committees' discussion.*

The meeting was adjourned at approximately 4:04 p.m.