

**Food and Drug Administration  
Center for Drug Evaluation and Research**

**Summary Minutes of the Drug Safety and Risk Management Advisory Committee and the  
Anesthetic and Analgesic Drug Products Advisory Committee Joint Meeting  
May 3-4, 2016**

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

Topic: On May 3 and 4, 2016, the committees discussed results from assessments of the extended-release and long-acting (ER/LA) Opioid Analgesics REMS. The Agency sought the committees' comments as to whether this REMS with ETASU assures safe use, is not unduly burdensome to patient access to the drugs, and to the extent practicable, minimizes the burden to the healthcare delivery system. The ER/LA Opioid Analgesics REMS requires that prescriber training will be made available to healthcare providers who prescribe ER/LA opioid analgesics. Training is considered "REMS-compliant" if: (1) It, for training provided by continuing education providers, is offered by an accredited provider to licensed prescribers, (2) it includes all elements of the FDA Blueprint for Prescriber Education for ER/LA Opioid Analgesics (Blueprint), (3) it includes a knowledge assessment of all the sections of the Blueprint, and (4) it is subject to independent audit to confirm that conditions of the REMS training have been met. The Agency sought the committees' input on possible modifications to the ER/LA Opioid Analgesics REMS, including expansion of the scope and content of prescriber training and expansion of the REMS program to include immediate-release opioids.

These summary minutes for the May 3-4, 2016, joint meeting of the Drug Safety and Risk Management Advisory Committee and the Anesthetic and Analgesic Drug Products Advisory Committee of the Food and Drug Administration were approved on June 30, 2016.

I certify that I attended the May 3-4, 2016, joint meeting of the Drug Safety and Risk Management Advisory Committee of the Food and Drug Administration and the Anesthetic and Analgesic Drug Products Advisory Committee and that these minutes accurately reflect what transpired.

\_\_\_\_\_/s/  
Stephanie L. Begansky, PharmD  
Designated Federal Officer, AADPAC

\_\_\_\_\_/s/  
Almut Winterstein, PhD  
Chairperson, DSaRM

**Summary Minutes of the  
Joint Meeting of the Drug Safety and Risk Management Advisory Committee and the  
Anesthetic and Analgesic Drug Products Advisory Committee  
May 3-4, 2016**

The following is the final report of the joint meeting of the Drug Safety and Risk Management Advisory Committee and the Anesthetic and Analgesic Drug Products Advisory Committee, held on May 3-4, 2016. A verbatim transcript will be available in approximately six weeks, sent to the Office of Safety and Epidemiology and the Division of Analgesia, Anesthesia and Addiction Products, and posted on the FDA website at:

<http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/ucm486856.htm> and  
<http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/AnestheticAndAnalgesicDrugProductsAdvisoryCommittee/ucm486848.htm>.

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

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The Drug Safety and Risk Management Advisory Committee and the Anesthetic and Analgesic Drug Products Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research, met on May 3-4, 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 REMS Programs Companies (RPC). The meeting was called to order by Almut Winterstein, RPh, PhD, FISPE (Chairperson). The conflict of interest statement was read into the record by Stephanie Begansky, PharmD (Designated Federal Officer). There were approximately 300 people in attendance each meeting day. There were 22 Open Public Hearing (OPH) speaker presentations.

**Issue:** The Food and Drug Administration Amendments Act of 2007 ([Public Law 110-85](#)) requires FDA to bring, at least annually, one or more drugs with Risk Evaluation and Mitigation Strategies (REMS) with Elements to Assure Safe Use (ETASU) before its Drug Safety and Risk Management Advisory Committee (DSaRM). On May 3 and 4, 2016, the committees discussed results from assessments of the extended-release and long-acting (ER/LA) Opioid Analgesics REMS. The Agency sought the committees' comments as to whether this REMS with ETASU assures safe use, is not unduly burdensome to patient access to the drugs, and to the extent practicable, minimizes the burden to the healthcare delivery system. The ER/LA Opioid Analgesics REMS requires that prescriber training will be made available to healthcare providers who prescribe ER/LA opioid analgesics. Training is considered "REMS-compliant" if: (1) It, for training provided by continuing education providers, is offered by an accredited provider to licensed prescribers, (2) it includes all elements of the FDA Blueprint for Prescriber Education for ER/LA Opioid Analgesics (Blueprint), (3) it includes a knowledge assessment of all the sections of the Blueprint, and (4) it is subject to independent audit to confirm that conditions of the REMS training have been met. The Agency sought the committees' input on possible modifications to the ER/LA Opioid Analgesics REMS, including expansion of the scope and

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content of prescriber training and expansion of the REMS program to include immediate-release opioids.

**Attendance:**

**Drug Safety and Risk Management Advisory Committee Members Present (Voting):**

Niteesh K. Choudhry, MD, PhD; Tobias Gerhard, PhD, RPh; Jeanmarie Perrone, MD, FACMT; Marjorie Shaw Phillips, MS, RPh, FASHP; Linda Tyler, PharmD, FASHP; Almut G. Winterstein, RPh, PhD, FISPE (Chairperson)

**Drug Safety and Risk Management Advisory Committee Members Not Present (Voting):**

Kelly Besco, PharmD, FISMP, CPPS; Christopher H. Schmid, PhD; Andy S. Stergachis, PhD, RPh; Til Sturmer, MD, MPH, PhD

**Drug Safety and Risk Management Advisory Committee Member Present (Non-Voting):**

Linda Scarazzini, MD, RPh (Industry Representative)

**Anesthetic and Analgesic Drug Products Advisory Committee Members Present (Voting):**

Brian T. Bateman, MD, MSc; Raeford E. Brown, Jr., MD, FAAP; David S. Craig, PharmD; Charles W. Emala Sr., MS, MD; Jeffrey L. Galinkin, MD, FAAP; 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):** Rafael V. Miguel, MD

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

**Temporary Members (Voting):** Warren B. Bilker, PhD; Amy Bohnert, PhD, MHS; Chester 'Trip' Buckenmaier III, MD, COL (ret), MC, USA; James Floyd, MD, MS; Michael Fry, PharmD; Martin Garcia-Bunuel, MD; Erika Lee Hoffman, MD; Heidi Israel, PhD, FNP; Alan D. Kaye, MD, PhD; Steven H. Krasnow, MD; Mary Ellen McCann, MD; Elaine H. Morrato, DrPH, MPH, CPH; Joseph O'Brien, MBA (Patient Representative); Ruth M. Parker, MD, MACP; Trivellore Ragunathan, PhD; Paul E. Stander, MD, MBA

**FDA Participants (Non-Voting):** Doug Throckmorton, MD; Cynthia LaCivita, PharmD; Claudia Manzo, PharmD; Sharon Hertz, MD; Ellen Fields, MD; Judy Staffa, PhD, RPh

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

**Open Public Hearing Speakers:** Tracy Rupp, PharmD, MPH, RD (National Center for Health Research); Phyllis Arn Zimmer, MN, FNP, FAANP, FAAN (Nurse Practitioner Healthcare Foundation); Julian Phillips, MBA; Peter Pitts (Center for Medicine in the Public Interest); Maria Lowe (PatientsLikeMe); Shruti Kulkarni (Center for Lawful Access and Abuse Deterrence); Wendy Foster (US Pain Foundation); Sidney Wolfe (Public Citizen); Matthew Horn, MD (Rockpointe); Andrew Rosenberg (CME Coalition); Bob Twillman, PhD, FAPM (American

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Academy of Pain Management); Justine Wittenauer, MD (American Academy of Addiction Psychiatry); Anna Lembke, MD (Stanford Addiction Medicine); Anna Lembke, MD on behalf of Andrew Kolodny, MD (Phoenix House); Chris Johnson, MD (Steve Rummeler Hope Foundation); Reyn Archer, MD (Adapt Pharma); JT Fallon (New England High Intensity Drug Trafficking Task Force); Joseph Adams, MD (American Board of Addiction Medicine); Joseph Brodine (National Physician's Alliance); Dean Beals (Chronic Pain Treatment Program at Johns Hopkins); Joseph Adams, MD on behalf of Don Flattery (Virginia Governor's Task Force on Prescription Drug and Heroin Abuse); Jan Chambers (National Fibromyalgia & Chronic Pain Association).

*The agenda was as follows:*

**Day 1: Tuesday, May 3, 2016**

Call to Order and Introduction of Committees

**Almut Winterstein, MD**  
Chairperson, DSaRM

Conflict of Interest Statement

**Stephanie L. Begansky, PharmD**  
Designated Federal Officer, AADPAC

FDA Introductory Remarks

**Janet Woodcock, MD**  
Director  
CDER, FDA

**FDA PRESENTATIONS**

Development of the 2012 Extended-Release and Long-Acting (ER/LA) Opioid Analgesic REMS

**Terry Toigo, MBA, RPh**  
Associate Director for Drug Safety Operations  
CDER, FDA

Risk Evaluation and Mitigation Strategy (REMS) Authority and Extended-Release and Long-Acting (ER/LA) REMS

**Cynthia LaCivita, PharmD**  
Director, Division of Risk Management (DRISK)  
Office of Surveillance and Epidemiology (OSE)  
CDER, FDA

**NIH PRESENTATION**

Responding to the Opioid Morbidity and Mortality

**Wilson Compton, MD, MPE**  
Deputy Director  
National Institute on Drug Abuse (NIDA)  
National Institutes of Health (NIH)

Clarifying Questions

**BREAK**

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**INDUSTRY PRESENTATIONS**

Introduction/REMS Design

**REMS Programs Companies (RPC)**

**Paul M. Coplan, ScD, MBA**

Head of Medical Affairs Strategic Research  
Purdue Pharma

Adjunct Assistant Professor of Epidemiology, University of  
Pennsylvania School of Medicine

REMS Continuing Education Progress and Results

**Marsha Stanton, PhD, MS, RN**

Executive Director of Medical Affairs  
Pernix Therapeutics

Perspective of a Pain Medicine Physician and  
Educator

**Charles E. Argoff, MD**

Professor of Neurology, Albany Medical College  
Director of the Comprehensive Pain Center  
Albany Medical Center

REMS Assessment Metrics Progress and Results

**M. Soledad Cepeda, MD, PhD**

Director of Epidemiology  
Janssen Research & Development

Surveillance Data of the Public Health Impact

**Richard C. Dart, MD, PhD**

Executive Director, RADARS System  
Director, Rocky Mountain Poison and Drug Center  
Professor of Emergency Medicine,  
University of Colorado School of Medicine

Lessons Learned and Recommendations

**Laura Wallace, MPH**

Director, Risk Management & Epidemiology  
Purdue Pharma

Conclusions

**Paul M. Coplan, ScD, MBA**

Clarifying Questions

**LUNCH**

**FDA PRESENTATIONS**

Introduction to FDA Reviews of the Extended-  
Release and Long-Acting (ER/LA) Opioid  
Analgesic REMS  
36-month Assessment

**Igor Cerny, PharmD**

REMS Assessment Analyst  
DRISK, OSE, CDER, FDA

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**FDA PRESENTATIONS (CONT.)**

Extended-Release and Long-Acting (ER/LA)  
Opioid Analgesics REMS  
36 month Assessment: Review of Prescriber and  
Patient Surveys

**Shelly Harris, MPH**  
REMS Assessment Analyst  
Division of Risk Management (DRISK)  
OSE, CDER, FDA

**Catherine (Ya-Hui) Hsueh, PhD**  
Mathematical Statistician  
Division of Biometrics VII (DB-VII)  
Office of Biostatistics (OB)  
Office of Translational Sciences (OTS), CDER, FDA

Extended-Release and Long Acting (ER/LA)  
Opioid Analgesic REMS  
36 month Assessment: Review of Epidemiologic  
and Drug Utilization Surveillance Studies

**Jana McAninch, MD, MPH, MS**  
Medical Officer  
Division of Epidemiology II (DEPI-II)  
OSE, CDER, FDA

Extended-Release and Long-Acting (ER/LA)  
Opioid Analgesic REMS 36 month Assessment:  
FDA Conclusions and Considerations for Next  
Steps

**Igor Cerny, PharmD**

Clarifying Questions

**BREAK**

**ORGANIZATIONS' PRESENTATIONS**

CO\*RE: Report From the Frontlines

**Cynthia Kear**  
Senior VP, California Academy of Family Physicians  
Project Lead, Collaboration for REMS Education (CO\*RE)

ER/LA Opioid REMS Education: A Clinical  
Perspective

**Kevin Zacharoff, MD**  
Faculty, SUNY Stony Brook School of Medicine  
Medical Director, PainEDU.org

Educating Clinicians in ER/LA Opioid REMS:  
Experiences of the Conjoint Committee on  
Continuing Education

**Norman Kahn, MD**  
Executive Vice President and CEO  
Council of Medical Specialty Societies (CMSS)  
Convener, Conjoint Committee for Continuing Education

Clarifying Questions

**ADJOURNMENT**

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**Day 2: Wednesday, May 4, 2016**

Call to Order and Introduction of the Committees

**Almut Winterstein, MD**  
Chairperson, DSaRM

Conflict of Interest Statement

**Stephanie L. Begansky, PharmD**  
Designated Federal Officer, DSARM

FDA Introductory Remarks

**Cynthia LaCivita, PharmD**

**ORGANIZATIONS' PRESENTATIONS**

A Coordinated Regulatory and Educational Approach to the Public Health Crisis of Chronic Pain and Addiction

**Joanna G. Katzman, MD, MSPH**  
University of New Mexico Health Sciences Center

Promoting Best Practices and the Public Health with Accredited CE

**Graham McMahon, MD**  
President and CEO  
Accreditation Council for Continuing Medical Education (ACCME)

Clarifying Questions

**FDA PRESENTATION**

Considerations for Modifications to the ER/LA Opioid Analgesic REMS

**Doris Auth, PharmD**  
REMS Assessment Team Leader  
Division of Risk Management (DRISK)  
OSE, CDER, FDA

Clarifying Questions

**BREAK**

**OPEN PUBLIC HEARING**

**LUNCH**

Charge to the Committee

**Doris Auth, PharmD**

Questions to the Committee/Committee Discussion

**BREAK**

Questions to the Committee/Committee Discussion (cont.)

**ADJOURNMENT**

***Questions to the Committee:***

1. **DISCUSSION:** Considering the number of participants and completers in the Extended-Release (ER) and Long-Acting (LA) Opioid Analgesics Risk Evaluation and Mitigation Strategy (REMS) continuing education (CE) programs in the first 3 years of the program, please discuss:

- A. The expectations for the reach of an education program that is voluntary for prescribers, and whether the number of completers and participants is satisfactory.
- B. Whether the goal of training 80,000 prescribers of ER/LA opioid analgesics within 2 years was appropriate. If not, what is a reasonable expectation in light of the many competing programs?

*Committee Discussion: Overall, the committee agreed that the goal of training 80,000 prescribers on the ER/LA opioid analgesics was not too high but some suggested that it may have been too low. Committee members stated that this goal, along with the voluntary nature of the training, may not have addressed prescribers with the greatest need for the training. The committee also noted that the outreach and design of the training, including the structure and length, should be revised to appeal to more prescribers, especially if the training remains voluntary. There was concern expressed that science changes too rapidly to rely solely on prior training and it was stated that there is a need for continuous training on opioid issues. Some committee members indicated that opioid abuse is a national epidemic and every patient should be able to expect they will receive adequate care from a trained prescriber. Please see the transcript for details of the committee discussion.*

2. **DISCUSSION:** The effectiveness of the data sources and methodologies (e.g., surveys, surveillance, and drug utilization) used by the RPC to evaluate the impact of the ER/LA opioid analgesics REMS, particularly:

- a. The expectations for the reach of an education program that is voluntary for prescribers, and whether the number of completers and participants is satisfactory.
- b. Whether there are more effective short and long-term approaches to measure the success of the ER/LA Opioid Analgesics REMS in reducing serious outcomes resulting from inappropriate prescribing, misuse, and abuse of ER/LA opioid analgesics while maintaining patient access to pain medications.
- c. Whether the potential effects of the ER/LA Opioid Analgesics REMS on reducing abuse, misuse, addiction, overdose, and death can be differentiated from the many federal, state, local and health-system activities with similar goals.
- d. What is the anticipated length of time for an educational intervention to broadly impact prescriber knowledge and behaviors?



**Committee Discussion:** *The committee stated that the potential for the effectiveness of the educational intervention was there; however, the RPC's efforts to evaluate the intervention were disappointing. The committee was also concerned, however, that there was a false expectation that a CME program in itself will fix such a huge problem; however, they agreed that there is a continued need to evaluate the reach and impact of the program. Several committee members stated that measuring outcomes using surveys that evaluate knowledge don't appropriately evaluate the quality or effectiveness of the REMS itself on impacting appropriate prescribing. The committee suggested that there be drug utilization and patient outcomes data tied to the educational program to see how the REMS directly affects physician and patient behavior, and pre vs. post comparisons on those changes in behavior. The committee struggled with how to define appropriateness of prescribing, using only available data. It was the sense of the committee that collaboration with other agencies and even at a state level may be needed for standardizing training programs and conducting appropriate evaluations. The committee also agreed that once an effective REMS is put into place, the anticipated length of time for an educational intervention to broadly impact prescriber knowledge and behaviors, if there is a direct link to consequence, would be minimal. Please see the transcript for details of the committee discussion.*

3. **DISCUSSION:** Please discuss the impact of the ER/LA Opioid Analgesics REMS on patient access to opioid analgesics; provide examples of how best to evaluate patient access.

**Committee Discussion:** *The committee expressed that it is not known whether the ER/LA Opioid Analgesics REMS has had an impact on patient access to opioid analgesics, but likely not. One committee member stated that it is and will continue to be difficult to evaluate patient access in this area without defining appropriateness of prescribing. Please see the transcript for details of the committee discussion.*

4. **DISCUSSION:** Considering the information provided today regarding the current ER/LA Opioid Analgesics REMS, please discuss:
  - a. Whether the REMS is meeting its stated goal to reduce serious adverse outcomes resulting from inappropriate prescribing, misuse, and abuse of extended-release or long-acting (ER/LA) opioid analgesics while maintaining patient access to pain medications.
  - b. Whether the REMS assures safe use of ER/LA opioid analgesics.
  - c. Whether the REMS is unduly burdensome on patient access to ER/LA opioid analgesics.
  - d. To the extent practicable, whether the REMS is minimizing burden on the healthcare delivery system.

**Committee Discussion:** *Overall, the committee stated that it is very difficult to evaluate if the current REMS meets its goal or not because of the lack of data. The committee agreed that safe use is not assured by the REMS, as evidence by the continuing opioid abuse epidemic. The committee also stated that it is difficult to draw the line at what FDA can regulate and what falls outside of the purview of the FDA, but diversion and abuse may not ever be*

*preventable. They also stated that the current REMS is not burdensome on patient access or on the healthcare delivery system but it is important to consider the potential burden when moving forward with changes to the REMS. Please see the transcript for details of the committee discussion.*

5. **DISCUSSION:** Discuss whether the scope of the current FDA Blueprint is sufficient. If not, what should be added or deleted from the blueprint?

***Committee Discussion:** It was the general consensus of the committee that the FDA Blueprint is very important to assure that appropriate information is covered in any training. The committee also agreed that coordination of education across agencies and states must occur in order to have one clear message conveyed. The committee recommended more emphasis and guidance on appropriate and inappropriate prescribing of opioids and other treatment modalities, in the larger context of pain management. There were several committee members who commented on the structure of the FDA Blueprint and having more focus on management of pain rather than opioid prescribing itself. One panel member also stated that the Agency should consider adding a blueprint for patient education. Please see the transcript for details of the committee discussion.*

6. **DISCUSSION:** Discuss whether the current Medication Guide and Patient Counseling Document are sufficient. If not, what should be added or deleted?

***Committee Discussion:** The committee stated that they like the current Medication Guide and Patient Counseling Document as available resources; however, they expressed concern that the actual use and delivery of the medication guide was lacking. The committee proposed that the REMS include a mechanism for patients to sign indicating receipt of a medication guide from their prescriber, similar to that of a pain contract. Innovative ways for delivery of this information such as through YouTube videos or other interactive media was also discussed by the committee. Please see the transcript for details of the committee discussion.*

7. **DISCUSSION:** Discuss whether a REMS for the immediate release (IR) opioid analgesics should be required to ensure their benefits outweigh their risks.

***Committee Discussion:** The committee overwhelmingly agreed that a REMS for immediate release (IR) opioid analgesics should be required to ensure their benefits outweigh their risks. One committee member stated that the boxed warnings of IR products have already been expanded but if they don't have REMS as well, the FDA will need to answer why. Please see the transcript for details of the committee discussion.*

8. **DISCUSSION:** Discuss whether prescriber education should be required in order to prescribe an ER/LA or ER/LA and IR opioid analgesic. If so, considering any burden on the healthcare delivery system and patient access, discuss mandatory prescriber education via a restricted closed-system REMS or some other mechanisms by which education should be required ( e.g., via DEA registration and renewal process, state licensing and renewal process).

**Committee Discussion:** *The committee agreed that mandatory prescriber education should be required in order to prescribe an ER/LA or ER/LA and IR opioid analgesic. The committee stated that this mandate should be linked with something that doesn't require a secondary check, such as licensure or DEA registration. One committee member noted that prescribers are required to have continuing education in many specific areas already, such as HIPPA, and this should be no different. Another committee member suggested that though the prescriber education should be mandatory, there might be benefit to an option of allowing prescribers to test out of the requirement. Although committee members preferred that mandatory education be provided through mechanisms outside of FDA REMS authorities, if those mechanisms could not be implemented, then FDA should use its REMS authorities to require it. Please see the transcript for details of the committee discussion.*

9. **VOTE:** Considering all available information, which one of the following options do you recommend FDA pursue regarding the ER/LA Opioid Analgesics REMS?
- A. Continue without modifications
  - B. Eliminate the REMS
  - C. Modify the REMS

After the vote, please describe the rationale for your recommended option. If you vote to modify the REMS, please discuss your rationale and provide specific recommendations for how it should be modified.

**Vote:      A: 0              B: 0              C: 30**

**Committee Discussion:** *The committee unanimously voted "C", to modify the REMS. As mentioned in previous discussion questions, several committee members stated that IR opioids should be a part of the change and that the training should be mandatory. Others suggested that there be an improved content to the blueprint, and improved patient education. . One committee member stated that additional restrictive elements to the REMS should be considered. There was also suggestions to improve the evaluation of the effectiveness of the REMS. Please see the transcript for details of the committee discussion.*

10. **DISCUSSION:** If any modifications are recommended, discuss how you would assess their impact on the safe use of ER/LA opioid analgesics; include how the impact of these modifications on patient access and healthcare delivery system burden could be assessed, if these differ from your responses to questions 2 and 3.

**Committee Discussion:** *Based on the committees' discussion of question #9, there was no need to discuss question #10. Please see the transcript for details of the committee discussion.*

The meeting was adjourned at approximately 5:03 p.m. on May 3, 2016 and 5:00 p.m. on May 4, 2016.