Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes of the Pharmacy Compounding Advisory Committee Meeting September 12, 2018

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

Topic: The committee received compounding updates and review, including information to follow up on the following discussions from previous PCAC meetings: balancing the criteria for the 503A bulk drug substance evaluation and dietary supplements nominated for use in compounding. The committee also discussed five bulk drug substances nominated for inclusion on the 503A Bulks List: alpha lipoic acid, coenzyme Q10, creatine monohydrate, pyridoxal 5 phosphate, and quercetin dihydrate.

Drugs	*Uses Reviewed*
alpha lipoic acid	*Diabetic neuropathy and associated pain, acute liver toxicity from Amanita spp. mushroom poisoning and other toxins, hepatitis C, cancer, cirrhosis, fibromyalgia, and muscle pain*
coenzyme Q10	*Mitochondrial disorders*
creatine monohydrate	*Mitochondrial disorders*
pyridoxal 5 phosphate	*Epilepsy and seizure disorders*
quercetin dihydrate	*Asthma, allergy, cancer prevention and treatment, and hypertension*

These summary minutes for the September 12, 2018 meeting of the Pharmacy Compounding Advisory Committee of the Food and Drug Administration were approved on October 4, 2018.

I certify that I attended the September 12, 2018, meeting of the Pharmacy Compounding Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/
Jay R. Fajiculay, PharmD
Acting Designated Federal Officer
Pharmacy Compounding Advisory Committee

/s/
Allen Vaida, BSc, PharmD
Acting Chairperson
Pharmacy Compounding Advisory Committee

Summary Minutes of the
Pharmacy Compounding Advisory Committee Meeting
September 12, 2018

The Pharmacy Compounding Advisory Committee (PCAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on September 12, 2018 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 Allen J. Vaida, BSc, PharmD, (Acting Chairperson). The conflict of interest statement was read into the record by Jay R. Fajiculay, PharmD (Acting Designated Federal Officer). There were approximately 95 people in attendance. There were five Open Public Hearing (OPH) speaker presentations.

A verbatim transcript will be available, in most instances, at approximately ten to twelve weeks following the meeting date.

Agenda: The committee received compounding updates and review, including information to follow up on the following discussions from previous PCAC meetings: balancing the criteria for the 503A bulk drug substance evaluation and dietary supplements nominated for use in compounding. The committee also discussed five bulk drug substances nominated for inclusion on the 503A Bulks List: alpha lipoic acid, coenzyme Q10, creatine monohydrate, pyridoxal 5 phosphate, and quercetin dihydrate.

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Attendance:

Pharmacy Compounding Advisory Committee Members Present (Voting): Robin Bogner, PhD; Michael Carome, MD, FASHP (Consumer Representative); Seemal Desai, MD, FAAD; Padma Gulur, MD (via phone); Stephen Hoag, PhD; William Humphrey, BSPh, MBA, MS; Elizabeth Jungman, JD; Kuldip Patel, PharmD; Allen Vaida, BSc, PharmD, FASHP (Acting Chairperson); Jurgen Venitz, MD, PhD (via phone); Donna Wall, PharmD (National Association of Boards of Pharmacy Representative)

Pharmacy Compounding Advisory Committee Member Not Present (Voting): Gigi Davidson, BSPh, DICVP

Pharmacy Compounding Advisory Committee Member Present (Non-Voting): William Mixon, RPh, MS, FIACP (Industry Representative)

Pharmacy Compounding Advisory Committee Member Not Present (Non-Voting): Ned Braunstein, MD (Industry Representative)

Temporary Members (Voting): Thomas Chelimsky, MD (participation in alpha lipoic acid, coenzyme Q10, and creatine monohydrate discussions); Marc Gregory Ghany, MD, MHSc, FAASLD (participation in alpha lipoic acid, coenzyme Q10, and creatine monohydrate discussions); Hrissanthi (Chris) Ikonomidou, MD, PhD (participation in alpha lipoic acid, coenzyme Q10, creatine monohydrate, and pyridoxal 5 phosphate monohydrate discussions); Sandeep Khurana, MBBS (participation in alpha lipoic acid, coenzyme Q10, and creatine monohydrate discussions); Jeanne Sun, PharmD (U.S. Pharmacopeia Representative)

Acting Industry Representative to the Committee (Non- Voting): Christopher Smalley, PhD, MS, MBA

FDA Participants (**Non-Voting):** Julie Dohm, JD, PhD; Ruey Ju, JD, PharmD; Frances Gail Bormel, RPh, JD; Sara Rothman, MPH; Rosilend Lawson, VMD, JD; Charles Ganley, MD; Susan Johnson, PharmD, PhD; Michael Brave, MD (morning session only)

Acting Designated Federal Officer (Non-Voting): Jay Fajiculay, PharmD

Open Public Hearing Speakers: Mark Filosi, RPh (Political Capital, LLC; Medisca; alpha lipoic acid session); Tami Wahl, JD (alpha lipoic acid session); Doug Tran, PharmD (McGuff Compounding Pharmacy Services, Inc.; alpha lipoic acid session); Mark Korson, MD (VMP Genetics, LLC; coenzyme Q10 and creatine monohydrate sessions); Alan Dumoff, JD, MSW (Integrative Medicine Consortium (consisting of American Association of Naturopathic Physicians American Academy of Environmental Medicine, American College for Advancement in Medicine and International College of Integrative Medicine); quercetin dihydrate session); Virginia Osbourne, ND, RN (American Association of Naturopathic Physicians and Integrative Medicine Consortium; quercetin dihydrate session)

The Agenda proceeded as follows:

Call to Order and Introduction of Committee	**Allen Vaida, BSc, PharmD** Acting Chairperson, PCAC
Conflict of Interest Statement	**Jay Fajiculay, PharmD** Acting Designated Federal Officer Division of Advisory Committee and Consultant Management (DACCM), CDER, FDA
FDA Introductory Remarks	**Julie Dohm, JD, PhD** Senior Science Advisor for Compounding, CDER Agency Lead on Compounding, FDA

FDA PRESENTATION

Compounding Updates and Review	**Sara Rothman, MPH** Senior Policy Advisor Office of Unapproved Drugs and Labeling Compliance Office of Compliance, CDER, FDA

Clarifying Questions from the Committee

SECTION 503A BULK DRUG SUBSTANCES LIST - FDA PRESENTATIONS

Alpha Lipoic Acid	**Michael Brave, MD** Medical Officer Division of Oncology Products 1 Office of Hematology and Oncology Products Office of New Drugs (OND), CDER, FDA

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS	**Alan Berkson, MD** Integrative Medical Center of New Mexico

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

BREAK

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

Coenzyme Q10	**Susan Johnson, PharmD, PhD** Associate Director Office of Drug Evaluation IV (ODE IV) OND, CDER, FDA

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS	**A.J. Day, PharmD** Professional Compounding Centers of America

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

LUNCH

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

Creatine monohydrate	**Susan Johnson, PharmD, PhD**
Clarifying Questions from the Committee	
NOMINATOR PRESENTATIONS	**A.J. Day, PharmD**
Clarifying Questions from the Committee	
OPEN PUBLIC HEARING	
COMMITTEE DISCUSSION AND VOTE	
BREAK	

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

Pyridoxal 5 phosphate monohydrate	**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	

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

Quercetin dihydrate	**Charles Ganley, MD** Director ODE IV, OND, CDER, FDA
Clarifying Questions from the Committee	
NOMINATOR PRESENTATIONS	**Paul Anderson, NMD** Anderson Medical Specialty Associates
Clarifying Questions from the Committee	

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

ADJOURNMENT

Questions to the Committee:

Morning Session

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

1. **VOTE:** FDA is proposing that alpha lipoic acid solid oral dosage forms be INCLUDED on the 503A Bulks List. Should alpha lipoic acid solid oral dosage forms be placed on the list?

   Vote Result: ***YES: 16*** ***NO: 0*** ***ABSTAIN: 0***

   Committee Discussion: *The committee unanimously agreed that alpha lipoic acid (ALA) solid oral dosage forms should be included on the 503A Bulks List. Many were compelled by the positive data presented about ALA's usage in diabetic neuropathy. Most of the committee members stated that while today they were voting on the inclusion of solid oral dosage forms, they would like to see ALA's IV formulation brought back for discussion in the future. Additionally, multiple panel members stressed the importance of evaluating the IV formulation more closely, especially in regards to the product's stability. One panel member stated concern with how prescribers know about adverse effects and other information about ALA since it is compounded and has no label. Another panel member suggested that the compound not be used for chronic Hepatitis C patients because there are already safe and effective products for these patients. Please note votes were originally misstated (YES: 17; NO: 0; Abstain: 0) but corrected during the meeting. The count listed above reflects the corrected vote result. Please see the transcript for details of the committee discussion.*

2. **VOTE:** FDA is proposing that coenzyme Q_{10} (ubiquinone) for oral administration be INCLUDED on the 503A Bulks List. Should coenzyme Q_{10} (ubiquinone) for oral administration be placed on the list?

   Vote Result: ***YES: 16*** ***NO: 0*** ***ABSTAIN: 0***

   Committee Discussion: *The committee unanimously agreed that coenzyme Q_{10} (ubiquinone) for oral administration be included on the 503A Bulks List. The committee members stated that there was a place in therapy for treating mitochondrial disorders and thus coenzyme Q_{10} helped many patients suffering from these disorders. Furthermore, the data presented met evaluation criteria and adequately supported the product's inclusion into the Bulks List. It was also noted that coenzyme Q_{10} is well characterized and has a USP dietary supplement monograph. Additionally, two committee members cited concerns with the stability and bioavailability of the substance and suggested that more detailed presentations into these subjects would be helpful. Please note votes were originally*

misstated (YES: 17; NO: 0; Abstain: 0) but corrected during the meeting. The count listed above reflects the corrected vote result. Please see the transcript for details of the committee discussions.

Afternoon Session

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

3. **VOTE:** FDA is proposing that creatine monohydrate solid oral dosage forms be INCLUDED on the 503A Bulks List. Should creatine monohydrate solid oral dosage forms be placed on the list?

   Vote Result: ***YES: 16*** ***NO: 0*** ***ABSTAIN: 0***

   Committee Discussion: *The committee unanimously agreed that creatine monohydrate solid oral dosage forms be included on the 503A Bulks List. Most committee members acknowledged that although the evidence presented was weak and there is risk of renal injury, the substance still suggested some benefit to a patient population that has no effective therapy for their disorder. However, many committee members urged the FDA to consider what an optimal dosage of creatine monohydrate would be. One committee member suggested that the substance have no qualifications for dosage form and route of administration and also noted that stability data exists for other dosage forms of creatine monohydrate. Another committee member stressed the importance of doctors and pharmacists closely monitoring their patients while taking creatine monohydrate. Please note votes were originally misstated (YES: 17; NO: 0; Abstain: 0) but corrected during the meeting. The count listed above reflects the corrected vote result. Please see the transcript for details of the committee discussion.*

4. **VOTE:** FDA is proposing that pyridoxal 5 phosphate monohydrate (intravenous and oral dosage forms) be INCLUDED on the 503A Bulks List. Should pyridoxal 5 phosphate monohydrate (intravenous and oral dosage forms) be placed on the list?

   Vote Result: ***YES: 13*** ***NO: 0*** ***ABSTAIN: 0***

   Committee Discussion: *The committee unanimously agreed that pyridoxal 5 phosphate monohydrate (intravenous and oral dosage forms) be included on the 503A Bulks List. The committee stated that pyridoxal 5 phosphate clearly has a life or death benefit for a rare disease. The committee also commented that the substance is well characterized and well supported with efficacy and safety data. One committee member expressed concern about the indication straying from the rare disease it is currently used in. Please note votes were originally misstated (YES: 14; NO: 0; Abstain: 0) but corrected during the meeting. The count listed above reflects the corrected vote result. Please see the transcript for details of the committee discussion.*

5. **VOTE:** FDA is proposing that quercetin dihydrate NOT be included on the 503A Bulks List. Should quercetin dihydrate be placed on the list?

   Vote Result: ***YES: 0*** ***NO: 11*** ***ABSTAIN: 0***

Committee Discussion: *The committee unanimously agreed that quercetin dihydrate NOT be included on the 503A Bulks List. Many committee members expressed concerns with the lack of reasonable data supporting the use of quercetin dehydrate in its proposed indications, the amount of known drug interactions with this product, and the number of products that are currently available for these conditions that are already proven to be safe and efficacious. Several committee members also noted that the product is widely available over-the-counter as an oral dietary supplement, and in the future, more substantial data would be needed to consider an IV formulation. Please note that one committee member was not present for the vote. Please see the transcript for details of the committee discussion.*

The meeting was adjourned at approximately 4:35 p.m.