

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

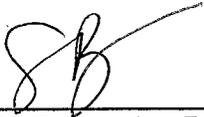
**Summary Minutes  
Anesthetic and Analgesic Drug Products Advisory Committee Meeting  
November 6, 2015**

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

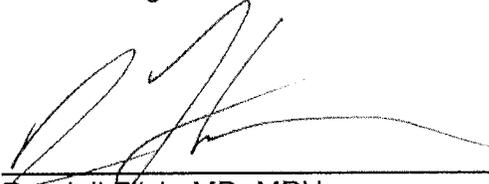
Topic: The committee will discuss new drug application (NDA) 022225, sugammadex sodium injection, submitted by Organon USA Inc., a subsidiary of Merck & Co., Inc., for the proposed indication of reversal of moderate or deep neuromuscular blockade (NMB) induced by rocuronium or vecuronium.

These summary minutes for the November 6, 2015, meeting of the Anesthetic and Analgesic Drug Products Advisory Committee of the Food and Drug Administration were approved on 12/2/2015.

I certify that I attended the November 6, 2015, meeting of the Anesthetic and Analgesic Drug Products Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.



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



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Randall Flick, MD, MPH  
*Chairperson, AADPAC*

**Summary Minutes of the  
Anesthetic and Analgesic Drug Products Advisory Committee Meeting  
November 6, 2015**

The following is final report of the Anesthetic and Analgesic Drug Products Advisory Committee meeting, held on November 6, 2015. A verbatim transcript will be available in approximately six weeks, sent to the Division of Analgesia, Anesthesia and Addiction Products and posted on the FDA website at:

<http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/AnestheticAndAnalgesicDrugProductsAdvisoryCommittee/ucm433361.htm>.

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

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The Anesthetic and Analgesic Drug Products Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research, met on November 6, 2015, 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 Randall Flick, MD, MPH (Chairperson). The conflict of interest statement was read into the record by Stephanie Begansky, PharmD (Designated Federal Officer). There were approximately 70 people in attendance on November 6, 2015. There was one Open Public Hearing (OPH) speaker.

**Issue:** The committee discussed new drug application (NDA) 022225, sugammadex sodium injection, submitted by Organon USA Inc., a subsidiary of Merck & Co., Inc., for the proposed indication of reversal of moderate or deep neuromuscular blockade (NMB) induced by rocuronium or vecuronium.

**Attendance:**

**Anesthetic and Analgesic Drug Products Advisory Committee Members Present (Voting):** Randall P. Flick, MD, MPH (Chairperson); David S. Craig, PharmD; Charles W. Emala Sr., MS, MD; Jennifer G. Higgins, PhD (Consumer Representative); Alan D. Kaye, MD, PhD; Rafael V. Miguel, MD; Abigail B. Shoben, PhD; Gary A. Walco, PhD

**Anesthetic and Analgesic Drug Products Advisory Committee Members Not Present (Voting):** Brian T. Bateman, MD, MSc; Raeford E. Brown, Jr., MD, FAAP; Jeffrey L. Galinkin, MD, FAAP

**Temporary Members (Voting):** Stanley Deden, CRNA, MBA (Patient Representative); Brian Erstad, PharmD, MCCM; Anita Gupta, DO, PharmD; Dennis R. Ownby, MD; Marjorie Shaw Phillips, MS, RPh, FASHP; Stanley J. Szeffler, MD

**Acting Industry Representative to the Committee (Non-Voting):** Michelle Hummel, PhD

**FDA Participants (Non-Voting):** Curtis J. Rosebraugh, MD, MPH; Sharon Hertz, MD; Rigoberto Roca, MD; Leah Crisafi, MD; Erika Torjusen, MD, MHS

**Open Public Hearing Speaker:** Tracy Rupp, PharmD, MPH, RD (National Center for Health Research)

*The agenda was as follows:*

Call to Order and Introduction of Committee	<b>Randall P. Flick, MD, MPH</b> Chairperson, AADPAC
Conflict of Interest Statement	<b>Stephanie L. Begansky, PharmD</b> Designated Federal Officer, AADPAC
FDA Introductory Remarks	<b>Rigoberto Roca, MD</b> Deputy Director Division of Anesthesia, Analgesia and Addiction Products (DAAAP) Office of Drug Evaluation II (ODEII) Office of New Drugs (OND), CDER, FDA
<b>APPLICANT PRESENTATIONS</b>	<b>Merck &amp; Co., Inc.</b>
Introduction and Overview	<b>David Michelson, MD</b> Vice President, Clinical Neuroscience Merck
Unmet Medical Need	<b>Glenn Murphy, MD</b> Director, Clinical Research NorthShore University Health System Clinical Professor University of Chicago Pritzker School of Medicine
Summary of Pharmacological Profile and Overview of Clinical Efficacy	<b>W. Joseph Herring, MD, PhD</b> Executive Director, Clinical Neuroscience Merck
Overview of Clinical Safety and Tolerability	<b>K. Chris Min, MD, PhD</b> Director, Translational Medicine Merck
Benefit-Risk Assessment	<b>David Michelson, MD</b>
Clarifying Questions	
<b>BREAK</b>	

## **FDA PRESENTATIONS**

Clinical Evaluation of Sugammadex:  
Efficacy and Safety

**Leah Crisafi, MD**  
Medical Officer  
DAAAP, ODEII, OND, CDER, FDA

Clinical Evaluation of Sugammadex:  
Anaphylaxis and Hypersensitivity

**Erika Torjusen, MD, MHS**  
Clinical Reviewer  
Division of Pulmonary, Allergy and Rheumatology  
Products (DPARP)  
ODEII, OND, CDER, FDA

Summary of Efficacy & Safety

**Leah Crisafi, MD**

Clarifying Questions

## **LUNCH**

Open Public Hearing

Charge to the Committee

**Rigoberto Roca, MD**

Questions to the Committee/Committee Discussion

## **BREAK**

Questions to the Committee/Committee Discussion (cont.)

## **ADJOURNMENT**

### ***Questions to the Committee:***

1. **VOTE:** Has the Applicant presented sufficient information to characterize the risk of hypersensitivity/anaphylaxis?

**Vote:      Yes = 13      No = 1      Abstain = 0**

***Committee Discussion:*** *The majority of the committee voted “Yes”, agreeing that the Applicant presented sufficient information to characterize the risk of hypersensitivity/anaphylaxis. The committee expressed concerns with the risk of hypersensitivity in vulnerable populations including pediatric, obstetric, obese, and elderly patients, and suggested further studies with regard to those populations. The committee member who voted “No” stated that there is a lack of information available to predict in which populations the hypersensitivity may occur. Please see the transcript for details of the committee discussion.*

2. **VOTE:** Has the Applicant presented sufficient information to characterize the risk of cardiac dysrhythmias?

**Vote:      Yes = 14      No = 0      Abstain = 0**

***Committee Discussion:** The committee unanimously agreed that the Applicant presented sufficient information to characterize the risk of cardiac dysrhythmias. It was stated that considerations have to be taken into context of the current practice and the role that sugammadex will play because current drugs for similar uses also have the potential to cause dysrhythmias. One committee member recommended that monitoring should be in place for potential drug interactions. Please see the transcript for details of the committee discussion.*

3. **DISCUSSION:** Are there issues not addressed in the supportive data that warrant the need for additional studies and, if so, should these studies be conducted before or after approval?

***Committee Discussion:** The committee noted that, additional studies, including but not limited to a large prospective or retrospective single or multicenter study, intended to better characterize adverse events of interest, would be helpful. The committee stated that the events of interest include coagulopathy, dysrhythmias and hypersensitivity (particularly in vulnerable populations including pediatrics, obstetrics, obese and the elderly). Committee members noted that additional studies to better elucidate the mechanism of hypersensitivity/anaphylactic reactions observed would be helpful. The committee stated that, of additional importance, is to better characterize those patients who appeared to be non-responders in studies 301 and 302. Please see the transcript for details of the committee discussion.*

4. **VOTE:** Does the efficacy, safety and overall risk-benefit profile of sugammadex support the approval of this application?

**Vote:      Yes = 14      No = 0      Abstain = 0**

***Committee Discussion:** The committee unanimously agreed that the efficacy, safety, and overall risk-benefit profile of sugammadex support the approval of this application. The committee commented that, the applicant has clearly demonstrated efficacy and though there are safety concerns, the overall benefit to risk profile is supported and does favor approval. The committee stated that the data suggest that the drug is safe in the populations in which it has been studied and that post-marketing data is imperfect but may provide further information. The committee emphasized that the labeling should reflect that specific populations may be at greater risk and this drug should be used with caution in populations which have not been studied. These specific populations might include pediatrics, obstetrics, obese, elderly, and other vulnerable populations in whom the risk-benefit profile may not be as favorable. Please see the transcript for details of the committee discussion.*

The meeting was adjourned at approximately 2:00 p.m.