Food and Drug Administration
Center for Drug Evaluation and Research

Final Summary Minutes of the Joint Meeting of the Anesthetic and Analgesic Drug Products and the Drug Safety and Risk Management Advisory Committee December 17-18, 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 provided input and advice on strategies to increase the availability of naloxone products intended for use in the community. The committees were asked to consider various options for increasing access to naloxone, weighing logistical, economic, and harm reduction aspects and whether naloxone should be co-prescribed with all or some opioid prescriptions to reduce the risk of overdose death. Because of the potential, significant costs and burdens that may be associated with naloxone co-prescribing (e.g., economic costs to consumers and health systems, adjusting to manufacturing volume growth, drug shortages), the committees were also asked to consider the potential burdens that may be associated with naloxone co-prescribing for all or some prescription opioid patients.

These summary minutes for the December 17-18, 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 February 4, 2019.

I certify that I attended the December 17-18, 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/**
Jennifer Shepherd, RPh	Raeford E. Brown, Jr., MD, FAAP
Acting Designated Federal Officer, AADPAC	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
December 17-18, 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 December 17-18, 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 Industry participants. The meeting was called to order by Raeford Brown, MD (Chairperson). The conflict of interest statement was read into the record by Jennifer Shepherd, RPh (Acting Designated Federal Officer). There were approximately 150 people in attendance on December 17, 2018, and approximately 85 people in attendance on December 18, 2018. There were sixteen Open Public Hearing speaker presentations.

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

Agenda: The committees provided input and advice on strategies to increase the availability of naloxone products intended for use in the community. The committees were asked to consider various options for increasing access to naloxone, weighing logistical, economic, and harm reduction aspects and whether naloxone should be co-prescribed with all or some opioid prescriptions to reduce the risk of overdose death. Because of the potential, significant costs and burdens that may be associated with naloxone co-prescribing (e.g., economic costs to consumers and health systems, adjusting to manufacturing volume growth, drug shortages), the committees were also asked to consider the potential burdens that may be associated with naloxone co-prescribing for all or some prescription opioid patients.

Attendance:

Anesthetic and Analgesic Drug Products Advisory Committee Members Present (Voting): Brian T. Bateman, MD, MSc; Raeford E. Brown, Jr., MD, FAAP (Chairperson); Basavana G. Goudra, MD, FRCA, FCARSCI; Mary Ellen McCann, MD, MPH; Abigail B. Shoben, PhD; Kevin L. Zacharoff, MD, FACIP, FACPE, FAAP

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): Ronald S. Litman, DO, ML; Lonnie Zeltzer, MD

Drug Safety and Risk Management Advisory Committee Members Present (Voting): Kelly Besco, PharmD, FISMP, CPPS**;** Denise M. Boudreau, PhD, RPh**;** Sonia Hernandez-Diaz, MD, MPH, DrPH**;** Steven B. Meisel, PharmD, CPPS; Suzanne B. Robotti (Consumer Representative)

Drug Safety and Risk Management Advisory Committee Members Not Present (Voting): 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): Maryann E. Amirshahi, MD, PharmD, MPH; Jordan Marie Ballou, PharmD, BCACP; Paul Brand, PharmD, AE-C; Daniel Ciccarone, MD, MPH; Nabarun Dasgupta, MPH, PhD; Mark D. Faul, PhD, MA; Martin Garcia-Bunuel, MD; Tobias Gerhard, BSPharm, PhD; Erin E. Krebs, MD, MPH; Jeffrey T. Macher, PhD; Sabrina Numann (Patient Representative); Paul Pisarik, MD, MPH

FDA Participants (Non-Voting): Joshua Lloyd, MD; Sharon Hertz, MD; Alex Secora, MPH; Judy Staffa, PhD, RPh; Douglas C. Throckmorton, MD

Designated Federal Officer (Non-Voting): Jennifer Shepherd, RPh

Open Public Hearing Speakers: Eliza Wheeler (Harm Reduction Coalition); Michael Hufford, PhD (Harm Reduction Therapies); James Lott, PharmD and Straker Carryer (Fiduscript); Erin Haas, MPH (Maryland Department of Health); Barbara Kochanowski, PhD (Consumer Healthcare Products Association); Megan McLemore, JD, LLM (Human Rights Watch); Jennifer Plumb, MD, MPH; Jeffrey Bratberg, PharmD (University of Rhode Island College of Pharmacy); Grant Smith (Drug Policy Alliance); Peter Maybarduk (Public Citizen); Mark Tripodi (Venebio); Traci Green, PhD; Fred Wells Brason II (Project Lazarus); Robert Twillman, PhD, FAPM (Academy of Integrative Pain Management); Karla Wagner, PhD; Alice Bell (Prevention Point Pittsburgh)

The agenda was as follows:

<u>Day 1: Monday, December 17, 2018</u>

Call to Order and Introduction of Committee	**Raeford E. Brown, Jr., MD, FAAP** Chairperson, AADPAC
Conflict of Interest Statement	**Jennifer Shepherd, RPh** Acting Designated Federal Officer, AADPAC
FDA Opening Remarks: Overview of the Issues in Question	**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

INDUSTRY PRESENTATIONS

Naloxone Co-prescribing	**Robert G. Kramer** President & Chief Operating Officer Adapt Pharma/Emergent Biosolutions
Co-prescribing of Naloxone	**Dean Mariano, DO** Senior Director, Clinical Development/Medical Affairs Insys Therapeutics, Inc.
Role of Naloxone in the Opioid Overdose Public Health Crisis	**Charles E. Argoff, MD** Professor of Neurology Albany Medical College
Role of Naloxone in the Opioid Overdose Public Health Crisis	**Omar Khalil** General Manager, Neurology & Addiction kaléo, Inc.
Clarifying Questions	

FDA PRESENTATIONS

Clinical and Regulatory Overview of Naloxone Products Intended for Use in the Community	**Timothy Jiang, MD, PhD** Medical Officer DAAAP, ODE-II, OND, CDER, FDA
Drug Utilization of Naloxone	**Shekhar Mehta, PharmD, MS** Drug Utilization Analyst, Division of Epidemiology II Office of Pharmacovigilance and Epidemiology Office of Surveillance and Epidemiology (OSE) CDER, FDA
Estimates of the Annual Health System Costs of Naloxone Co-Prescribing	**Matthew Rosenberg, MSPPM** Operations Research Analyst, Economics Staff Office of Program and Strategic Analysis Office of Strategic Programs, CDER, FDA
Clarifying Questions	

BREAK

SPEAKER PRESENTATION

Candidates for Naloxone: What the Data Tell Us	**Christopher M. Jones, PharmD, MPH** CAPT, US Public Health Service Senior Advisor and Director of Strategy and Innovation National Center for Injury Prevention and Control U.S. Centers for Disease Control and Prevention (CDC)

GUEST SPEAKER PRESENTATIONS

Naloxone Dispensing via Retail Pharmacies	**Alexander Y. Walley, MD, MSc** Associate Professor of Medicine Boston University School of Medicine Director, Addiction Medicine Fellowship Boston Medical Center Medical Director Opioid Overdose Prevention Pilot Program Massachusetts Department of Public Health
Naloxone Co-prescribing	**Phillip O. Coffin, MD, MIA, FACP, FIDSA** Director of Substance Use Research San Francisco Department of Public Health Assistant Professor University of California San Francisco
Clarifying Questions	

LUNCH

SPEAKER PRESENTATION

Opioid Overdose Education and Naloxone Distribution (OEND) Within the Veterans Health Administration	**Elizabeth M. Oliva, PhD** VA National OEND Coordinator VA Program Evaluation and Resource Center VA Office of Mental Health and Suicide Prevention U.S. Department of Veterans Affairs (VA)

GUEST SPEAKER PRESENTATIONS

Take-Home Naloxone Use in New Mexico	**Joanna Girard Katzman, MD, MSPH** Senior Associate Director, ECHO (Extension for Community Healthcare Outcomes) Institute Project ECHO Professor, Neurology University of New Mexico School of Medicine, UNM Health Sciences Center
Development, Manufacturing, and Commercialization Costs for Naloxone and Other Nasal Sprays	**Daniel Wermeling, PharmD, FCCP, FASHP** Emeritus Professor University of Kentucky College of Pharmacy
Clarifying Questions	

BREAK

SPEAKER PRESENTATION

Legal Regimes: Naloxone Access	**Joy E. Gamber, PharmD, BCPP** Clinical Pharmacy Specialist, Mental Health Veterans Affairs North Texas Health Care System

GUEST SPEAKER PRESENTATIONS

Narcan Distribution Collaborative: Expanding Access in Hamilton County, Ohio and the Impacts	**Tim Ingram, MS** Health Commissioner Hamilton County Public Health
Community Naloxone Programs	**Peter Davidson, PhD** Associate Professor Department of Medicine University of California at San Diego
Clarifying Questions	

FDA PRESENTATION

Nonprescription Model Drug Facts Label Project	**Barbara R. Cohen, MPA** Social Science Analyst Division of Nonprescription Drug Products Office of Drug Evaluation IV, OND, CDER/FDA
Clarifying Questions	

ADJOURNMENT

Day 2: Tuesday, December 18, 2018

Call to Order and Introduction of Committee	**Raeford E. Brown, Jr., MD, FAAP** Chairperson, AADPAC
Conflict of Interest Statement	**Jennifer Shepherd, RPh** Acting Designated Federal Officer, AADPAC
FDA Opening Remarks: Overview of the Issues in Question	**Sharon Hertz, MD** Director, DAAAP ODE-II, OND, CDER, FDA

OPEN PUBLIC HEARING

BREAK

Charge to the Committee	**Sharon Hertz, MD**
Questions to the Committee/ Committee Discussion	

LUNCH

Questions to the Committee/
Committee Discussion

BREAK

Questions to the Committee/
Committee Discussion

ADJOURNMENT

Questions to the Committee:

1. **DISCUSSION:** Naloxone is currently available through individual prescriptions for patients from their healthcare providers (e.g., pain clinics and opioid treatment programs) and without individual prescriptions through community-based programs offering overdose education and naloxone distribution and by direct access from pharmacies under programs such as statewide naloxone standing orders or collaborative practice agreements. Discuss the comparative and collective effectiveness of these programs with regard to prevention of overdose death and their ability to get naloxone where it is most needed in communities to save lives.

   Committee Discussion*: The committees noted that the overwhelming majority of deaths occur in those using illicit opioids or prescription opioids without therapeutic purpose, and that this group, as well as patients prescribed opioids for therapeutic purpose, must be considered in order to provide the maximum public health benefit. The committees also commented that co-prescribing of naloxone with opioids could provide some benefit, but would be expensive with no model suggesting the extent of effectiveness that could be expected. One panel member discussed that education at the time of opioid prescribing may be as effective as providing a prescription for naloxone itself. Several committee members discussed that community-based programs have been very effective but lack the resources to expand their efforts. The committees expressed that, for the Agency to help maximize the impact of naloxone, assisting these community groups would seem to be the best use of scarce resources. Several committee members stated that FDA efforts should also include facilitating more rapid availability of over-the-counter (OTC) naloxone and generic naloxone products, and considering using Departmental authorities to enhance the distribution of naloxone by the federal government. Please see the transcript for details of the Committees' discussion.*

2. **DISCUSSION:** Discuss potential burdens and barriers associated with co-prescribing naloxone concurrently with opioid prescriptions for all or some patients or with targeted prescribing for individuals considered at high risk for overdose. Discuss how these burdens or barriers may affect implementation of co-prescription or targeted prescribing and what steps could be taken to mitigate these impacts.

***Committee Discussion**: The committees discussed that the major burden to co-prescribing is cost, which includes cost to the patient, the healthcare system, and secondary costs. It was noted that secondary burdens are also failure to address the larger public health issue of increasing illicit opioid deaths and the stigma of revealing a need for naloxone to a healthcare provider. The committees stated that targeting high-risk populations is a problem because it is difficult to define what constitutes a high-risk population; this approach may require a separate situational targeting model. Several committee members expressed that offering naloxone rather than co-prescribing naloxone may be more effective. The committees discussed that drug shortages may be a problem and that capacity will need to be expanded dramatically to meet the needs of any expansion in naloxone distribution; however, it was noted that this will likely not be something that industry will be able to keep up with and will require the intervention of the federal government, including FDA and other aspects of the Department of Health and Human Services (HHS). The committees also commented on the lack of parity between the branded and generic naloxone products in terms of community use and suggested updating generic labels to emphasize that they can also be used in community settings. Please see the transcript for details of the Committees' discussion.*

3. **DISCUSSION:** Because of the significant costs for patients and the health care system associated with increasing naloxone availability, prioritization of strategies will likely be needed. Discuss, in terms of available data on effectiveness and costs, which, if any, of the following approaches may be beneficial for public health:

    a. Relying on alternate approaches for increasing naloxone availability (e.g., community-based distribution programs, statewide standing orders)

    b. Limiting co-prescribing or targeted prescribing to certain populations that may potentially benefit the most from having naloxone available (i.e., those at highest risk for overdose or death due to overdose). If so, identify those populations, along with the evidence supporting this benefit**.**

***Committee Discussion**: The committees discussed many approaches for increasing naloxone availability, including identifying high-risk populations as a possibility that would reduce the amount of naloxone that was required, using the Automated External Defibrillator (AED) model to distribute naloxone geographically rather than to individuals, use of voucher programs for persons without any fixed address, and bulk purchase of IV naloxone from major distributors mainly by the federal government. The committees also discussed the possibility of FDA using its authorities to expand capacity and make OTC naloxone available in the shortest possible time. The committees noted that if changes to the market were made, consideration should be given to ensure those who need naloxone, such as community-based programs, are still able to get the drug at a reasonable cost. Please see the transcript for details of the Committees' discussion.*

4. **DISCUSSION:** Discuss any potential unintended consequences that should be considered if naloxone is co-prescribed to all or some patients prescribed opioids, and what steps can be taken to mitigate them.

Committee Discussion*: The committees discussed several unintended consequences of co-prescribing naloxone for all patients including the overall cost to the healthcare system, the specific costs for doses of naloxone and other drugs as capacity is transferred to naloxone, and the effect that these impacts could have on availability and prescribing. The committees noted that by changing the labeling, there could be changes to the standard of care, including a possible increase in liability risk to clinicians. The committees commented that some may take the position that co-prescribing naloxone may extend the perceived risk of addiction to a larger population, creating unintended consequences such as the denial of life insurance policies recently reported in the news. It was also discussed that there is a need to educate the public about the acute effects of opioid withdrawal following the administration of naloxone. Please see the transcript for details of the Committees' discussion.*

5. **VOTE:** Would labeling language that recommends co-prescription of naloxone for all or some patients prescribed opioids, or more targeted prescribing for patients otherwise at high risk for death from opioid overdose be an effective method for expanding access to naloxone and improving public health?

    a. If so, which populations do you believe should be included in such labeling?

    Vote Result: Yes: 12 No: 11 Abstain: 0

    Committee Discussion: *A slim majority of the committee voted "Yes" that labeling language that recommends co-prescription of naloxone for all or some patients prescribed opioids, or more targeted prescribing for patients otherwise at high risk for death from opioid overdose, would be an effective method for expanding access to naloxone and improving public health. Many committee members who voted "Yes" stated that while labeling may be an effective strategy to expand access to naloxone, it would not be the most effective strategy; some of these members suggested initially prioritizing efforts to expand availability of OTC and generic naloxone products. Many voting "Yes" also stated that their vote was contingent on identifying and targeting high-risk populations (e.g., high dose opioid use, concomitant benzodiazepines, history of substance use disorder, mental health disorder, or prior overdose) to maximize the public health benefit. Several committee members who voted "No" stated that changing labeling to include the recommendation of co-prescribing was not an effective or efficient way to provide naloxone to those patients who need it most. One member who voted "No" stated that not enough research has been done on the potential impacts of labeling recommendations for co-prescribing on harm reduction programs. Please see the transcript for details of the Committees' discussion.*

The meeting was adjourned at approximately 4:55 p.m. on December 17, 2018 and at approximately 3:50 p.m. on December 18, 2018.