Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes of the Pharmacy Compounding Advisory Committee Meeting

May 8-9, 2017

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

Topic: On May 8-9, 2017, the committee received updates on certain issues to follow up on discussions from previous meetings, including quality standards and conditions at certain compounding facilities. In addition, the committee discussed the following nominated bulk drug substances: nicotinamide adenine dinucleotide (NAD,) nicotinamide adenine dinucleotide disodium reduced (NADH,) nettle (Urtica dioica) whole plant, ubiquinol, vanadyl sulfate, and artemisinin. The nominators of these substances were invited to make a short presentation supporting the nomination. The committee also discussed oral solid modified release drug products that employ coated systems (MRC), which were nominated for the Difficult to Compound (DTC) List. The nominators were invited to make a short presentation supporting the nomination.

These summary minutes for the May 8-9, 2017 meeting of the Pharmacy Compounding Advisory Committee of the Food and Drug Administration were approved on ____6/26/17_____.

I certify that I attended the May 8-9, 2017 meeting of the Pharmacy Compounding Advisory Committee and that these minutes accurately reflect what transpired.

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

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

Summary Minutes of the Pharmacy Compounding Advisory Committee Meeting
May 8-9, 2017

The following is a final report of the Pharmacy Compounding Advisory Committee (PCAC) meeting held on May 8-9, 2017. 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:

https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/PharmacyCompoundingAdvisoryCommittee/ucm553328.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 May 8-9, 2017 from 8:30 a.m. until 4:30 p.m. on May 8th and 8:30 a.m. until 12:00 p.m. on May 9th, at the FDA White Oak Campus, Building 31 Conference Center, The Great Room (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) Chee, PharmD (Designated Federal Officer). There were approximately 40 persons in attendance in the audience section. There were six (6) Open Public Hearing presentations.

Issue:
On May 8-9, 2017, the committee received updates on certain issues to follow up on discussions from previous meetings, including quality standards and conditions at certain compounding facilities. In addition, the committee discussed the following nominated bulk drug substances: nicotinamide adenine dinucleotide (NAD,) nicotinamide adenine dinucleotide disodium reduced (NADH,) nettle (Urtica dioica) whole plant, ubiquinol, vanadyl sulfate, and artemisinin. The nominators of these substances were invited to make a short presentation supporting the nomination. The committee also discussed oral solid modified release drug products that employ coated systems (MRC), which were nominated for the Difficult to Compound (DTC) List. The nominators were invited to make a short presentation supporting the nomination.

Attendance:
PCAC Members Present (Voting):
Michael Carome, MD, FACP (Consumer Representative) (all topics except DTC); Gigi Davidson, BSPh, DICVP (US Pharmacopeial Convention Representative); John DiGiovanna, MD; Padma Gulur, MD (May 8th); Stephen Hoag, PhD (May 8th- all topics except nicotinamide adenine dinucleotide); William Humphrey, BSPharm, MBA, MS (May 9th-via phone); Katherine Pham, PharmD, BCPS; Jürgen Venitz, MD, PhD (Chairperson); Donna Wall, PharmD (National Association of Boards of Pharmacy Representative)

PCAC Members Present (Non-Voting): Ned Braunstein, MD (Industry Representative)

PCAC Members Not Present (Voting): Padma Gulur, MD (May 9th); Stephen Hoag, PhD (May 9th); William Humphrey, BSPharm, MBA, MS (May 8th); Allen Vaida, BSc, PharmD, FASHP

PCAC Members Not Present (Non-Voting): William Mixon, RPh, MS, FIACP (Industry Representative)

Temporary Members (Voting): Robert J. Smith, MD (nettle, ubiquinol, vanadyl sulfate topics only) Elizabeth Unger, MD, PhD (NAD and NADH topics only); Peter Weina, MD, PhD, FACP, FIDSA (artemisinin topic only)

FDA Participants (**Non-Voting):** Muhammad Ashraf, PhD; Frances Gail Bormel, RPh, JD; Yen-Ming Chan, PhD; Julie Dohm, JD, PhD; Charles Ganley, MD; Michael Ghobrial, PharmD, JD; Wafa Harrouk, PhD; Susan Johnson, PharmD, PhD; Corrine Kulick, PharmD; Rosilend Lawson, VMD, JD; Bindi Nikhar, MD, FAAP; Jennifer Shiang, PhD; Ahmed Zidan, PhD

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

Open Public Hearing Speakers:
May 8th: Doreen D'Agostino; Col. Jeffery Johnson (Ret.), RPh, MBA, ND, PharmD (Medisca Inc.); Ronna Hauser, PharmD (National Community Pharmacists Association)
May 9th: Col. Jeffery Johnson (Ret.), RPh, MBA, ND, PharmD (Medisca Inc.)

The agenda proceeded as follows:

May 8, 2017 a.m. session:

Call to Order and Introduction of Committee	**Jürgen Venitz, MD, PhD** Chairperson, PCAC
Conflict of Interest Statement	**Cindy (Hong) Chee, PharmD** Designated Federal Officer, PCAC
FDA INTRODUCTORY REMARKS	**Julie Dohm, JD, PhD** Senior Science Advisor for Compounding, CDER Agency Lead on Compounding, FDA
FDA PRESENTATION	
Compounders Under Section 503A of the FD&C Act: Quality Standards and FDA Findings	**Sarah Rothman, MPH** Senior Policy Advisor Office of Unapproved Drugs and Labeling Compliance
Clarifying Questions from the Committee	

SECTION 503A BULK DRUG SUBSTANCES LIST – FDA PRESENTATIONS

Nicotinamide Adenine Dinucleotide

Yen-Ming Chan, PhD
ORISE Fellow
Office of Drug Evaluation (ODE) IV
Office of New Drugs (OND)

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS

John Humiston, MD
Fagron

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

BREAK

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

Nicotinamide Adenine Dinucleotide Disodium Reduced

Corrine Kulick, PharmD
Clinical Analyst (Detail)
ODE IV, OND

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS

Tom Wynn, RPh
Fagron

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

LUNCH

May 8, 2017 p.m. session

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

Nettle

Jennifer Shiang, PhD
ORISE Fellow
ODE IV, OND

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

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

Ubiquinol — **Susan Johnson, PharmD, PhD**
Associate Director
ODE IV, OND

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS — **Tom Wynn, RPh**
Fagron

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

BREAK

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

Vanadyl Sulfate — **Susan Johnson, PharmD, PhD**

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

ADJOURNMENT

May 9, 2017 a.m. session

Call to Order and Introduction of Committee — **Jürgen Venitz, MD, PhD**
Chairperson, PCAC

Conflict of Interest Statement — **Cindy (Hong) Chee, PharmD**
Designated Federal Officer, PCAC

SECTION 503A BULK DRUG SUBSTANCES LIST – FDA PRESENTATIONS

Artemisinin — **Wafa Harrouk, PhD**
Bindi Nikhar, MD, FAAP
ODE IV, OND

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

BREAK

DEMONSTRABLY DIFFICULT TO COMPOUND LIST— FDA PRESENTATION

Oral Solid Modified Release Drug Products that Employ Coated Systems — **Muhammad Ashraf, PhD**
Office of Testing and Research
Office of Pharmaceutical Quality

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

ADJOURNMENT

Questions to the Committee:

May 8, 2017, a.m. session

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

1. FDA is proposing that nicotinamide adenine dinucleotide NOT be included on the 503A Bulks List. Should nicotinamide adenine dinucleotide be placed on the list?

   YES: 1 NO: 7 ABSTAIN: 0

Committee Discussion: *The majority of the committee agreed that NAD should not be included on the 503A Bulks List. Members commented on the need for clinical trials and the ambiguity in its efficacy when given with other supplements and the fact that NAD is not stable under ordinary storage conditions. The one member who voted "YES" commented about the efficacy seen in chronic fatigue patients and its safety. Please see the transcript for details of the committee discussion.*

2. FDA is proposing that nicotinamide adenine dinucleotide disodium reduced NOT be included on the 503A Bulks List. Should nicotinamide adenine dinucleotide disodium reduced be placed on the list?

   YES: 0 NO: 9 ABSTAIN: 0

   Committee Discussion: *The committee unanimously agreed that NADH should not be included on the 503A list. The panel expressed concerns with the stability, formulation, delivery of the drug substance, and potential safety issues. Please see the transcript for details of the committee discussion.*

May 8, 2017, p.m. session

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

1. FDA is proposing that nettle NOT be included on the 503A Bulks List. Should nettle be placed on the list?

   YES: 0 NO: 9 ABSTAIN: 0

   Committee Discussion: *The committee unanimously agreed that nettle should not be included on the 503A list. The panel expressed concerns with variability in formulations, lack of efficacy, and the lack of clinical protocol. Please see the transcript for details of the committee discussion.*

2. FDA is proposing that ubiquinol NOT be included on the 503A Bulks List. Should ubiquinol be placed on the list?

   YES: 2 NO: 6 ABSTAIN: 1

   Committee Discussion: *The majority of the committee agreed that ubiquinol should not be included on the 503A list. The panel expressed need for additional safety and efficacy data. The panel members who voted "YES" commented that there are uncertainties to safety, but not enough to rule out ubiquinol's use. The members who voted "YES" noted ubiquinol's similarity to CoQ10. Please see the transcript for details of the committee discussion.*

3. FDA is proposing that vanadyl sulfate NOT be included on the 503A Bulks List. Should vanadyl sulfate be placed on the list?

   YES: 0 NO: 9 ABSTAIN: 0

Committee Discussion: *The committee unanimously agreed that vanadyl sulfate should not be included on the 503A list. The panel expressed concerns with serious safety signals and the lack of evidence of efficacy, while noting the abundance of currently available therapies. Please see the transcript for details of the committee discussion.*

May 9, 2017, a.m. session

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

1. FDA is proposing that artemisinin NOT be included on the 503A Bulks List. Should artemisinin be placed on the list?

   YES: 0 NO: 8 ABSTAIN: 0

   Committee Discussion: *The committee unanimously agreed that artemisinin should not be included on the 503A list. The panel expressed concerns with the limited data on safety of chronic use and noted that the animal data cannot be translated to humans. Members also commented on the lack of efficacy and potential for drug resistance. Please see the transcript for details of the committee discussion.*

Questions for PCAC Regarding Whether to Include Certain Drug Products or Categories of Drug Products on the Difficult to Compound List

1. FDA is proposing that oral solid modified release drug products that employ coated systems be INCLUDED on the Difficult to Compound List under sections 503A and 503B of the FD&C Act. Should oral solid modified release drug products that employ coated systems be placed on the list?

   YES: 6 NO: 0 ABSTAIN: 0

   Committee Discussion: *The committee unanimously agreed that oral solid modified release drug products that employ coated systems should be included on the Difficult to Compound (DTC) List under sections 503A and 503B of the FD&C Act. The panel commented that due to the complexity of the system's coating principles and characteristics necessary to release active ingredient at a predetermined rate, pattern and onset, MRC should be included on the DTC List and adequately defined in the proposed rulemaking in the Federal Register. Please see the transcript for details of the committee discussion.*

The meeting was adjourned at approximately 3:30 p.m. on May 8, 2017 and at 11:40 a.m. on May 9, 2017.