



U.S. Food and Drug Administration

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**Summary Minutes of the  
Joint Meeting of the Anesthetic and Life Support Drugs Advisory  
Committee (ALSDAC) and the Drug Safety and Risk Management Advisory  
Committee (DSaRM)  
July 22-23, 2010  
UMUC Inn and Conference Center by Marriott  
3501 University Boulevard East, Adelphi, Maryland**

All external requests for the meeting transcript should be submitted to the CDER, Freedom of Information office. These summary minutes for the Joint Anesthetic and Life Support Drugs Advisory Committee (ALSDAC) and the Drug Safety and Risk Management Advisory Committee (DSaRM) meeting of the Food and Drug Administration were approved on August 1, 2010.

I certify that I attended the July 22-23, 2010 Joint Meeting of the Anesthetic and Life Support Drugs Advisory Committee (ALSDAC) and the Drug Safety and Risk Management Advisory Committee (DSaRM) meeting of the Food and Drug Administration and that these minutes accurately reflect what transpired.

\_\_\_\_\_/s/\_\_\_\_\_  
**Kristine Khuc, Pharm.D.**  
Designated Federal Official,  
ALSDAC

\_\_\_\_\_/s/\_\_\_\_\_  
**Jeffrey Kirsch, M.D.**  
Committee Chair,  
ALSDAC

**FOOD AND DRUG ADMINISTRATION (FDA)**  
*Center for Drug Evaluation and Research (CDER)*  
*Joint Meeting of the Anesthetic and Life Support Drugs (ALSDAC)*  
*& Drug Safety and Risk Management Advisory Committee (DSaRM)*  
July 22-23, 2010

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Summary Minutes

The Anesthetic and Life Support Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee met on July 22-23, 2010 at the Marriott Inn and Conference Center at the University of Maryland University College, 3501 University Boulevard East, Adelphi, Maryland. Prior to the meeting, the members and the invited consultants had been provided the background material from the FDA. The meeting was called to order by Jeffrey Kirsch, M.D., (Chair); the conflict of interest statement was read into the record by Kristine Khuc, Pharm.D. (Acting Designated Federal Official). There were approximately 250 persons in attendance. There were 26 speakers for the Open Public Hearing session.

**Attendance:**

**Anesthetic and Life Support Drugs Advisory Committee Members Present (Voting):**

Sorin Brull, M.D., Edward Covington, M.D., Jayant Deshpande, M.D., M.P.H., Randall Flick, M.D., M.P.H., Jeffrey Kirsch, M.D. (Chair), John Markman, M.D., Knox Todd, M.D., M.P.H.,

**Anesthetic and Life Support Drugs Advisory Committee Members Present (Non-Voting):** (Industry Representative)

Bartholomew Tortella, M.D., M.B.A.

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

Elaine Morrato, Dr.P.H., Lewis Nelson, M.D., Allen Vaida, Pharm.D., Sidney Wolfe, M.D. (Consumer Representative)

**Special Government Employee Consultants Present (Temporary Voting Members):**

Jane Ballantyne, M.D., Patrick Beardsley, Ph.D., Warren Bickel, Ph.D., Edward Boyer, M.D., Lawrence Carter, Ph.D., David Craig, Pharm.D., John Farrar, M.D., Ph.D., Roland Gray, M.D., Dorothy Hatsukami, Ph.D., Mori Krantz, M.D., Susan Krivacic (Patient Representative), Edward Michna, M.D., Mary Ellen Olbrisch, Ph.D., Carol Peairs, M.D., Gregory Terman, M.D., Ph.D., Dennis Turk, Ph.D., James Woods, Ph.D., Timothy Mark Woods, Pharm.D.

**Regular Government Employee Consultants Present (Voting):**

Ann Berger, M.D., Richard Denisco, M.D., Robert Kerns, Ph.D., Thomas Kosten, M.D., Cynthia Morris-Kukoski, Pharm.D., Linda Porter, Ph.D.

**Speakers (Non-voting):**

Robert Anderson, Ph.D., Richard Boyd, Kevin Conway, Ph.D., Rollin Gallagher, M.D., A. Thomas McLellan, Ph.D., Leonard Paulozzi, M.D., M.P.H., Nicholas Reuter, M.P.H.

**Guest Speakers (Non-voting):**

Murray Kopelow, M.D., Peter Vlases, Pharm.D., D.Sc. (Hon.)

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**FDA Participants Present (Non-Voting):**

Jane Axelrad, J.D., Gerald Dal Pan, M.D., John Jenkins, M.D., Bob Rappaport, M.D., Douglas Throckmorton, M.D.

**Open Public Hearing Presenters:**

Nathaniel Katz, M.D., Tufts University School of Medicine, Analgesic Solutions; Penney Cowan, American Chronic Pain Association; Stephen Porada, Aventine HealthSciences; Ronna Hauser, Pharm.D., National Community Pharmacists Association; Carlton Brown, R.N., Ph.D., Oncology Nursing Society; Jack Gorman, M.D., Care Management Technologies; Will Rowe, American Pain Foundation; Betts Tully; Simon Budman, Ph.D., Inflexxion, Inc.; Sydney Dy, M.D., American Society of Clinical Oncology; Theresa Grimes, MN, RN-BC, American Society for Pain Management Nursing; Sidney Schnoll, M.D., Ph.D., Pinney Associates; Art Van Zee, M.D., Stone Mountain Health Services; Cynthia Kear, CCMEP, California Academy of Family Physicians; Lynne White-Shim, M.S., D.V.M., American Veterinary Medical Association; Robin Burns-Lambert, M.D.; Philip Saigh, Jr., American Academy of Pain Medicine; Justine Coffey, J.D., LLM, American Society of Health-System Pharmacists; Kevin Nicholson, R.Ph., J.D., National Association of Chain Drug Stores; Marcie Bough, Pharm.D., American Pharmacists Association; Rosemary Orr, M.D., Seattle Children's Hospital and University of Washington; Rebecca Kirch, American Cancer Society Cancer Action Network; Jacqueline Watson, D.O., M.B.A., Federation of State Medical Boards; Mr. Mohler for Dean Hart, NanoGaurdian, a Division of NanoInk, Inc.; Fred Wells Brason II, Project Lazarus, Chronic Pain Initiative; Seddon Savage, M.D., American Pain Society

**Acting Designated Federal Official:**

Kristine Khuc, Pharm.D.

**Issue:** The joint committee met to discuss Risk Evaluation and Mitigation Strategies (REMS) for extended-release and long-acting opioid analgesics. As a part of the materials for the meeting, FDA anticipates presenting a proposal for a class-wide opioid REMS and will solicit feedback from the Advisory Committee and public on the components of that proposal. The need for adequate pain control is an element of good medical practice. In this context, some persons suffering from pain need access to potent opioid drug products; however, inappropriate prescribing, addiction and death due to prescription opioid abuse and misuse have been increasing over the last decade.

**The agenda was as follows:**

**-DAY ONE- July 22, 2010**

8:00 a.m.	Call to Order Introduction of Committee	Jeffrey Kirsch, M.D. Chair, ALSDAC
	Conflict of Interest Statement	Kristine Khuc, Pharm.D. Acting Designated Federal Official, ALSDAC
	Opening Remarks	John Jenkins, M.D. Director, Office of New Drugs CDER, FDA

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Improving Functional Outcomes in Chronic Pain: The Importance of Appropriate, Safe Opioid Analgesia	Rollin Gallagher, M.D. (Speaker) Deputy National Program Director for Pain Management Veterans Affairs Health System Philadelphia Veterans Affairs Medical Center
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Questions for Clarification

**Nature of the Problem of Prescription Opioid Misuse and Abuse**

**FDA**

Outpatient Opioid Utilization Patterns	Laura Governale, Pharm.D., M.B.A. Drug Utilization Analysis Team Leader Division of Epidemiology (DEPI) Office of Surveillance and Epidemiology (OSE) CDER, FDA
Opioid Abuse and Misuse Data From Drug Abuse Warning Network (DAWN) and National Survey on Drug Use and Health (NSDUH)	Cathy Dormitzer, Ph.D., M.P.H. Epidemiologist DEPI, OSE CDER, FDA

**NIDA**

Community Epidemiology Working Group (CEWG) & Monitoring the Future	Kevin P. Conway, Ph.D. (Speaker) Deputy Director Division of Epidemiology, Services and Prevention Research National Institute on Drug Abuse (NIDA)
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Questions for Clarification

**Summary of Efforts to Address Problem**

**FDA**

Extended-Release and Long-Acting Opioid Labeling and Risk Management	Bob Rappaport, M.D. Director Division of Anesthesia and Analgesia Products Office of Drug Evaluation II (ODE II) CDER, FDA
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FDA/CDER Education Campaigns on Misuse of Pain Relievers	Ellen Frank Director, Division of Public Affairs Office of Communications CDER, FDA
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BREAK

**SAMHSA**

SAMHSA Initiatives to Reduce Prescription Drug Abuse, Morbidity, and Mortality	Nicholas Reuter, M.P.H. (Speaker) Senior Public Health Analyst Substance Abuse and Mental Health Services Administration (SAMHSA) U.S. Public Health Service
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**DEA**

The DEA Registration Process	Richard Boyd (Speaker) Chief, Registration and Program Support Office of Diversion Control Drug Enforcement Agency (DEA)
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**ONDCP**

Public Service Program	A. Thomas McLellan, Ph.D. (Speaker) Deputy Director Office of National Drug Control Policy (ONDCP)
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Questions for Clarification

**FDA**

Requirements under Food and Drug Administration Amendments Act (FDAAA)	Jane A. Axelrad, J.D. Associate Director for Policy CDER, FDA
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Development of the Opioid REMS	Bob Rappaport, M.D.
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1. Original Proposal Letter
2. Summary of Docket –Number, Source, Themes of Comments
3. Internal Process
  - a. Timeline
  - b. Working Group Summaries
  - c. Go Away

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- d. Discussion of Differences between the Final Working Group Recommendations and the Final REMS Proposal
- e. Rationale for Final REMS and Included Products

Questions for Clarification

Lunch

**Final REMS Proposal**

Elements of the REMS	Bob A. Rappaport, M.D.
1. Medication Guide	
2. Elements to ensure safe use (ETASU) –Prescriber Training Educational Messages	

**Metrics for Evaluation**

Metrics for Opioid REMS	Mary Willy, Ph.D. Deputy Director Division of Risk Management OSE, CDER
Tracking the Opioid REMS Impact Using Prescription Drug Monitoring Program (PDMP)	Leonard Paulozzi, M.D., M.P.H. (Speaker) Division of Unintentional Injury Prevention National Center for Injury Prevention and Control Centers for Disease Control and Prevention
The Challenge of Mortality Data	Robert N. Anderson, Ph.D. (Speaker) Chief, Mortality Statistics Branch Division of Vital Statistics National Center for Health Statistics Centers for Disease Control and Prevention

**The Safe Use Initiative**

The Safe Use Initiative: Opportunities to Complement the REMS	Karen Weiss, M.D., M.P.H. Associate Director for Medical Affairs CDER, FDA
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BREAK

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**Continuing Education**

ACCME Accredited Continuing Education as a Strategic Asset To REMS	Murray Kopelow, M.D., M.S. (Guest Speaker) Chief Executive and Secretary Accreditation Council for Continuing Medical Education (ACCME)
REMS and Continuing Pharmacy Education	Peter H. Vlasses, Pharm.D., D.Sc. (Hon) (Guest Speaker) Executive Director Accreditation Council for Pharmacy Education
Questions for Clarification	

**Industry Presentations**

**INDUSTRY WORKING GROUP (IWG)**

Risk Evaluation and Mitigation Strategies (REMS) for Extended-Release and Long-Acting Opioid Products-Industry Working Group (IWG) Introduction	Martin A. Lessem, J.D. Senior Regulatory Associate Ranbaxy, Inc.
REMS Components	Eric H. Davis, M.D. Associate Director Medical Services Product Safety & Risk Management Mylan Pharmaceuticals
REMS Assessments	Paul Coplan, D.Sc. Executive Director Risk Management and Epidemiology Purdue Pharma L.P.

**COVIDIEN**

Our Experience in EXALGO Risk Management	Herbert Neuman, M.D. Vice President of Medical Affairs and Chief Medical Officer, Covidien
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Questions for Clarification

Adjourned at approximately 5:00 p.m.

**Day 2- July 23, 2010**

8:00 a.m.	Call to Order Introduction of Committee	Jeffrey Kirsch, M.D. Chair, ALSDAC
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Conflict of Interest Statement

Kristine Khuc, Pharm.D.  
Acting Designated Federal Official, ALSDAC

Open Public Hearing

BREAK

Continue Clarification Questions

Presentation of Questions for the Committee

Discussion/Vote by Committee

LUNCH

Continue Discussion/Vote by Committee

Adjourned at approximately 3:35 p.m.

Questions to the Committee:

1. Please discuss the problem of misuse and abuse of the extended-release and long-acting opioid analgesics and its impact on public health.

*The committee consensus is that there is a significant concern regarding the misuse and abuse of both extended-release (ER) and immediate-release (IR) opioid analgesics and that this problem has a huge impact on public health. The vast majority of the members wanted to see a REMS for both the ER and IR opioid analgesic products and a few suggested that a REMS for the ER products should at least be implemented as a first step followed by a REMS for the IR products. Overall, the committee agreed that a concerted public health campaign should involve prescribers, pharmacies, patients, and industry.*

(Please see transcript for a detailed discussion)

2. Please discuss the goals of the proposed REMS, the appropriateness of the REMS components to address the misuse and abuse of extended-release and long-acting opioid analgesics, and the potential burden of the proposed REMS on the healthcare system and patient access to these analgesics.

The Chair proposed that the question apply to both the ER and IR opioid analgesics based on the committee consensus that both the misuse and abuse of ER and IR opioid analgesics are a public health concern.

*The committee unanimously agreed that the goals of the REMS are appropriate, however, the individual components of the REMS are insufficient to address the misuse and abuse of ER opioid analgesics. Committee members strongly stressed the need for appropriate and adequate legislation*

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*to further the collaboration with other federal agencies since voluntary training and education efforts have not worked. Many members suggested that mandatory prescriber education and mandatory patient counseling are needed. The majority of the committee members opined that there are significant amount of expenses (financial costs) associated with the proposed REMS on the healthcare system, but, the proposed REMS is a reasonable first step. The committee members also offered suggestions of a pilot study and appropriate, realistic time assessments are needed.*

(Please see transcript for a detailed discussion)

3. **(VOTE)** Please vote on whether you agree with the Agency's proposed REMS for extended-release and long-acting opioid analgesics and discuss the rationale for your vote.

YES= 10            NO= 25            ABSTAIN= 0

*Committee members who voted "Yes" felt that the proposed REMS is a good start to capture data, despite the insufficiencies of the REMS.*

*The majority of the committee members who voted "No" commented that the REMS does not adequately address the problems. These members felt that the REMS should encompass both the ER and IR opioid analgesics. These members also commented that elements to ensure safe use need to be more robust, that pilot studies should be undertaken, and educational training programs must be mandatory.*

(Please see transcript for a detailed discussion)

4. Please discuss how we should work with sponsors to develop the necessary educational program for prescribers and patients. Include the following in your discussion:
- a. How this might be achieved to avoid the concerns that have been raised regarding the manufacturers' involvement in the development of these tools
  - b. The value of a common set of educational materials for all products versus individual product-specific material
  - c. Potential incentives to improve prescriber participation

*The Committee members suggested the following:*

- *FDA develop the content of the training/education material and utilize experts from both academia and stakeholders to assist in development;*
- *Having both a common set and an individual set of educational materials;*
- *Prescriber participation should be mandatory and no incentives are needed for prescriber participation;*
- *Need to conduct real-time audit feedback and surveillance maps*

(Please see transcript for a detailed discussion)

5. Please discuss how to assess the impact of the REMS. Include the following in your discussion:

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- a. Specific metrics that should be used and sources for data on those metrics
- b. The changes in those metrics that would constitute evidence of success for the REMS
- c. The changes in those metrics that would suggest a need to make changes to the REMS
- d. The appropriate period of follow up for initial evaluation to determine if the REMS is working
- e. How to distinguish the effects of the REMS from other efforts to address misuse and abuse of these analgesics

*Committee members commented on the following:*

- *Utilize the existing outcomes measures and existing databases;*
- *Need to determine new variables to specifically address outcomes for morbidity and mortality;*
- *Establish a new set of data to be collected in order to capture patient level data on use, storage, and perceived use;*
- *Need to establish definitions and better interpret mortality data concerning opioids and look at state level data;*
- *Appropriate follow-up of existing metrics should be done at least quarterly to yearly and newer metrics could be followed even more frequently;*
- *Prefer not to have specific registries;*
- *Measure and track pharmacy audits (including medication errors), home audits, prescriber and patient knowledge behavior, patient and community attitudes, process measures similar to the Veterans Administration (VA) system, surrogate markers such as ER visits;*
- *Utilize old drug abuse data to identify problematic drugs;*
- *Hard to distinguish the effects of the REMS from other efforts*

(Please see transcript for a detailed discussion)

Following the formal discussions and vote on the FDA questions, the Committee Chair announced that several of the members informed him that they would like to propose and vote on a "Committee Statement". The Chair read the proposed statement into the record (with the statement being projected) and a prolonged discussion regarding the wording of the statement took place. After much discussion, the Chair stated that he believed that when the members voted and discussed the questions earlier, many of the members expressed the same issues raised in the proposed statement. He further stated that because of the multiple and varied comments made regarding the statement, that with the large number of committee members involved in the meeting, it would be difficult to "word-smith" the statement so that all would be in agreement. The decision was made to not continue the discussion on the statement and the Chair stated that he did not want to vote on the statement. The meeting was adjourned without further discussion or vote.

Meeting adjourned at approximately 3:35 p.m.