Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes of the Joint Meeting of the Nonprescription Drugs Advisory Committee and the Pediatric Advisory Committee

May 17-18, 2011

Topic: The committees reviewed pertinent pharmacokinetic (how drugs are absorbed, distributed, used, and eliminated by the body), safety and efficacy data, and discussed whether new dosing information for oral over-the-counter (OTC) drug products containing acetaminophen should be added to the label for children less than 2 years of age. In addition, the committees considered adding a weight-based dosing regimen to the existing age-based dosing regimen for children 2 to 12 years of age. Dosing for children 12 years of age and older was not discussed. Lastly, the committees discussed ways that administration by caregivers can be improved so that medication errors can be minimized.

These summary minutes for the May 17-18, 2011 joint meeting of the Nonprescription Drugs Advisory Committee and the Pediatric Advisory Committee were approved on May 31, 2011.

I certify that I attended the May 17-18, 2011 joint meeting of the Nonprescription Drugs Advisory Committee and the Pediatric Advisory Committee and that these minutes accurately reflect what transpired.

_____*-signed-*_____
Diem-Kieu H. Ngo, Pharm.D., BCPS
(Designated Federal Officer)

_____*-signed-*_____
Richard Neill, M.D.
(Acting Chair)

Summary Minutes of the Joint Meeting of the Nonprescription Drugs Advisory Committee and the Pediatric Advisory Committee
May 17-18, 2011

The following is the final report of the joint meeting of the Nonprescription Drugs Advisory Committee and the Pediatric Advisory Committee held on May 17-18, 2011. A verbatim transcript will be available in approximately six weeks, sent to the Division and posted on the FDA website at http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/NonprescriptionDrugsAdvisoryCommittee/ucm246438.htm

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

The Nonprescription Drugs Advisory Committee and the Pediatric Advisory Committee of the Food and Drug Administration met jointly on May 17-18, 2011, at the Hilton Washington DC/Silver Spring, The Ballrooms, 8727 Colesville Road, Silver Spring, Maryland. Prior to the meeting, the members and temporary voting members were provided the background materials from the FDA, Consumer Healthcare Products Association (CHPA), and McNeil Consumer Healthcare. On both days, the meeting was called to order by Richard Neill, M.D. (Acting Chair) and the conflict of interest statement was read into the record by Diem-Kieu H. Ngo, Pharm.D., BCPS (Designated Federal Officer). There were approximately 150 people in attendance on May 17th and approximately 100 people in attendance on May 18th. There were four Open Public Hearing (OPH) speakers.

Issue: The committees reviewed pertinent pharmacokinetic (how drugs are absorbed, distributed, used, and eliminated by the body), safety and efficacy data, and discussed whether new dosing information for oral over-the-counter (OTC) drug products containing acetaminophen should be added to the label for children less than 2 years of age. In addition, the committees considered adding a weight-based dosing regimen to the existing age-based dosing regimen for children 2 to 12 years of age. Dosing for children 12 years of age and older was not discussed. Lastly, the committees discussed ways that administration by caregivers can be improved so that medication errors can be minimized.

Attendance:
Nonprescription Drugs Advisory Committee members present (voting): Steven C. Curry, M.D. Janet P. Engle, Pharm.D., FAPhA; Neil J. Farber, M.D., FACP; Winifred A. Landis, R.Ph., C.D.E.; Norma Martínez Rogers, Ph.D., R.N., FAAN (Consumer Representative); Leslie R. Walker-Harding, M.D. Dorraine D. Watts, Ph.D., R.N.

Nonprescription Drugs Advisory Committee members present (non-voting): Edward B. Nelson, M.D., FACP (Industry Representative)

Pediatric Advisory Committee members present (voting): Daniel A. Notterman, M.A., M.D.; Alexander T. Rakowsky, M.D.; Geoffrey L. Rosenthal, M.D., Ph.D.; Victor Santana, M.D.; Kenneth E. Towbin, M.D.; Joseph L. Wright, M.D., M.P.H.

Pediatric Advisory Committee members not present: Carl D'Angio, M.D.; Jeffrey P. Krischer, Ph.D.; Kathleen Motil, M.D., Ph.D.; Michael D. Reed, Pharm.D., FCCP, FCP; Jeffrey Wagener, M.D.

Pediatric Advisory Committee members present (non-voting): Henry Farrar, M.D. (Pediatric Health Organization Representative); Brahm Goldstein, M.D., M.C.R. (Industry Representative)

Temporary Members (voting): Amy J. Celento (Patient Representative); Susan S. Baker, M.D., Ph.D.; Michael R. Cohen, R.Ph., M.S., Sc.D.; Marie R. Griffin, M.D., M.P.H.; Richard Neill, M.D. (Acting Chair); Ruth M. Parker, M.D.; Marcus M. Reidenberg, M.D., FACP; Gary A. Walco, Ph.D., ABPP

Speaker (non-voting, presented only): Maria Suarez-Almazor, M.D., Ph.D.

FDA Participants (non-voting): M. Scott Furness, Ph.D.; Sharon Hertz, M.D.; RADM Sandra Kweder, M.D.; Dianne Murphy, M.D.

Open Public Hearing Speakers: Kevin N. Nicholson, R.Ph., J.D. (National Association of Chain Drug Stores); Mike A. Royal, M.D., J.D., M.B.A. (Cadence Pharmaceuticals, Inc.); Daniel Frattarelli, M.D., FAAP (American Academy of Pediatrics); Brian Kaplan, M.D. (Accudial Pharmaceutical, Inc.)

The agenda was as follows:

Day 1: May 17, 2011

Call to Order and Opening Remarks, Introduction of Committee	***Richard Neill, M.D.*** *Acting Chair, Nonprescription Drugs Advisory Committee*
Conflict of Interest Statement	***Diem-Kieu H. Ngo, Pharm.D., BCPS*** *Designated Federal Officer*
FDA Introductory Remarks	***M. Scott Furness, Ph.D.*** *Director* *Division of Nonprescription Regulation Development (DNRD), Office of Drug Evaluation IV (ODE-IV)* *Office of New Drugs (OND), CDER, FDA*
FDA PRESENTATION	
Regulatory History of Pediatric Acetaminophen Dosing	***Kathleen M. Phelan, R.Ph.*** *Interdisciplinary Scientist* *DNRD, ODE-IV, OND, CDER, FDA*
Review of Extrapolation: What It Is and Why We Use It	***Lisa Mathis, M.D.*** *Associate Director, Pediatric and Maternal Health Staff* *OND, CDER, FDA*
Clarifying Questions	
FDA PRESENTATION (CONT.)	
Clinical Pharmacology Findings of Acetaminophen in Pediatric Patients	***Ping Ji, Ph.D.*** *Senior Clinical Pharmacologist* *Division of Clinical Pharmacology II* *Office of Clinical Pharmacology (OCP)* *Office of Translational Sciences (OTS), CDER, FDA*
Literature Review: Efficacy and Safety of Acetaminophen in Children 6 months to 2 years of Age	***Jane Filie, M.D.*** *Medical Officer* *DNRD, ODE-IV, OND, CDER, FDA*

Clarifying Questions

BREAK

FDA PRESENTATION (CONT.)

Introduction to Office of Surveillance and Epidemiology Presentations	***Irene Z. Chan, Pharm.D., BCPS*** *Team Leader* *Division of Medication Error Prevention and Analysis (DMEPA)* *Office of Surveillance and Epidemiology (OSE)* *CDER, FDA*
Single-Ingredient Acetaminophen Utilization Patterns	***Tracy Pham, Pharm.D.*** *Drug Use Analyst* *Division of Epidemiology II (DEPI-II), OSE, CDER, FDA*
Acetaminophen-Exposure Associated Problems in Children in the U.S.: A Review of U.S. Poison Control Center Calls Data for 2002-2008	***Margie Goulding, Ph.D.*** *Epidemiologist* *DEPI-II, OSE, CDER, FDA*

Clarifying Questions

FDA PRESENTATION (CONT.)

Hospitalization Rates for Acetaminophen-Associated Poisonings in Children	***Syed Rizwanuddin Ahmad, M.D., M.P.H.*** *Medical Epidemiologist* *DEPI-II, OSE, CDER, FDA*
Acetaminophen Overdose Among Children	***Maria E. Suarez-Almazor, M.D., Ph.D.*** *Barnts Family Distinguished Professor* *University of Texas MD Anderson Cancer Center* *Houston, Texas*

Clarifying Questions

FDA PRESENTATION (CONT.)

Review of Acetaminophen Postmarketing Adverse Event Reports and Medical Literature	***Peter Waldron, M.D.*** *Medical Officer* *Division of Pharmacovigilance II, OSE, CDER, FDA*
Medication Errors Associated with Pediatric Use of Oral Acetaminophen	***Irene Z. Chan, Pharm.D., BCPS*** *Team Leader, DMEPA, OSE, CDER, FDA*

Clarifying Questions

LUNCH

INDUSTRY PRESENTATION

Introductory Remarks	***Barbara Kochanowski, Ph.D.*** *Vice President, Regulatory Affairs* *Consumer Healthcare Products Association (CHPA)*

Acetaminophen Pharmacokinetic Data in Children	***Cathy Gelotte, Ph.D.*** *Senior Director, Clinical Pharmacology* *McNeil Consumer Healthcare*
Acetaminophen Efficacy and Safety, and Weight-Based Dosing	***Ed Kuffner, M.D.*** *Vice President, Medical Affairs and Clinical Research,* *McNeil Consumer Healthcare*
Safe Use of OTC Acetaminophen in Children	***Randall Bond, M.D.*** *Director* *Cincinnati Children's Hospital Medical Center*
Industry Initiatives, Concluding Remarks	***Barbara Kochanowski, Ph.D.***
Clarifying Questions	
BREAK	
Open Public Hearing	
Adjournment	

Day 2: May 18, 2011

Call to Order and Opening Remarks *Introduction of Committee*	***Richard Neill, M.D.*** *Acting Chair* *Nonprescription Drugs Advisory Committee*
Conflict of Interest Statement	***Diem-Kieu H. Ngo, Pharm.D., BCPS*** *Designated Federal Officer*
FDA Introductory Remarks	***M. Scott Furness, Ph.D.*** *Director, DNRD, ODE-IV, OND, CDER, FDA*
Panel Discussions/Questions	
BREAK	
Panel Discussions/Questions	
Adjournment	

Questions to the Committee:

1. Should weight-based dosing directions be added to the existing age-based labeled dosing directions for children ages 2-12? YES/NO/ABSTAIN

   YES: 21 NO: 0 ABSTAIN: 0

   a. If the answer is yes, how should dosing directions be written using incremental increases in dosing based on age and weight?

Committee Discussion: *The committees unanimously agreed that weight-based dosing directions should be added to the existing age-based labeled dosing directions for children 2-12 years old. In*

summary, the committees recommended the following regarding a revised label that includes weight-based dosing directions:

- *The dosing instructions should be simple and use language that is at the lowest reading level possible and/or pictograms*
- *The dosing chart should list youngest age to oldest age group, and also include the dosing frequency*
- *The weight-based dosing chart should be listed first, then the age-based dosing chart; additionally, the label should clearly state that weight-based dosing is preferred*
- *The dosing chart should be simple with fewer dosing increments*
- *The active ingredient(s) should be listed next to or in close proximity to the dosing chart*
- *The maximum daily dose should be more prominent and clear on the label*
- *The label on the medication bottle should include the dosing chart*
- *The new label should be rigorously tested in different populations and various languages*

Please see the transcript for details of the committees' discussion.

2. Do the pharmacokinetic (PK), safety, and efficacy data support the addition of new labeled dosing directions corresponding to a 10-15 mg/kg dose for children 6 months to 2 years of age? YES/NO/ABSTAIN

   YES: 21 NO: 0 ABSTAIN: 0

   a. *Based on the discussions that transpired, question 2a was revised during the meeting to the following:* If the answer is yes, should the new labeling include an antipyretic claim? YES/NO/ABSTAIN

   YES: 21 NO: 0 ABSTAIN: 0

   b. *Based on the discussions that transpired, the following question was added during the meeting:* If the answer is yes, should the new labeling include an analgesic claim? YES/NO/ABSTAIN

   YES: 5 NO: 16 ABSTAIN: 0

   Committee Discussion: *The committees unanimously agreed that the pharmacokinetic, safety, and efficacy data support the addition of new labeled dosing directions corresponding to a 10-15 mg/kg dose for children 6 months to 2 years of age. The committees also unanimously agreed that new labeling should include an antipyretic claim. However, the majority of the committees agreed that new labeling should not include an analgesic claim because there is no substantial/conclusive evidence that acetaminophen is efficacious in relieving pain in children 6 months to 2 years of age. Please see the transcript for details of the committees' discussion.*

3. In what ways can the labeling, packaging, and the container/closure system be improved such that medication errors can be minimized?

   Committee Discussion: *In summary, the committees recommended that the following be done in order to minimize acetaminophen-related medication errors:*

   - *Packaging: use of a flow restrictor or some other system to minimize/eliminate excessive dosing*
   - *Dosing devices: dosing devices should be appropriate for the formulation and use "mL" only; markings on the device should be consistent with the recommended dosing; inclusion of the weight ranges next to the corresponding dose on the dosing device*

- *Label: simple label that clearly states the indication and active ingredient(s); use of the icon system to alert consumers to the presence of acetaminophen; addition of the weight-based dosing charts on the label; placement of the maximum daily dose and dosing frequency close to the dosing chart; use of pictorial instructions if possible*
- *Use of a safety dosing syringe in order to reduce accidental ingestion by children*
- *Inclusion of active ingredient(s) and dosing information on the medication bottle, not just on the packaging*
- *Members expressed concern about how an attached measuring device might be cleaned between administrations*
- *Members raised the issue of concerns with combination products with acetaminophen but were asked to please focus on the single ingredient product at this time and the combination product issue would be addressed subsequently*

Please see the transcript for details of the committees' discussion.

4. Restricting liquid formulations to a single concentration was a recommended intervention discussed at a recent (2009) advisory committee meeting addressing acetaminophen safety. Should the agency consider similar measures for pediatric acetaminophen-containing solid oral dosage forms? YES/NO/ABSTAIN

   YES: 17 NO: 3 ABSTAIN: 1

   Committee Discussion: *The majority of the committees felt that the Agency should consider similar measures for pediatric acetaminophen-containing solid oral dosage forms. Please see the transcript for details of the committees' discussion.*

The meeting was adjourned at approximately 5:00 p.m. on May 17th and at approximately 11:40 a.m. on May 18th.