

Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes of the Pharmacy Compounding Advisory Committee Meeting

October 27-28, 2015

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

Topic: On October 27, 2015, during the morning and afternoon sessions, the committee discussed five bulk drug substances nominated for inclusion on the section 503A bulk drug substances list. FDA intends to discuss the following nominated bulk drug substances: Methylsulfonylmethane (MSM), curcumin, germanium sesquioxide, rubidium chloride, and deoxy-D-glucose. The nominators of these substances will be invited to make a short presentation supporting the nomination

On October 28, 2015, during the morning and afternoon sessions, the committee discussed four bulk drug substances nominated for inclusion on the section 503A bulk drug substances list. FDA intends to discuss the following nominated bulk drug substances: Alanyl-L-glutamine, glutaraldehyde, glycyrrhizin, and domperidone. Other nominated substances will be discussed at future committee meetings.

These summary minutes for the October 27-28, 2015 meeting of the Pharmacy Compounding Advisory Committee of the Food and Drug Administration were approved on April 25, 2016.

I certify that I attended the October 27-28, 2015 meeting of the Pharmacy Compounding Advisory Committee and that these minutes accurately reflect what transpired.

_____/s/_____
Cindy Hong, PharmD
Designated Federal Officer
Pharmacy Compounding
Advisory Committee (PCAC)

_____/s/_____
Jürgen Venitz, MD, PhD
Chairperson, PCAC

Summary Minutes of the Meeting of the Pharmacy Compounding Advisory Committee October 27-28, 2015

The following is the final report of the Pharmacy Compounding Advisory Committee (PCAC) meeting held on October 27-28, 2015. A verbatim transcript will be available in approximately six weeks, sent to the Office of Compliance, to the Agency Lead on Pharmacy Compounding and posted on the FDA website at:

<http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/PharmacyCompoundingAdvisoryCommittee/ucm431285.htm>

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

The Pharmacy Compounding Advisory Committee (PCAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on October 27 and 28, 2015 from 10:00 a.m. until 5:30 p.m. and from 8:30 a.m. to approximately 4:45 p.m., respectively, at the FDA White Oak Campus, Building 31, the Great Room, White Oak Conference Center (Rm. 1503), Silver Spring, Maryland. Prior to the meeting, members and temporary voting members were provided copies of the briefing materials from the FDA. The meeting was called to order by Jürgen Venitz, MD, PhD (Chairperson); the conflict of interest statement was read into the record by Cindy Hong, PharmD (Acting Designated Federal Officer). There were approximately 80 persons in attendance in the audience section. There were five (5) Open Public Hearing presentations over the two days.

Issue:

On October 27, 2015, during the morning and afternoon sessions, the committee discussed five bulk drug substances nominated for inclusion on the section 503A bulk drug substances list. FDA discussed the following nominated bulk drug substances: Methylsulfonylmethane (MSM), curcumin, germanium sesquioxide, rubidium chloride, and deoxy-D-glucose.

On October 28, 2015, during the morning and afternoon sessions, the committee discussed four bulk drug substances nominated for inclusion on the section 503A bulk drug substances list. FDA discussed the following nominated bulk drug substances: Alanyl-L-glutamine, glutaraldehyde, glycyrrhizin, and domperidone. Other nominated substances will be discussed at future committee meetings.

Attendance:

PCAC Members Present (Voting):

Michael Carome, MD (Consumer Representative); Gigi Davidson, BSpH, (USP Representative); John DiGiovanna, MD; Padma Gulur, MD; William Humphrey, BSpHarm, MBA; Elizabeth Jungman, JD; Katherine Pham, PharmD; Allen Vaida, PharmD; Jürgen Venitz, MD, PhD (Chairperson); Donna Wall, PharmD (NABP Representative).

PCAC Members Present (Non-Voting): Ned Braunstein, MD and William Mixon, RPh (excluding domperidone) (Industry Representatives)

PCAC Member Not Present (Voting): October 27 and October 28: Robert DeChristoforo, MS; Stephen Hoag, PhD

Temporary Members (Voting): October 27: John Cush, MD (MSM only); Antonio Tito Fojo, MD, PhD (germanium, curcumin, deoxy-D-glucose, and rubidium only), Vincent Lo Re III, MD (deoxy-D-glucose only). October 28: Lin Chang, MD (alanyl-L-glutamine and domperidone only), Vincent Lo Re III, MD (glycyrrhizin only)

FDA Participants (Non-Voting): Jane Axelrad, JD; Frances Gail Bormel, RPh, JD; Jeffrey Murray, MD, MPH; Christine Nguyen, MD; Sandra Casak, MD; Anjelina Pokrovnichka, MD; James Flahive, JD; John Brad Pace, JD; Sau (Larry) Lee, PhD; Sanjeeve Balasubramaniam, MD, MPH; Joyce Korvick, MD, MPH; Hon Sum Ko, MD; Sarah Connelly, MD; Catherine Sewell, MD, MPH; Leslie McKinney, PhD; Anil Rajpal, MD

Acting Designated Federal Officer (Non-Voting): Cindy Hong, PharmD

Open Public Hearing Speakers:

10/27/15 p.m. session:

Bona Benjamin, MD (American Society of Health-System Pharmacists); Spencer Malkin (Vividus, LLC); David Miller, RPh (International Academy of Compounding Pharmacists)

10/28/15 a.m. and p.m. sessions: Alan Diamond, MD (Capital Digestive Care); Baxter Phillips III; Mark Birns, MD (Capital Digestive Care)

The agenda proceeded as follows:

October 27, 2015:

Call to Order and Introduction of Committee

Jürgen Venitz, MD, PhD
Chairperson, PCAC

Conflict of Interest Statement

Cindy Hong, PharmD
Acting Designated Federal Officer, PCAC

FDA INTRODUCTORY REMARKS

Jane A. Axelrad, JD
Associate Director for Policy, CDER and Agency Lead on Compounding

Clarifying Questions

FDA PRESENTATIONS

Dietary Supplements as Bulk Drug Substances

John Brad Pace, JD
Chief
Health Fraud Branch
Division of Non-Prescription Drugs & Health Fraud
Office of Unapproved Drugs and Labeling Compliance, Office of Compliance, CDER

Botanical Evaluation as Active Pharmaceutical
Ingredients

Sau (Larry) Lee, PhD
Acting Associate Director for Science
Acting Team Leader for Office of
Pharmaceutical Quality (OPQ) Botanical
Review Team, Immediate Office, OPQ, CDER

Clarifying Questions from the Committee

**SECTION 503A BULK DRUG SUBSTANCES LIST
FDA PRESENTATIONS**

Methylsulfonylmethane

Anjelina Pokrovnichka, MD
Medical Officer
Division of Anesthesia, Analgesia, and
Addiction Products (DAAAP)
Office of Drug Evaluation II (ODE II), Office
of New Drugs (OND), CDER

Clarifying Questions from the Committee

Curcumin

Sandra Casak, MD
Medical Officer
Division of Oncology Products (DOP) 2
Office of Hematology and Oncology Products
(OHOP), OND, CDER

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS

Methylsulfonylmethane

A.J. Day, PharmD
Professional Compounding Centers of
American (PCCA)

Christopher L. Gruber, PharmD
Fagron

October 27, 2015 (*Beginning of Session 2, afternoon of October 27th*)

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

**SECTION 503A BULK DRUG SUBSTANCES LIST
FDA PRESENTATIONS**

Germanium Sesquioxide

Sanjeeve Balasubramaniam, MD, MPH
Medical Officer
DOP 1, OHOP, OND, CDER

Clarifying Questions from the Committee

October 27-28, 2015
Meeting of the Pharmacy Compounding Advisory Committee

Rubidium Chloride

Sanjeeve Balasubramaniam, MD, MPH

Clarifying Questions from the Committee

Deoxy-D-Glucose

Sanjeeve Balasubramaniam, MD, MPH

Jeffrey Murray, MD

Deputy Division Director
Division of Antiviral Products (DAVP)
Office of Antimicrobial Products (OAP),
OND, CDER

Clarifying Questions from the Committee

BREAK

NOMINATOR PRESENTATIONS

Deoxy-D-Glucose

A.J. Day, PharmD
PCCA

Richard B Moon PharmD, RPh, FIACP
National Community Pharmacists Association
(NCPA)

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

ADJOURNMENT

October 28, 2015:

Call to Order and Introduction of Committee

Jürgen Venitz, MD, PhD
Chairperson, PCAC

Conflict of Interest Statement

Cindy Hong, PharmD
Acting Designated Federal Officer, PCAC

**SECTION 503A BULK DRUG SUBSTANCES LIST
FDA PRESENTATIONS**

Alanyl-L-Glutamine

Joyce Korvick, MD, MPH
Deputy Director for Safety
Division of Gastroenterology and Inborn
Errors Products (DGIEP), ODE III, OND,
CDER

Clarifying Questions from the Committee

October 27-28, 2015
Meeting of the Pharmacy Compounding Advisory Committee

Glutaraldehyde

Hon Sum Ko, MD
Medical Officer
Division of Dermatology and Dental Products
(DDDP), ODE III, OND, CDER

Clarifying Questions from the Committee

Glycyrrhizin

Sarah Connelly, MD
Medical Officer
DAVP, OAP, OND, CDER

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS

BREAK

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

LUNCH

October 28, 2015 (*Beginning of Session 2, afternoon of October 28th*)

**SECTION 503A BULK DRUG SUBSTANCES LIST
FDA PRESENTATIONS**

Domperidone

Catherine Sewell, MD, MPH
Medical Officer
Division of Bone, Reproductive and Urologic
Products (DBRUP), ODE III, OND, CDER

Leslie McKinney, PhD
Pharmacology/Toxicology Reviewer
DBRUP, ODE III, OND, CDER

Anil Rajpal, MD
Lead Medical Officer
DGIEP, ODE III, OND, CDER

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS

Domperidone

A.J. Day, PharmD
PCCA

Richard B. Moon PharmD, RPh, FIACP
NCPA

OPEN PUBLIC HEARING

BREAK

COMMITTEE DISCUSSION AND VOTE

ADJOURNMENT

Questions to the Committee:

October 27, 2015, PM Session

Questions for PCAC Regarding Whether to Include Certain Bulk Drug Substances on the 503A Bulk List:

VOTE: YES, NO, or ABSTAIN for each question

1. FDA is proposing that methylsulfonylmethane (MSM) NOT be placed on the list of bulk drug substances that can be used in pharmacy compounding in accordance with section 503A of the FD&C Act (“the 503A bulk list”). Should methylsulfonylmethane be placed on the list?

YES: 1 NO: 10 ABSTAIN: 0

Committee Discussion: Majority of the committee agreed that MSM should not be placed on the list of bulk drug substances. Members of the committee who voted “NO” commented on the lack of data on efficacy and they saw no utility of MSM as a product for any structure function claim or any medical indication for the treatment of musculoskeletal pain or arthritis. Most members noted that there were safety concerns with MSM. The one member who voted “Yes” commented that there was sufficient evidence in terms of safety and that MSM should be restricted to oral and topical use only. Please see the transcript for details of the committee discussion.

2. FDA is proposing that curcumin NOT be placed on the 503A bulk list. Should curcumin be placed on the list?

YES: 4 NO: 6 ABSTAIN: 1

Committee Discussion: A slight majority of the committee agreed that curcumin should not be placed on the 503A bulk list. Members voting “Yes” commented on the utility of curcumin for individual patients with leukoplakia and suggested making it available as an option for oral or topical use only. Members who voted “No” commented on the lack of safety/efficacy for the proposed indication and the difficulty in compounding this substance. Please see the transcript for details of the committee discussion.

3. FDA is proposing that germanium sesquioxide NOT be placed on the 503A bulk list. Should germanium sesquioxide be placed on the list?

YES: 0 NO: 11 ABSTAIN: 0

***Committee Discussion:** The committee unanimously voted against placing germanium on the 503A bulk list. All members of the committee commented on safety concerns and the lack of efficacy. Please see the transcript for details of the committee discussion.*

4. FDA is proposing that rubidium chloride NOT be placed on the 503A bulk list. Should rubidium chloride be placed on the list?

YES: 0 NO: 11 ABSTAIN: 0

***Committee Discussion:** The committee unanimously voted against placing rubidium on the 503A bulk list. All members of the committee commented on the lack of convincing safety and efficacy data. Please see the transcript for details of the committee discussion.*

5. FDA is proposing deoxy-D-glucose NOT be placed on the 503A bulk list. Should deoxy-D-glucose be placed on the list?

YES: 3 NO: 9 ABSTAIN: 0

***Committee Discussion:** Majority of the committee agreed that deoxy-D-glucose should not be placed on the 503A bulk list. The committee members voting "NO" commented on the safety concerns with intravenous use and lack of antiviral data and noted on the availability of currently available options. The members who voted "YES" commented on some antiviral efficacy and suggested restricting to topical or oral use only. Please see the transcript for details of the committee discussion.*

October 28, 2015, AM Session

Questions for PCAC Regarding Whether to Include Certain Bulk Drug Substances on the 503A Bulk List

VOTE: YES, NO, or ABSTAIN for each question

1. FDA is proposing that alanyl-L-glutamine NOT be placed on the 503A bulk list. Should alanyl-L-glutamine be placed on the list?

YES: 0 NO: 11 ABSTAIN: 0

***Committee Discussion:** The committee unanimously agreed that alanyl-L-glutamine should not be placed on the 503A bulk list. The members stated that the quality of this substance cannot be adequately assessed and also noted on the risk of contaminants. One member who had originally*

voted "YES" subsequently noted during the explanation of the vote that she meant to vote "NO". The record was corrected to reflect a unanimous vote. The vote count above records her vote as "NO." Please see the transcript for details of the committee discussion.

2. FDA is proposing that glutaraldehyde for topical use be placed on the 503A bulk list. Should glutaraldehyde for topical use be placed on the list?

YES: 9 NO: 1 ABSTAIN: 0

Committee Discussion: *The majority of the committee members agreed that glutaraldehyde for topical use should be placed on the 503A bulk list. The members voting "YES" commented on sufficient evidence of safety, as well as some clinical efficacy and supported the topical only use. Please see the transcript for details of the committee discussion.*

3. FDA is proposing that glycyrrhizin NOT be placed on the 503A bulk list. Should glycyrrhizin be placed on the list?

YES: 0 NO: 11 ABSTAIN: 0

Committee Discussion: *The committee members unanimously agreed that glycyrrhizin should not be placed on the 503A bulk list. The panel commented that the substance demonstrated no antiviral activity and poses significant hypokalemia safety risk. Please see the transcript for details of the committee discussion.*

October 28, 2015, PM Session

Questions for PCAC Regarding Whether to Include Certain Bulk Drug Substances on the 503A Bulk List

VOTE: YES, NO, or ABSTAIN for each question

1. FDA is proposing that domperidone NOT be placed on the 503A bulk list. Should domperidone be placed on the list?

YES: 3 NO: 8 ABSTAIN: 0

Committee Discussion: *The majority of the committee members agreed that domperidone should not be placed on the 503A bulk list. The members who voted "NO" commented on the strong safety signal of QTc prolongation and the availability of the drug through the Investigational New Drug process. The members voting "YES" suggested REMS or Black Box warning being attached to domperidone and acknowledged the presence of safety risks, but noted that they are found in elderly patients with comorbidities. Please see the transcript for complete details of the committee discussion.*

The meeting was adjourned at approximately 4:30 p.m. on October 27, 2015 and at 3:30 p.m. on October 28, 2015.