Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes of the Pharmacy Compounding Advisory Committee Meeting

March 8-9, 2016

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

Topic: On March 8, 2016, the committee discussed six bulk drug substances nominated for inclusion on the section 503A bulk drug substances list. FDA discussed the following nominated bulk drug substances: quinacrine hydrochloride, boswellia, aloe vera 200:1 freeze dried, D-ribose, chondroitin sulfate, and acetyl-L-carnitine.

On March 9, 2016, the committee discussed two categories of drug products nominated for the list of drug products that present demonstrable difficulties for compounding. These categories of drug products were metered dose inhalers and dry powder inhalers.

These summary minutes for the March 8-9, 2016 meeting of the Pharmacy Compounding Advisory Committee of the Food and Drug Administration were approved on ___May 2, 2016____.

I certify that I attended the March 8-9, 2016 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/_____
Padma Gulur, MD
Acting Chairperson, PCAC

Summary Minutes of Meeting of the Pharmacy Compounding Advisory Committee
March 8-9, 2016

The following is the final report of the Pharmacy Compounding Advisory Committee (PCAC) meeting held on March 8-9, 2016. 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/ucm486094.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 March 8 and 9, 2016 from 8:30 a.m. until 4:30 p.m. and from 8:30 a.m. to 1:00 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 Padma Gulur, MD (Acting Chairperson); the conflict of interest statement was read into the record by Cindy Hong, PharmD (Designated Federal Officer). There were approximately 80 persons in attendance in the audience section. There were two (2) Open Public Hearing presentations scheduled over the two days.

Issue:

On March 8, 2016, the committee discussed six bulk drug substances nominated for inclusion on the section 503A bulk drug substances list. They were: quinacrine hydrochloride, boswellia, aloe vera freeze dried 200:1, D-ribose, chondroitin sulfate, and acetyl-L-carnitine.

On March 9, 2016, the committee discussed two categories of drug products nominated for the list of drug products that present demonstrable difficulties for compounding. These categories of drug products were metered dose inhalers and dry powder inhalers.

Attendance:
PCAC Members Present (Voting):
Michael Carome, MD (Consumer Representative) (all topics except chondroitin and difficult to compound); Gigi Davidson, BSPh, (USP Representative); John DiGiovanna, MD; Padma Gulur, MD (Acting Chairperson); Stephen Hoag, PhD; William Humphrey, BSPharm, MBA; Elizabeth Jungman, JD; Katherine Pham, PharmD; Allen Vaida, PharmD; Donna Wall, PharmD (NABP Representative)

PCAC Members Present (Non-Voting): Ned Braunstein, MD (Industry Representative) (March 8th p.m. session and March 9th session); William Mixon, RPh (Industry Representative)

PCAC Member Not Present (Voting): Jürgen Venitz, MD, PhD (Chairperson)

Temporary Members (Voting): March 8: Lenore Buckley, MD, MPH (quinacrine, boswellia, D-ribose, and chondroitin only); Jeffrey Cohen, MD (acetyl-L-carnitine only via telephone)

Acting Industry Representative to the Committee (Non- Voting): Christopher Smalley, PhD, MS, MBA (March 8th a.m. session only)

FDA Participants (**Non-Voting):** Jane Axelrad, JD; Frances Gail Bormel, RPh, JD; James Flahive, JD; Shrimant Mishra, MD; Keith M. Hull, MD, PhD; Ronald Orleans, MD; Susan S. Johnson, PharmD, PhD; Janet Maynard, MD, MHS; David Kettl, MD; Shari Targum, MD; CDR Javier Muniz, MD; Kenneth Bergmann, MD; LCDR Cyrus Agarabi, PharmD, RPh, MBA, PhD; Brian Rogers, PhD; Craig M. Bertha, PhD; Khelin Eure, JD

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

Open Public Hearing Speakers:
3/8/16 a.m. session:
Victoria Werth, MD (University of Pennsylvania); Benjamin Chong, MD (University of Texas Southwestern Medical Center)

The agenda proceeded as follows:

March 8, 2016:

Call to Order and Introduction of Committee	**Padma Gulur, MD** Acting Chairperson, PCAC
Conflict of Interest Statement	**Cindy Hong, PharmD** Designated Federal Officer, PCAC
FDA INTRODUCTORY REMARKS	**Frances Gail Bormel, RPh, JD** Director (Acting) Division of Prescription Drugs Office of Unapproved Drugs and Labeling Compliance Office of Compliance, CDER
503A BULK DRUG SUBSTANCES LIST – FDA PRESENTATIONS	
Quinacrine Hydrochloride	**Shrimant Mishra, MD** Medical Officer Division of Anti-Infective Products Office of Antimicrobial Products (OAP) Office of New Drugs (OND), CDER

Quinacrine Hydrochloride (cont.)

Keith M. Hull, MD, PhD
Medical Officer
Division of Pulmonary, Allergy, and Rheumatology Products (DPARP)
Office of Drug Evaluation (ODE) II, OND, CDER

Ronald Orleans, MD
Medical Officer
Division of Bone, Reproductive, and Urologic Products (DBRUP)
ODE III, OND, CDER

Susan S. Johnson, PharmD, PhD
Associate Director
ODE IV, OND, CDER

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS

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

BREAK

503A BULK DRUG SUBSTANCES LIST – FDA PRESENTATIONS (cont.)

Boswellia

Janet Maynard, MD, MHS
Lead Medical Officer
DPARP, ODE II, OND, CDER

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS

Kimberly Kieffer
Fagron

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

LUNCH

March 8, 2016 *(Beginning of Session 2, afternoon of March 8th)*

SECTION 503A BULK DRUG SUBSTANCES LIST – FDA PRESENTATIONS

Aloe Vera Freeze Dried 200:1

David Kettl, MD
Lead Medical Officer
Division of Dermatology and Dental Products
ODE III, OND, CDER

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS

Kimberly Kieffer
Fagron

Clarifying Questions from the Committee

D-Ribose

Shari Targum, MD
Lead Medical Officer
Division of Cardiovascular and Renal Products
ODE I, OND, CDER

Janet Maynard, MD, MHS

Susan S. Johnson, PharmD, PhD

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS

Kimberly Kieffer
Fagron

Clarifying Questions from the Committee

BREAK

SECTION 503A BULK DRUG SUBSTANCES LIST – FDA PRESENTATIONS (cont.)

Chondroitin Sulfate

CDR Javier Muniz, MD
Medical Officer
Division of Anesthesia, Analgesia, and
Addiction Products, ODE II, OND, CDER

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS

Clarifying Questions from the Committee

Acetyl-L-Carnitine

Kenneth Bergmann, MD
Medical Officer, Division of Neurology
Products
ODE I, OND, CDER

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS	**A.J. Day, PharmD** PCCA

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

ADJOURNMENT

March 9, 2016

Call to Order and Introduction of Committee	**Padma Gulur, MD** Acting Chairperson, PCAC
Conflict of Interest Statement	**Cindy Hong, PharmD** Designated Federal Officer, PCAC
FDA PRESENTATIONS- INTRODUCTION OF DEMONSTRABLY DIFFICULT TO COMPOUND AND REVIEW OF CRITERIA	**LCDR Cyrus Agarabi, PharmD, RPh, MBA, PhD** Senior Regulatory Research Review Officer Division of Biotechnology Review and Research II, Office of Pharmaceutical Quality (OPQ), CDER

DEMONSTRABLY DIFFICULT TO COMPOUND – FDA PRESENTATIONS

Metered Dose Inhalers	**Brian Rogers, PhD** Chemistry, Manufacturing, and Controls (CMC) Reviewer Process Assessment Branch IV Division of Process Assessment II Office of Process and Facilities OPQ, CDER

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS

Clarifying Questions from the Committee

BREAK

DEMONSTRABLY DIFFICULT TO COMPOUND – FDA PRESENTATIONS (cont.)

Dry Powder Inhalers	**Craig M. Bertha, PhD** CMC Lead New Drug Products Branch IV

Division of New Drug Products II
Office of New Drug Products, OPQ, CDER

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

ADJOURNMENT

Questions to the Committee:

March 8, 2016, a.m. 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 quinacrine hydrochloride 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 quinacrine hydrochloride be placed on the list?

YES: 5 NO: 6 ABSTAIN: 0

Committee Discussion: *A slight majority of the committee agreed that quinacrine should not be placed on the list of bulk drug substances. Members of the committee who voted "NO" commented that although there is evidence of efficacy for lupus, this drug would be best used with more oversight or under the Investigational New Drug (IND) process due to its safety profile and the difficulty with placing limitations on the bulk list. The members who voted "YES" commented that there is evidence of efficacy and safety and could be safely used with patient education by the practitioner and pharmacist. The committee also expressed concerns with the IND program and commented that it is not an ideal way to treat patients. Please see the transcript for details of the committee discussion.*

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

YES: 0 NO: 11 ABSTAIN: 0

Committee Discussion: *The committee unanimously agreed that boswellia should not be placed on the 503A bulk list. Members commented on the variability in composition and quality, limited*

efficacy data, drug interactions, and multiple alternatives available. Please see the transcript for details of the committee discussion.

March 8, 2016, p.m. 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 Aloe Vera freeze dried 200:1 NOT be placed on the 503A bulk list. Should Aloe Vera freeze dried 200:1 be placed on the list?

YES: 1 NO: 9 ABSTAIN: 0

Committee Discussion: *The majority of the committee agreed that Aloe Vera freeze dried 200:1 should not be placed on the list. The one member who voted "YES" commented that there is a use for aloe vera and the risk is very minimal. The members voting "NO" commented on the lack of data in humans, difficulty in obtaining consistency in the products, lack of characterization, and lack of evidence for efficacy. Please see the transcript for details of the committee discussion.*

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

YES: 1 NO: 10 ABSTAIN: 0

Committee Discussion: *The majority of the committee agreed that D-ribose should not be placed on the list. The one member who voted "YES" commented that the product would not have negative effects when used by chronic fatigue patients. The members voting "NO" commented on the lack of efficacy data for the proposed uses. Please see the transcript for details of the committee discussion.*

3. FDA is proposing that chondroitin sulfate for topical use NOT be placed on the 503A bulk list. Should chondroitin sulfate be placed on the list?

YES: 0 NO: 10 ABSTAIN: 0

Committee Discussion: *The committee unanimously agreed that chondroitin sulfate should not be placed on the list. They commented on the lack of efficacy data, unlikeliness of the compound to be absorbed topically, and the availability of alternatives on the market. Please see the transcript for details of the committee discussion.*

4. FDA is proposing that acetyl-L-carnitine NOT be placed on the 503A bulk list. Should acetyl-L-carnitine be placed on the list?

YES: 1 NO: 10 ABSTAIN: 0

Committee Discussion: *The majority of the committee agreed that acetyl-L-carnitine should not be placed on the list. The one member who voted "YES" commented on the potential use for some patients with chronic pain, peripheral pain, and HIV. The members voting "NO" commented on the lack of evidence of efficacy and similar toxicity profile compared to the already available L-carnitine. Please see the transcript for details of the committee discussion.*

March 9, 2016
Questions for PCAC Regarding Whether to Include Two Categories of Drug Products on the Demonstrable Difficult to Compound List

VOTE: YES, NO, or ABSTAIN for each question

1. FDA is proposing that metered dose inhalers (MDIs) be placed on the list of drug products that present demonstrable difficulties for compounding in accordance with sections 503A and 503B of the FD&C Act ("the difficult to compound list"). Should metered dose inhalers be placed on the list?

YES: 9 NO: 0 ABSTAIN: 0

Committee Discussion: *The committee unanimously agreed that metered dose inhalers be placed on the list of drug products that present demonstrable difficulties for compounding in accordance with sections 503A and 503B of the FD&C Act. The members commented on the complexities of MDIs and agreed with FDA's assessment of MDI's. Please see the transcript for details of the committee discussion.*

2. FDA is proposing that dry powder inhalers be placed on the difficult to compound list. Should dry powder inhalers be placed on the list?

YES: 9 NO: 0 ABSTAIN: 0

Committee Discussion: *The committee unanimously agreed that dry powder inhalers be placed on the difficult to compound list and agreed with FDA's assessment. There were also comments that dosage forms to be delivered by dry powder inhalers should also not be compounded. Please see the transcript for details of the committee discussion.*

The meeting was adjourned at approximately 4:15 p.m. on March 8, 2016 and at 10:00 a.m. on March 9, 2016.