Food and Drug Administration
Center for Drug Evaluation and Research

Final Summary Minutes of the Joint Meeting of the Drug Safety and Risk Management Advisory Committee (DSaRM) and the Anesthetic and Analgesic Drug Products Advisory Committee (AADPAC) June 11-12, 2019

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

Topic: FDA sought public input on the clinical utility and safety concerns associated with the higher range of opioid analgesic dosing (both in terms of higher strength products and higher daily doses) in the outpatient setting. FDA was interested in better understanding current clinical use and situations that may warrant use of higher doses of opioid analgesics. We were also interested in discussing the magnitude and frequency of harms associated with higher doses of opioid analgesics relative to lower doses, as well as optimal strategies for managing these risks while ensuring access to appropriate pain management for patients.

FDA frequently hears from patients and healthcare providers that higher dose opioid analgesics continue to be a unique and necessary part of effective pain management for some patients. FDA was also cognizant of serious safety concerns associated with both higher strengths and higher daily doses of opioid analgesics, both in patients and in others who may access these drugs. Higher strength products may be more harmful in cases of accidental exposure and overdose and may also be more sought out for misuse and abuse. Along with a number of other factors, a higher daily opioid dose is associated with greater risk of overdose. Concerns have also been raised that higher dose opioid regimens may carry a higher risk of addiction, although robust evidence for a causal relationship is lacking. There is a strong association between higher opioid dose and duration/persistence of opioid analgesic therapy and assessing temporal relationships and independent effects of opioid dose and duration on the risks of both addiction and overdose is challenging. In addition, FDA acknowledged the complex and evolving landscape of the opioid epidemic, with myriad Federal, State, local, and payer efforts to encourage more judicious prescribing of opioid analgesics, and the growing threat of highly lethal illicit opioids.

To better understand both the clinical utility and harms of higher dose opioid analgesics in the current environment, and to discuss the advantages and disadvantages of various potential risk management strategies, FDA brought these issues to an advisory committee to seek input and advice from the clinical, patient, public health, and research communities.

In particular, FDA sought to discuss: (1) The current clinical use and situations that may warrant pain management with opioid analgesics at higher product strengths and daily doses, factors influencing prescribing practices, and specific patient populations for whom there may be utility in prescribing these medications at higher doses; (2) the magnitude and frequency of harms associated with opioid analgesics at higher product strengths and daily doses, relative to lower strengths and daily doses, including the role of opioid dose in adverse health outcomes in both patients and in others who may access the drugs (e.g., risk for developing addiction, fatal

overdose), the relevance of therapy duration and physical opioid dependence, and risks in different subpopulations (e.g., patients with chronic non-cancer pain, young children, adolescents); and (3) possible FDA interventions and their expected impact on patients and public health more broadly, including, for example, potential effects on prescribing and pain management practices, patient experience and behaviors, and adverse outcomes such as addiction and overdose.

These summary minutes for the June 11-12, 2019 joint meeting of the Drug Safety and Risk Management (DSaRM) Advisory Committee and the Anesthetic and Analgesic Drug Products Advisory Committee (AADPAC) of the Food and Drug Administration were approved on August 1, 2019.

I certify that I attended the June 11-12, 2019 joint meeting of the Drug Safety and Risk Management Advisory Committee the Anesthetic and the Analgesic Drug Products Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/	**/s/**
Moon Hee V. Choi, PharmD	Sonia Hernandez-Diaz, MD, MPH, DrPH
Designated Federal Officer, AADPAC	Chairperson, DSaRM

Final Summary Minutes of the Joint Meeting of the Drug Safety and Risk Management Advisory Committee (DSaRM) and the Anesthetic and Analgesic Drug Products Advisory Committee (AADPAC) June 11-12, 2019

The Drug Safety and Risk Management Advisory Committee (DSaRM) and the Anesthetic and Analgesic Drug Products Advisory Committee (AADPAC) of the Food and Drug Administration, Center for Drug Evaluation and Research, met jointly on June 11-12, 2019, 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. The meeting was called to order by Sonia Hernandez-Diaz, MD, MPH, DrPH (Chairperson). The conflict of interest statement was read into the record by Moon Hee V. Choi, PharmD (Designated Federal Officer). There were approximately 120 people in attendance on June 11, 2019 and approximately 100 people in attendance on June 12, 2019. There were twelve Open Public Hearing presentations.

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

Agenda:

FDA sought public input on the clinical utility and safety concerns associated with the higher range of opioid analgesic dosing (both in terms of higher strength products and higher daily doses) in the outpatient setting. FDA was interested in better understanding current clinical use and situations that may warrant use of higher doses of opioid analgesics. We were also interested in discussing the magnitude and frequency of harms associated with higher doses of opioid analgesics relative to lower doses, as well as optimal strategies for managing these risks while ensuring access to appropriate pain management for patients.

FDA frequently hears from patients and healthcare providers that higher dose opioid analgesics continue to be a unique and necessary part of effective pain management for some patients. FDA was also cognizant of serious safety concerns associated with both higher strengths and higher daily doses of opioid analgesics, both in patients and in others who may access these drugs. Higher strength products may be more harmful in cases of accidental exposure and overdose and may also be more sought out for misuse and abuse. Along with a number of other factors, a higher daily opioid dose is associated with greater risk of overdose. Concerns have also been raised that higher dose opioid regimens may carry a higher risk of addiction, although robust evidence for a causal relationship is lacking. There is a strong association between higher opioid dose and duration/persistence of opioid analgesic therapy and assessing temporal relationships and independent effects of opioid dose and duration on the risks of both addiction and overdose is challenging. In addition, FDA acknowledged the complex and evolving landscape of the opioid epidemic, with myriad Federal, State, local, and payer efforts to encourage more judicious prescribing of opioid analgesics, and the growing threat of highly lethal illicit opioids.

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In particular, FDA sought to discuss: (1) The current clinical use and situations that may warrant pain management with opioid analgesics at higher product strengths and daily doses, factors influencing prescribing practices, and specific patient populations for whom there may be utility in prescribing these medications at higher doses; (2) the magnitude and frequency of harms associated with opioid analgesics at higher product strengths and daily doses, relative to lower strengths and daily doses, including the role of opioid dose in adverse health outcomes in both patients and in others who may access the drugs (e.g., risk for developing addiction, fatal overdose), the relevance of therapy duration and physical opioid dependence, and risks in different subpopulations (e.g., patients with chronic non-cancer pain, young children, adolescents); and (3) possible FDA interventions and their expected impact on patients and public health more broadly, including, for example, potential effects on prescribing and pain management practices, patient experience and behaviors, and adverse outcomes such as addiction and overdose.

Attendance:

Drug Safety and Risk Management Advisory Committee Members Present (Voting): Denise M. Boudreau, PhD, RPh; Marie R. Griffin, MD, MPH; Sonia Hernandez-Diaz, MD, MPH, DrPH (Chairperson); Steven B. Meisel, PharmD, CPPS; Suzanne B. Robotti (Consumer Representative); Terri L. Warholak, PhD, RPh, CPHQ, FAPhA (via phone)

Drug Safety and Risk Management Advisory Committee Member Present (Non-Voting): Linda Scarazzini, MD, RPh (Industry Representative)

Drug Safety and Risk Management Advisory Committee Members Not Present (Voting): Karim Anton Calis, PharmD, MPH, FASHP, FCCP; Laurel A. Habel, MPH, PhD; Martin Kulldorff, PhD; Anne-Michelle Ruha, MD, FACMT; Soko Setoguchi, MD, DrPh

Anesthetic and Analgesic Drug Products Advisory Committee Members Present (Voting): Basavana G. Goudra, MD, FRCA, FCARSCI; Jennifer Higgins, PhD (Consumer Representative); Maryam Jowza, MD; Ronald S. Litman, DO, ML; Maura S. McAuliffe, CRNA, MSN, MSNA, PhD, FAAN; Mary Ellen McCann, MD, MPH; Abigail B. Shoben, PhD; Michael Sprintz, DO, DFASAM; Richard D. Urman, MD, MBA; Kevin L. Zacharoff, MD, FACIP, FACPE, FAAP

Acting Industry Representative to the Anesthetic and Analgesic Drug Products Advisory Committee Present (Non-Voting): Michele Hummel PhD, RPh (Acting Industry Representative)

Anesthetic and Analgesic Drug Products Advisory Committee Member Not Present (Voting): Lonnie Zeltzer, MD

Anesthetic and Analgesic Drug Products Advisory Committee Member Not Present (Non-Voting): W. Joseph Herring, MD, PhD (Industry Representative)
Temporary Members (Voting): William C. Becker, MD; Martin Garcia-Bunuel, MD; Lee D. Hoffer, PhD, MPE; Joanna Girard Katzman, MD, MSPH; Timothy S. Lesar, PharmD; Sean Mackey, MD, PhD; Brandon DL Marshall, PhD; Christina A. Mikosz, MD, MPH, FACP; Lewis S. Nelson, MD; Joseph P. O'Brien, MBA; Kara Zivin, PhD, MS, MA

FDA Participants (Non-Voting)
Judy Staffa, PhD, RPh; Sharon Hertz, MD; Jana McAninch, MD, MPH, MS; Pamela Horn, MD; Sara Eggers, PhD

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

Open Public Hearing Speakers Present: Adriane Fugh-Berman MD (PharmedOut); Kristin McGarity; Kristen Ogden (Families for Intractable Pain Relief); Emily Walden (FED UP!); Lexi Reed Holtum (The Steve Rummler HOPE Network); Anthony J. LaGreca; April Rovero (National Coalition Against Prescription Drug Abuse); Daniel A. Busch, MD; Jane C. Ballantyne, MD, FRCA (Physicians for Responsible Opioid Prescribing); Leah Kaufman (Shatterproof); Anne Fuqua, BSN; David Egilman, MD, MPH

The agenda was as follows:

Day 1: Tuesday, June 11, 2019

Call to Order and Introduction of Committee	**Sonia Hernandez-Diaz, MD, MPH, DrPH** Chairperson, DSaRM
Conflict of Interest Statement	**Moon Hee V. Choi, PharmD** Designated Federal Officer, AADPAC
FDA Introductory Remarks	**Judy Staffa, PhD, RPh** Associated Director for Public Health Initiatives Office of Surveillance and Epidemiology (OSE) CDER, FDA
FDA PRESENTATIONS	
A Framework for Assessing the Impacts of Strategies to Manage Risks of Higher Dose and Higher Dosage Strengths Opioid Analgesic Products	**Sara Eggers, PhD** Operations Research Analyst Decision Support and Analysis Team Office of Program and Strategic Analysis Office of Strategic Programs, CDER, FDA

FDA PRESENTATIONS (CONT.)

Regulatory Background for Opioid Analgesics	**Ning Hu, MD, MS** Medical Officer Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) Office of Drug Evaluation II (ODE-II) Office of New Drugs (OND), CDER, FDA
Dispensing Patterns and Clinical Use of Higher Dose Opioid Analgesics in the U.S.	**Corinne Woods, RPh, MPH** Drug Utilization Team 4 Lead Division of Epidemiology II (DEPI-II) Office of Pharmacovigilance and Epidemiology (OPE), OSE, CDER, FDA
Review of Epidemiologic Studies of the Associations Between Higher Dose Opioid Analgesics and the Risks of Abuse, Addiction, and Overdose	**Rose Radin, PhD, MPH** Acting Team Lead, Drug Abuse Team 2 DEPI-II, OPE, OSE, CDER, FDA
Clarifying Questions	

BREAK

GUEST SPEAKER PRESENTATIONS: *Clinical Need and Risks Associated with Higher Daily Dose and Higher Dosage Strength Opioid Analgesics*

Clinician Perspectives

Dosing How Context Creates Dilemmas	**John Markman, MD** University of Rochester Professor of Neurosurgery and Neurology Director, Neuromedicine Pain Management Director, Translational Pain Research University of Rochester School of Medicine and Dentistry
Clinician and Clinical Research Perspectives on Opioid Analgesic Tolerance and Hyperalgesia	**Michael Rowbotham, MD** Chief Research Officer, Sutter Health Adjunct Professor of Anesthesia, Emeritus Professor of Neurology, UCSF

	Attending Neurologist UCSF Pain Management Center

GUEST SPEAKER PRESENTATIONS: ***Clinical Need and Risks Associated with Higher Daily Dose and Higher Dosage Strength Opioid Analgesics (cont.)***

Opioid Utilization Patterns by Home-Based Hospice Patients: A Longitudinal Review	**Mary Lynn McPherson, PharmD, MA, MDE, BCPE** Professor, Executive Director of Advanced Post-Graduate Education Executive Director, Online Master of Science and Graduate Certificates in Palliative Care Vice Chair of Teaching Development and Enhancement Department of Pharmacy Practice and Science University of Maryland School of Pharmacy Hospice and Palliative Care Consultant Pharmacist

Patient Perspectives

Chronic Pain	**Marianne Farrell**
Living "Lived Experience"	**Andrew Kiezulas**
Clarifying Questions	

LUNCH

GUEST SPEAKER PRESENTATIONS: ***Considering the Role of Opioid Dose and Dosage Strength in Abuse, Addiction, and Overdose***

Neurobiology of Addiction and the Role of Dose	**Sandra D. Comer, PhD** Professor of Neurobiology Department of Psychiatry Columbia University Irving Medical Center New York State Psychiatric Institute
Patient-Reported Pathways to Opioid Use Disorder	**Bobbi Jo Yarborough, PsyD** Investigator Kaiser Permanente Center for Health Research
Opioid Misuse and Diversion Among Chronic Substance Users: The Role of	**Hilary L. Surratt, PhD** Associate Professor

Dosage Strength, Potency, and Other Factors	University of Kentucky, College of Medicine

GUEST SPEAKER PRESENTATIONS: ***Considering the Role of Opioid Dose and Dosage Strength in Abuse, Addiction, and Overdose (cont.)***

Understanding Opioid Trajectories: Decision-Making and High Dosage Opioids	**Theodore J. Cicero, PhD** John P. Feighner Professor of Psychiatry Department of Psychiatry Washington University in St. Louis School of Medicine
Opioid-Involved Fatal Overdoses and the Role of Higher Dosage Strength Opioid Products: What We Do and Don't Know	**Bruce A. Goldberger, PhD** Division of Forensic Medicine Department of Pathology, Immunology and Lab Medicine University of Florida, College of Medicine

Clarifying Questions

BREAK

GUEST SPEAKER PRESENTATIONS: ***Efforts to Reduce High-Dose Opioid Prescribing—What Have We Learned?***

Veterans Health Experience	**Friedhelm Sandbrink, MD** National Program Director Pain Management, Veterans Health Administration
Controlled Evaluation of Group Health Opioid Risk Reduction Initiatives: 2006-2014	**Michael Von Korff, ScD** Senior Investigator Kaiser Permanente Washington Health Research Institute
Patient-Centered Opioid De-Prescribing	**Beth Darnall, PhD** Associate Professor Stanford University School of Medicine Anesthesiology, Perioperative and Pain Medicine Psychiatry and Behavioral Sciences (by courtesy) Principal Investigator, Stanford PCORI Project on Opioid and Pain Reduction (EMPOWER study)

Clarifying Questions

ADJOURNMENT

Day 2: Wednesday, June 12, 2019

Call to Order and Introduction of Committee	**Sonia Hernandez-Diaz, MD, MPH, DrPH** Chairperson, DSaRM
Conflict of Interest Statement	**Moon Hee V. Choi, PharmD** Designated Federal Officer, AADPAC
FDA Introductory Remarks	**Sharon Hertz, MD** Director DAAAP, ODE-II, OND, CDER, FDA

FDA PRESENTATION

Examples of FDA Regulatory Actions to Manage Risks Associated with Opioid Analgesics and a Framework for Evaluating Potential Impacts on Patient and Public Health	**Pamela Horn, MD** Clinical Team Leader DAAAP, ODE-II, OND, CDER, FDA

Clarifying Questions

BREAK

OPEN PUBLIC HEARING

LUNCH

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 Committees:

1. **DISCUSSION:** Discuss the role of higher daily doses and high dosage strength products of opioid analgesics in the management of pain.

    a. Discuss the settings or patient populations where there may be a clinical need for higher daily doses of opioid analgesics.

Committee Discussion: *The majority of the committee members agreed that there is a clinical need for higher range dosing of opioid analgesics. Some committee members noted the need to distinguish between first-time users and patients who are already on opioid analgesics, noting that there is no clinical indication to initiate high doses in opioid naïve patients. Committee members also discussed the importance of screening for patients who display signs of abuse or are at high risk of overdose. The majority of committee members agreed that patient populations who may require higher daily doses would be end of life, hospice or palliative care as well as those with debilitating illnesses, such as cancer and complex neurological and musculoskeletal conditions. These committee members agreed that for some patients, higher doses might reduce pain and improve mobility and quality of life. These committee members added that for some patients, when nothing else works, opioid analgesics might be the best option, and sometimes high doses may be needed. Some committee members agreed that higher daily doses are also indicated for "legacy" patients who already receive high doses of opioid analgesics, and for whom the benefits are determined to outweigh the risks in the context of a comprehensive pain management program, or for those who are in the process of tapering down to lower doses. Some committee members agreed that, for the small proportion of patients on opioid analgesics that need very high doses, primary care is not an appropriate setting and that these patients should be managed in settings with pain management expertise and also access to and expertise in addiction diagnosis and treatment. A minority of committee members stated that there is no role for very high doses of opioid analgesics, as they are not more effective than lower doses, and the benefits do not outweigh the risks (hyperalgesia, tolerance, overdose etc.). Please see the transcript for details of the committees' discussion.*

    b. Discuss the specific clinical utility of higher dosage strength opioid analgesic products, relative to lower dosage strength products.

Committee Discussion: *The majority of the committee members agreed there is a clinical need for higher dosage strength opioid analgesic products. Some stated that the availability of higher dosage strength products may help reduce the risk of diversion (i.e.., the more (low-dose) pills at home, the harder to keep track). It was further noted that the higher dosage strength could be more convenient and reduce pill burden for patients on higher daily doses, including those who have difficulty swallowing. Some committee members noted that higher dosage strength products may also help avoid issues with insurance that may limit coverage based on the number of pills dispensed. Several committee members disagreed with there being clinical utility for higher dosage*

strength products, stating their concern that a single dose of one of these could be lethal. These committee members further stated that the lower dosage strength products allow for dose adjustments using smaller increments; whereas, higher dosage strength opioid products with larger increments in available dosage strengths may lead to more dose escalation. Some committee members noted that, from a public health perspective, the increase number of deaths from overdose on higher dosage strength opioid weights more than the inconvenience from swallowing more pills. Please see the transcript for details of the committees' discussion.

2. **DISCUSSION:** Discuss the risks attributable to higher daily doses and higher dosage strength opioid analgesic products relative to lower daily doses and lower dosage strength products. In particular, discuss the differences in risks of misuse and abuse, addiction, and non-fatal or fatal overdose with high relative to lower daily doses or dose strengths.

   Include in your discussion the influence of therapy duration, physical opioid dependence, and other factors, as well as risks in different patient populations and to others who may access these drugs (e.g., young children, adolescents).

   Committee Discussion: *The majority of the committee members agreed that there are greater risks associated with higher daily doses and higher dosage strength opioid analgesic products relative to lower daily doses and lower dosage strength products. These committee members agreed that higher daily doses can increase the risk of non-fatal or fatal overdoses compared to lower daily doses. Some committee members noted that a greater proportion of patients are on lower doses, and thus the absolute number of overdoses predominantly occur in patients prescribed lower opioid analgesic doses (i.e., strategies should also pay attention to low doses). In addition, several committee members noted that for patients on higher daily doses, misuse and abuse risk may be greater with lower dosage strength opioid analgesics compared to higher dosage strength opioid analgesics due to the higher number of pills needed, because 1) it may be more difficult for patients to detect if they had already taken their dose and 2) more pills could increase the potential for diversion. Other committee members expressed concern that higher range dosing can be more dangerous if patients concomitantly use with other substances that can cause respiratory depression, such as alcohol and benzodiazepines. With regard to addiction, some committee members agreed that addiction data are difficult to interpret, as addiction is not measured well in most studies. Other committee members agreed that addiction risk may be greater with higher doses, as they increase stimulation of the brain reward system, and patients on higher doses may be more likely to develop tolerance and physical opioid dependence, particularly if therapy duration is prolonged. Some committee members expressed concerns that higher range dosing may result in additional adverse effects, such as hyperalgesia. Please see the transcript for details of the committees' discussion.*

3. **DISCUSSION:** Discuss the potential impact on patient health and public health more broadly if FDA were to take any regulatory actions that resulted in reduced prescribing, access to, and use of higher dosage strength opioid analgesic products, specifically.

Consider both positive and negative impacts on patients, healthcare delivery, and public health.

Committee Discussion: *The committee noted that negative impacts on patient health and public health if FDA were to take any regulatory actions that resulted in reduced prescribing, access to, and use of higher dosage strength opioid analgesic products might include inconvenience (e.g. more pills for patients and difficulties with insurance coverage), issues with swallowing a high number of pills, and increased potential for medication errors and diversion due to a higher volume of pills. Some committee members expressed concern about patients turning to heroin or other illicit substances if higher dosage strength opioid analgesics were restricted or no longer available. In addition, it was noted that alternatives such as compounding could have issues such as the absence of abuse deterrent technology. The main potential positive impact the committee noted was the potential to prevent some overdose cases where a single dose could be lethal. Please see the transcript for details of the committees' discussion.*

a. What currently available evidence is most compelling in predicting the impacts of taking such actions?

Committee Discussion: *Some committee members agreed that while data suggest that opioid analgesic prescribing and doses can be safely decreased in some patients, there is little evidence that this has reduced opioid overdoses. Higher quality data are needed to accurately predict impacts of potential FDA regulatory actions, as most of the available evidence is not from rigorous scientific studies, but from informed clinician and patient experiences. Please see the transcript for details of the committees' discussion.*

b. What are the most significant uncertainties (e.g., changes in prescribing behavior, rates of transition of patients to illicit drug use) in understanding the ultimate impact of such interventions on patients and public health?

Committee Discussion: *Some committee members agreed that the most significant uncertainty is whether higher daily dose or higher dosage strength products, or deprescribing of higher dose opioids, are leading to illicit opioid use and that more robust data are needed. Others stated that the issues are too complicated as to predict what one action would do. In addition, some committee members agreed that taking such actions can result in emergence of new problems that could be more severe and difficult to address than current problems. Other uncertainties noted by the committee members include the actual contribution of higher dose products to addiction and deaths, as well as other behavioral risk factors (e.g., alcohol use and previous illicit drug exposure) that are contributing to the opioid epidemic. Please see the transcript for details of the committees' discussion.*

c. What additional evidence could help address these uncertainties?

Committee Discussion: *To address these uncertainties, committee members suggested creating a registry to monitor prescribing patterns, patient use, overdose, tapering, etc. for those patients on high dosage strength opioids. Some committee members also suggested qualitative comparisons data, to compare patients who were screened vs not screened for substance use disorders or comprehensive data that stratify patients by their pain indications and clinical setting. Several committee members noted the need for a better understanding of the impact of deprescribing or tapering high doses on patient outcomes, particularly suicide. Please see the transcript for details of the committees' discussion.*

4. **DISCUSSION:** Considering the discussion on all the previous questions, discuss whether there would be value in FDA taking any new regulatory actions intended to target or reduce prescribing and use of higher dosage strength opioid analgesic products.

    a. If FDA were to consider potential new regulatory actions, how might FDA define the products that would be subject to such actions?

Committee Discussion: *Several committee members questioned the exact definition of what would be considered as "higher dosage strength opioid analgesics" in the management of pain. Some committee members recommended using the 90 morphine milligram equivalent (MME)/day threshold provided in the CDC Guideline for Prescribing Opioids for Chronic Pain, agreeing that this threshold would be consistent with the CDC guidelines, and noting that this value appears to be widely recognized and has already impacted prescribing practice. Committee members who did not support the 90 MME/day threshold noted that efforts should be focused on all doses of opioids as the use of higher dose products begins with lower dose products, and most opioid-related harms (e.g., overdoses) occur in patients on lower doses. Overall, the committee members agree that caution should be taken with any regulatory action, as it may be very destabilizing to patients who have a clinical need for higher dosage strengths, as the data show that this is a vulnerable population. Please see the transcript for details of the committees' discussion.*

    b. Discuss any other actions FDA should consider to improve the safety of higher dosage strength opioid analgesic products (i.e., actions not specifically intended to target or reduce prescribing and use).

Committee Discussion: *The recommendations made by committee members regarding other actions FDA should consider included improved communication and education for both providers and patients, as well as potential regulatory action. In terms of providing education on the potential dangers of higher dosage strength opioid analgesics, committee members suggested using simpler language, including information on medication disposal, establishing communication programs directed toward both clinicians and patients, implementing direct-to-consumer advertising from health agencies (e.g., public service announcements) vs companies, increasing awareness amongst high schoolers, and providing appropriate specialized training to medical*

school students and practitioners. In terms of regulation, committee members suggested changes to labeling and packaging, removing waivers to prescribe buprenorphine, implementing elements to assure safe use (ETASU) attached to risk evaluation and mitigation strategy (REMS) and mandating naloxone to be given with opioid medications. One committee member suggested that an anticoagulation clinic model be followed, such that the safety of opioid analgesic use can be increased while access is largely preserved. Please see the transcript for details of the committees' discussion.

The meeting was adjourned at approximately 5:22 p.m. on June 11, 2019 and at approximately 5:10 p.m. on June 12, 2019.