

Food and Drug Administration  
Center for Drug Evaluation and Research

Summary Minutes of the  
**Meeting of the Anesthetic and Life Support Drugs Advisory Committee**

May 7, 2008  
Holiday Inn, Gaithersburg  
Two Montgomery Village Avenue, Gaithersburg, MD.

**Anesthetic and Life Support Drugs Advisory Committee Consultants (voting):**

Diane Aronson, B.S. (Acting Consumer Representative), Alan L. Buchman, M.D., Lin Chang, M.D., Michael S. Epstein, M.D., Susan Krivacic (Patient Representative), Christine Sang, M.D., M.P.H., Sulpicio de Guzman Soriano, III, M.D.

**Industry Representative (non-voting):**

Charles McLeskey, M.D.

**Anesthetic and Life Support Drugs Advisory Committee Members Absent:**

Kanwaljeet J.S. Anand, M.D., Ph.D.

**FDA Participants:**

Curtis Rosebraugh, M.D., Rigo Roca, M.D., Lex Schultheis, M.D., Ph.D., and Srikanth Nallani, Ph.D.

**Open Public Hearing Speakers:**

Atul Shah, Stanford Plavin, Kumar Belani, Momen Wahidi, David Lubarsky, Todd Baron, Philip Grossman, Michael Weinstein, Gordon Downie, Thomas Henthorn, and Julie Cantor-Weinberg

**Executive Secretary**

Teresa A. Watkins

I certify that I attended the May 7, 2008 meeting of the Drug Safety and Risk Management Advisory Committee and that these minutes accurately reflect what transpired.

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Teresa A. Watkins  
Executive Secretary, ALSDAC

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John Farrar, M.D.  
Chair, ALSDAC

## **Minutes**

### **Anesthetic and Life Support Drugs Advisory Committee Meeting May 7, 2008**

A verbatim transcript will be available in approximately four to six weeks, sent to the Division and posted on the FDA website at:

<http://www.fda.gov/ohrms/dockets/ac/cder08.html#AnestheticLifeSupport>

All external requests for the meeting transcripts should be submitted to the CDER, Freedom of Information office.

Prior to the meeting, the members and the invited consultants were provided the background material from the FDA. The meeting was called to order by John T. Farrar, M.D. (Acting Chair, ALSDAC); the conflict of interest statement was read into the record by Teresa Watkins (Designated Federal Official). There were approximately 150 persons in attendance. There were 11 speakers for the Open Public Hearing Session

#### **Attendance:**

##### **Anesthetic and Life Support Drugs Advisory Committee Members Present (voting)**

John T. Farrar, M.D., Jeffrey R. Kirsch, M.D., Nancy A. Nussmeier, M.D., and Donald S. Prough, M.D.

##### **Anesthetic and Life Support Drugs Advisory Committee Consultants (voting):**

Diane Aronson, B.S. (Acting Consumer Representative), Alan L. Buchman, M.D., Lin Chang, M.D., Michael S. Epstein, M.D., Susan Krivacic (Patient Representative), Christine Sang, M.D., M.P.H., Sulpicio de Guzman Soriano, III, M.D.

##### **Industry Representative (non-voting):**

Charles McLeskey, M.D.

##### **Anesthetic and Life Support Drugs Advisory Committee Members Absent:**

Kanwaljeet J.S. Anand, M.D., Ph.D.

##### **FDA Participants:**

Curtis Rosebraugh, M.D., Rigo Roca, M.D., Lex Schultheis, M.D., Ph.D., and Srikanth Nallani, Ph.D.

##### **Open Public Hearing Speakers:**

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**Issue:**

*The committee discussed new drug application (NDA) 22-244, fospropofol disodium injection (35 mg/mL) (proposed tradename Aquavan), MGI Pharma, Inc., for the proposed indication of sedation in adult patients undergoing diagnostic or therapeutic procedures.*

**The agenda proceeded as follows:**

Call to Order

Introduction of Committee

**John T. Farrar, M.D.**

Acting Chair, ALSDAC

Conflict of Interest Statement

**Teresa Watkins, Pharm.D., R.Ph.**

Acting Designated Federal Officer,  
ALSDAC

Opening Remarks

**Rigoberto Roca, M.D.**

Deputy Director, Division of Anesthesia,  
Analgesia, and Rheumatology Products  
CDER/FDA

Sponsor Presentations

MGI Pharma, Inc.

Introduction

**Jacqueline M. Kline, Ph.D.**

Director, Regulatory Affairs  
MGI Pharma, Inc.

Medical Need

**Lawrence B. Cohen, M.D.**

Associate Clinical Professor,  
The Mount Sinai Hospital  
New York

Clinical Pharmacology

**Stephen Waters, Ph.D.**

Vice President, Science & Technology  
MGI Pharma, Inc.

Efficacy

**Jacqueline M. Kline, Ph.D.**

Director, Regulatory Affairs  
MGI Pharma, Inc.

Safety

**Michael T. Cullen, M.D.**

Chief Medical Officer,  
MGI Pharma, Inc.

Risk/Benefit Summary

**John Leslie, M.D., M.B.A**

Professor of Anesthesiology,  
Mayo Clinic College of Medicine

Questions from the committee to MGI

Break

FDA Presentation  
FDA Perspective on the Application

**Lex Schultheis, M.D., Ph.D.**  
Medical Officer, Division of Anesthesia,  
Analgesia, and Rheumatology Products  
CDER/FDA

Questions from the committee

Lunch

Open Public Hearing

Discussion

Questions to the committee and Recommendations

**Questions to the committee:**

1. *Do the clinical data support the adequacy of using purposeful responsiveness as a clinical sign to make appropriate and safe decisions regarding supplemental dosing of fospropofol disodium?*

*-If not, which other clinical responses should be incorporated in this assessment?*

Although no formal vote was taken, it was generally felt that more than a subjective sign of purposeful responsiveness was required and should be used in conjunction with other clinical signs (e.g., vital signs, oxygen saturation, and capnography).

2. *Adverse events, particularly respiratory adverse events were observed at a greater frequency among geriatric patients, patients categorized as ASAIII or IV, and patients weighing less than 60 kg. Are additional data needed for these patient populations in order to provide appropriate dosing guidelines for these subpopulations?*

*-If additional data are needed, what studies do you recommend?*

YES = 9

NO = 1

ABSTAIN = 0

TOTAL = 10

-Many wanted to see additional efficacy and safety trials in patients with end stage renal and/or hepatic disease, in obese patients, and in those with co-morbidities (e.g., cardiovascular disease), and in geriatric patients.

-Many also wanted dose range studies in patients who weigh less than 60 kg, in those with high ASA categories and those with renal and/or hepatic disease.

-Others recommended pediatric studies.

- Others wanted to study safety and efficacy of the drug when it is used for a longer period of time (such as 12-24 hours).
- Others want to evaluate the role patient size (e.g., weight) and gender plays.
- Others want to evaluate the safety and efficacy in patients whose end tidal CO<sub>2</sub> is in the 80-90% range.

**3. Do the data from clinical trials indicate that fospropofol disodium sedation can be safely managed by health care providers without training in general anesthesia? Please vote "YES" or "NO"**

***-If you voted "NO", what types of studies would best provide this data?***

YES = 2

NO = 8

ABSTAIN = 0

TOTAL = 10

- The safety of utilizing this product in those subpopulations at greater risk of having complications or a difficult airway needs to be established in the anesthesiologist's arena prior to expanding dosing privileges to other healthcare providers.
- Others felt there needs to be standardization of the difficult airway exclusion criteria which would mandate anesthesiologist administered sedation.
- Others felt there needs to be more clarification on what training would be required for non-anesthesiologists before they could administer fospropofol.
- Others had concerns with the possibility of dose stacking if dosing protocols for dose intervals were not adhered to by non-anesthesiologists.
- Others felt there needs to be a Risk Map.
- Others felt that a proactive diversion avoidance system needed to be in place for this medication.

**4. Do you recommend approval of fospropofol for the indication of sedation in adult patients undergoing diagnostic or therapeutic procedures? Please vote "Yes" or "No".**

***-If yes, are there any additional studies you recommend to be done post approval?***

***-If no, what additional data would you recommend is needed to gain approval?***

YES = 6

NO = 3

ABSTAIN = 1

TOTAL = 10

For those who voted yes, many expressed that they want it restricted to anesthesiologist use only for now. Others who voted yes, recommended that CO<sub>2</sub> monitoring be a requirement. Others who voted yes, also want pediatric studies.

For those who voted no, many said that more data in high risk populations (e.g., patients < 60 kg, older patients, and those with co-morbidities) are needed prior to approval. For those who voted no, some expressed there is no advantage of using fospropofol over

propofol if it is only going to be used by anesthesiologists. Others expressed concerns about adherence to post-marketing study commitments.

Adjourn approximately 3:15 pm

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