Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes of the Pharmacy Compounding Advisory Committee Meeting

November 20-21, 2017

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

Topic: On November 20-21, 2017, the committee discussed six bulk drug substances nominated for inclusion on the section 503A Bulks List. FDA discussed the following nominated bulk drug substances: L-citrulline, pregnenolone, 7-keto dehydroepiandrosterone (DHEA), astragalus, epigallocatechin gallate (EGCg), and resveratrol. The committee also discussed liposome drug products and drug products produced using hot melt extrusion for inclusion on the Difficult to Compound List. Drug products produced "by extrusion or nanotechnology" were nominated for inclusion on the Difficult to Compound List.

These summary minutes for the November 20-21, 2017 meeting of the Pharmacy Compounding Advisory Committee of the Food and Drug Administration were approved on __12/19/17_____.

I certify that I attended the November 20-21, 2017 meeting of the Pharmacy Compounding Advisory Committee and that these minutes accurately reflect what transpired.

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

_____/s/_____
Padma Gulur, MD
Acting Chairperson, PCAC

Summary Minutes of the Pharmacy Compounding Advisory Committee Meeting
November 20-21, 2017

The following is a final report of the Pharmacy Compounding Advisory Committee (PCAC) meeting held on November 20-21, 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 November 20-21, 2017 from 8:30 a.m. until 5:00 p.m. on November 20th and from 8:30 a.m. until 11:30 a.m. on November 21st, 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 Padma Gulur, MD (Acting Chairperson); the conflict of interest statement was read into the record by Cindy Chee, PharmD (Designated Federal Officer). There were approximately 35 persons in attendance in the audience section. There were three (3) Open Public Hearing presentations.

Issue:
On November 20-21, 2017, the committee discussed six bulk drug substances nominated for inclusion on the section 503A Bulks List. FDA discussed the following nominated bulk drug substances: L-citrulline, pregnenolone, 7-keto dehydroepiandrosterone (DHEA), astragalus, epigallocatechin gallate (EGCg), and resveratrol. The committee also discussed liposome drug products and drug products produced using hot melt extrusion for inclusion on the Difficult to Compound List. Drug products produced "by extrusion or nanotechnology" were nominated for inclusion on the Difficult to Compound List.

Attendance:
PCAC Members Present (Voting):
Robin Bogner, PhD; Michael Carome, MD, FACP (Consumer Representative); Gigi Davidson, BSPh, DICVP (US Pharmacopeial Convention Representative); Seemal Desai MD, FAAD (7-keto DHEA, astragalus, EGCg, and resveratrol topics only); Padma Gulur, MD (Acting Chairperson); Stephen Hoag, PhD; William Humphrey, BSPharm, MBA, MS; Elizabeth Jungman, JD, MPH; Kuldip Patel, PharmD; Allen Vaida, BSc, PharmD, FASHP (all topics except 7-keto DHEA); Jürgen Venitz, MD, PhD (L-citrulline, pregnenolone, 7-keto DHEA, astragalus, and EGCg topics only-via phone); Donna Wall, PharmD (National Association of Boards of Pharmacy Representative-via phone)

PCAC Members Present (Non-Voting): Ned Braunstein, MD (Industry Representative); William Mixon, RPh, MS, FIACP (Industry Representative)

PCAC Members Not Present (Voting): Seemal Desai, MD, FAAD (L-citrulline and pregnenolone and Day 2 topics); Jürgen Venitz, MD, PhD (resveratrol and Day 2 topics)

PCAC Members Not Present (Non-Voting): none

Temporary Members (Voting): Kenneth Burman, MD (L-citrulline, astragalus, EGCg, and resveratrol topics only); Jess Fiedorowicz, MD, PHD (pregnenolone topic only)

FDA Participants (**Non-Voting):** Frances Gail Bormel, RPh, JD; Michael Brave, MD; Celia Cruz, PhD; Julie Dohm, JD, PhD; Lesley Furlong, MD; Charles Ganley, MD; Michael Ghobrial, PharmD, JD; Wafa Harrouk, PhD; Susan Johnson, PharmD, PhD; Rosilend Lawson, VMD, JD; Sara Rothman, MPH; Tracy Rupp, PharmD; Katherine Tyner, PhD

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

Open Public Hearing Speakers:
Nov 20th: Col. Jeffery Johnson (Ret.), RPh, MBA, ND, PharmD (Medisca Inc.)
Nov 21st: Seth DePasquale, RPh (BET Pharm); Col. Jeffery Johnson (Ret.), RPh, MBA, ND, PharmD (Medisca Inc.)

The agenda proceeded as follows:

November 20, 2017 a.m. session:

Call to Order and Introduction of Committee	**Padma Gulur, MD** Acting Chairperson, PCAC
Conflict of Interest Statement	**Cindy Chee, PharmD** Designated Federal Officer, PCAC
FDA INTRODUCTORY REMARKS	**Julie Dohm, JD, PhD** Senior Science Advisor for Compounding, CDER Agency Lead on Compounding, FDA

SECTION 503A BULK DRUG SUBSTANCES LIST – FDA PRESENTATIONS

L-citrulline	**Susan Johnson, PharmD, PhD** Associate Director Office of Drug Evaluation IV (ODE IV) Office of New Drugs (OND), CDER, FDA

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS — **A. J. Day, PharmD**
Professional Compounding Centers of America (PCCA)

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

BREAK

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

Pregnenolone — **Wafa Harrouk, PhD**
Senior Pharmacologist
ODE IV, OND, CDER, FDA

Clarifying Questions from the Committee

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

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

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

7-Keto dehydroepiandrosterone — **Susan Johnson, PharmD, PhD**

Clarifying Questions from the Committee

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

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

LUNCH

November 20, 2017 p.m. session

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

Astragalus Extract 10:1

Michael Brave, MD
Clinical Reviewer
Division of Oncology Products 1
Office of Hematology and Oncology Products (OHOP)
OND, CDER, FDA

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS **Tom Wynn, RPh**

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

BREAK

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

Epigallocatechin gallate (EGCg) **Susan Johnson, PharmD, PhD**

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS **Kimberly Kieffer**
Fagron

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

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

Resveratrol

Charles Ganley, MD
Director
ODE IV, OND, CDER, FDA

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS

Jeffery A. Johnson, RPh, MBA, ND, PharmD Colonel (retired)
National Community Pharmacists Association (NCPA)

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

ADJOURNMENT

November 21, 2017

Call to Order and Introduction of Committee	**Padma Gulur, MD** Acting Chairperson, PCAC
Conflict of Interest Statement	**Cindy Chee, PharmD** Designated Federal Officer, PCAC

DEMONSTRABLY DIFFICULT TO COMPOUND LIST– FDA PRESENTATIONS

Liposome Drug Products	**Katherine Tyner, PhD** Associate Director for Science (Acting) Office of Pharmaceutical Quality (OPQ), CDER, FDA

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 PRESENTATIONS (cont.)

Drug Products Produced Using Hot Melt Extrusion	**Celia N. Cruz, PhD** Division Director Division of Product Quality Research Office of Testing and Research, OPQ, CDER, FDA

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

ADJOURNMENT

Questions to the Committee:

November 20, 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 L-citrulline for oral administration only be included on the 503A Bulks List. Should L-citrulline for oral administration only be placed on the list?

   YES: 12 NO: 0 ABSTAIN: 0 NO VOTE: 1

   Committee Discussion: *The committee unanimously agreed that L-citrulline should be included on the 503A Bulks List. The panel commented that the substance is stable, well characterized, and has a long history of use. One committee member was not present for the vote. Please see the transcript for details of the committee discussion.*

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

   YES: 6 NO: 5 ABSTAIN: 1

   Committee Discussion: *The committee was split on whether pregnenolone should be included on the 503A list. The panel expressed concerns with long term use safety signal, lack of evidence of effectiveness for the nominated uses, and the drug's oral availability as a dietary supplement that consumers can take without medical advice, while some members supported its use with pharmacist dispensing and physician supervision on an individual basis for difficult to treat situations. A majority of the committee voted to recommend placement of pregnenolone on the 503A bulks list contrary to FDA's recommendation against doing so. Please see the transcript for details of the committee discussion.*

3. FDA is proposing that 7-keto dehydroepiandrosterone NOT be included on the 503A Bulks List. Should 7-keto dehydroepiandrosterone be placed on the list?

   YES: 2 NO: 9 ABSTAIN: 0

   Committee Discussion: *A majority of the committee agreed that 7-keto dehydroepiandrosterone should not be included on the 503A list. The panel expressed concerns with a lack of evidence to demonstrate efficacy, its long-term safety, and difficulty in formulating the drug substance. Members voting "YES" commented that they did not see a significant negative safety profile and did not see a reason to limit access to patients. Please see the transcript for details of the committee discussion.*

November 20, 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 astragalus extract 10:1 NOT be included on the 503A Bulks List. Should astragalus extract 10:1 be placed on the list?

   YES: 0 NO: 13 ABSTAIN: 0

   Committee Discussion: *The committee unanimously agreed that astragalus should not be included on the 503A list. The panel expressed concerns with safety, lack of efficacy, and poor characterization of the formulation. Please see the transcript for details of the committee discussion.*

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

   YES: 0 NO: 13 ABSTAIN: 0

   Committee Discussion: *The committee unanimously agreed that EGCg should not be included on the 503A list. The panel expressed concern with the stability of the drug substance, lack of human data, impurities of the substance, and a lack of efficacy in most of the indications for which it was used. Please see the transcript for details of the committee discussion.*

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

   YES: 0 NO: 12 ABSTAIN: 0

   Committee Discussion: *The committee unanimously agreed that resveratrol should not be included on the 503A list. The panel expressed concerns with insufficient human clinical studies, issues with safety, and adverse drug interactions. Please see the transcript for details of the committee discussion.*

November 21, 2017

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 liposome drug products be INCLUDED on the Difficult to Compound List under sections 503A and 503B of the FD&C Act. Should liposome drug products be placed on the list?

   YES: 9 NO: 1 ABSTAIN: 0

   Committee Discussion: *A majority of the committee agreed that liposome drug products should be included on the Difficult to Compound (DTC) List under sections 503A and 503B of the FD&C Act. The panel commented on the complexity of the formulation, drug delivery, and lack of technology available to test these drug products, but did note that these products' placement on the DTC List should be reviewed as technology advances in the future. Please see the transcript for details of the committee discussion.*

2. FDA is proposing that drug products produced using hot melt extrusion be INCLUDED on the Difficult to Compound List under sections 503A and 503B of the FD&C Act. Should drug products produced using hot melt extrusion (HME) be placed on the list?

   YES: 7 NO: 2 ABSTAIN: 1

Committee Discussion: *A majority of the committee agreed that drug products produced using hot melt extrusion should be included on the DTC List under sections 503A and 503B of the FD&C Act. The panel members voting "YES" commented on the complexity of the systems, the need for in vivo testing, and the uncertain bioavailability of the drugs produced using HME. Members voting "NO" commented that prohibiting all HME is premature. Please see the transcript for details of the committee discussion.*

The meeting was adjourned at approximately 5:08 p.m. on November 20, 2017 and at 11:14 a.m. on November 21, 2017.