

Food and Drug Administration  
Center for Drug Evaluation and Research

**Summary Minutes of the Pharmacy Compounding Advisory Committee Meeting**

February 23-24, 2015

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

Topic: On February 23, 2015, during the morning session, the committee discussed proposed revisions to the list of drug products that may not be compounded because the drug products have been withdrawn or removed from the market because such drug products or components of such drug products have been found to be unsafe or not effective. The list of products is currently codified at § 216.24 (21 CFR 216.24) and FDA is proposing to revise and update the list at § 216.24 for purposes of both sections 503A and 503B.

On February 23, 2015, during the afternoon session and continuing to the next day, the committee discussed particular drug substances nominated for inclusion on the list of bulk drug substances that may be used to compound drug products in accordance with section 503A of the FD&C Act. At this inaugural meeting of the newly-constituted committee, FDA discussed the following six nominated bulk drug substances: cantharidin, diphenylcyclopropenone, piracetam, silver protein mild, squaric acid dibutyl ester, and thymol iodide. The nominators of these substances were invited to make a short presentation supporting their nomination. Other nominated substances were to be discussed at future committee meetings.

These summary minutes for the February 23-24, 2015 meeting of the Pharmacy Compounding Advisory Committee of the Food and Drug Administration were approved on May 5, 2016.

I certify that I attended the February 23-24, 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 February 23-24, 2015

The following is the final report of the Pharmacy Compounding Advisory Committee (PCAC) meeting held on February 23-24, 2015. A verbatim transcript is available 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.

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The Pharmacy Compounding Advisory Committee (PCAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on February 23 and 24, 2015 from 8:30 a.m. until 5:00 p.m. and from 8:15 a.m. to approximately 12:20 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 Jayne Peterson, JD (Designated Federal Officer). There were approximately 60 persons in attendance in the audience section. There were three (3) Open Public Hearing presentations over the two days.

### **Issue:**

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On February 23, 2015, during the afternoon session and continuing to the next day, the committee discussed particular drug substances nominated for inclusion on the list of bulk drug substances that may be used to compound drug products in accordance with section 503A of the FD&C Act. At this inaugural meeting of the newly-constituted committee, FDA discussed the following six nominated bulk drug substances: cantharidin, diphenylcyclopropanone, piracetam, silver protein mild, squaric acid dibutyl ester, and thymol iodide. The nominators of these substances were invited to make a short presentation supporting their nomination. Other nominated substances were to be discussed at future committee meetings.

### **Attendance:**

**PCAC Members Present (Voting):** Jürgen Venitz, MD, PhD (Chairperson); Michael Carome, MD (Consumer Representative), Gigi Davidson, BSPh, (USP Representative - 2/23/15 only), Robert DeChristoforo, MS, John DiGiovanna, MD, Padma Gulur, MD, William Humphrey, BSPharm, MBA, Stephen Hoag, PhD, Elizabeth Jungman, JD, Katherine Pham, PharmD, Allen Vaida, PharmD, Donna Wall, PharmD (NABP Representative)

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

**PCAC Members Not Present (Voting):** February 24<sup>th</sup>: Gigi Davidson (not present on February 24<sup>th</sup>); Stephen Hoag, PhD (not present for presentations on February 24<sup>th</sup> – arrived at the meeting at the start of the last vote call (cantharidin and piracetam) and did not vote on either of the two nominated substances).

**Temporary Members (Voting):** February 23<sup>rd</sup>: Michael Belin, MD (silver mild protein only); February 24<sup>th</sup>: Jeanne Sun, PharmD (alternate USP representative)

**FDA Participants (Non-Voting):** Kalah Auchincloss, JD, MPH, Jane Axelrad, JD, Kenneth Bergmann, MD, Frances Gail Bormel, RPh, JD, Patricia Brown, MD, Wiley Chambers, MD, Emily Helms Williams, JD, Dmitri Iarikov, MD, Hon-Sum Ko, MD, Mwango A. Kashoki, MD, MPH, Nancy Xu, MD, Olivia Ziolkowski, JD, MPH

**Designated Federal Officer (Non-Voting):** Jayne Peterson

**Open Public Hearing Speakers:**

**2/23/15 10:15 a.m. session:** A.J. Day, PharmD (Pharmacy Compounding Corporation of America)

**2/23/15 3:35 p.m. session:** Ronna Hauser, PharmD (National Community Pharmacists Association)

**2/24/15 9:30 a.m. session:** None

**2/24/15 11:45 a.m. session:** Matt Davidson, PhD (Verrica Pharmaceuticals)

*The agenda proceeded as follows:*

**February 23, 2015:**

Call to Order and Introduction of Committee

**Jürgen Venitz, MD, PhD**  
Chairperson, PCAC

Conflict of Interest Statement

**Jayne E. Peterson, BS Pharm, JD**  
Designated Federal Officer (acting), PCAC

FDA Introductory Remarks and  
Overview of Withdrawn and Removed List

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

**FDA PRESENTATIONS**

Identification of Drugs Withdrawn or Removed  
from the Market for Safety Reasons

**Mwango A. Kashoki, MD, MPH**  
Associate Director for Safety, Office of New  
Drugs (OND), Immediate Office, CDER, FDA

Clarifying Questions from the Committee

Adenosine Phosphate

**Nancy Xu, MD**  
Medical Officer, Division of Cardiovascular  
and Renal Products, Office of Drug Evaluation  
(ODE) I, OND, CDER, FDA

Clarifying Questions from the Committee

Chloramphenicol

**Dmitri Iarikov, MD, PhD**  
Clinical Team Leader (acting)  
Division of Anti-Infective Products, Office of  
Antimicrobial Products (OAP)  
OND, CDER, FDA

Clarifying Questions from the Committee

**BREAK**

**OPEN PUBLIC HEARING**

Committee Discussion and  
Vote on Withdrawn or Removed List

**LUNCH** (*End Session one*)

**February 23, 2015** (*Beginning of Session 2, afternoon of February 23<sup>rd</sup>*)

Call to Order

**Jürgen Venitz, MD, PhD**  
Chairperson, PCAC

Conflict of Interest Statement

**Jayne E. Peterson, BS Pharm, JD**  
Designated Federal Officer (acting), PCAC

FDA Introduction to List of Bulk Drug  
Substances That Can Be Used to Compound  
Drug Products Under the Conditions of  
Section 503A

**Kalah Auchincloss, JD, MPH**  
Director (acting), Office of Unapproved  
Drugs and Labeling Compliance, Office of  
Compliance, CDER, FDA

Committee Discussion of Proposed Criteria  
for the Section 503A Bulk Drug Substance List

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

Thymol Iodide

**Patricia Brown, MD, FAAD**  
Medical Officer, Division of Dermatology and  
Dental Products (DDDP), ODE III  
OND, CDER, FDA

Clarifying Questions from the Committee

Silver Protein Mild

**Wiley Chambers, MD**  
Deputy Director, Division of Transplant and  
Ophthalmology Products  
OAP, OND, CDER, FDA

Clarifying Questions from the Committee

**BREAK**

**NOMINATOR PRESENTATION**

Thymol Iodide  
Silver Protein Mild

**Craig Hitchman, RPh**  
Academy Director  
Fagron North America

**OPEN PUBLIC HEARING SESSION**

Committee Discussion and Vote  
Thymol Iodide  
Silver Protein Mild

**ADJOURNMENT**

**February 24, 2015 (session continued from the afternoon of February 23rd):**

Call to Order and Introduction of Committee

**Jürgen Venitz, MD, PhD**  
Chairperson, PCAC

Conflict of Interest Statement

**Jayne E. Peterson, BS Pharm, JD**  
Designated Federal Officer (acting), PCAC

**FDA PRESENTATIONS**

**SECTION 503A BULK DRUG SUBSTANCES**

Squaric Acid Dibutyl Ester

**Hon-Sum Ko, MD, FACP**  
Medical Officer, DDDP  
ODE III, OND, CDER, FDA

Diphenylcyclopropenone

Clarifying Questions from the Committee

**NOMINATOR PRESENTATIONS**

Squaric Acid Dibutyl Ester

**A. J. Day, PharmD, RPh**  
Director of Pharmacy Consulting  
Professional Compounding Centers  
of America (PCCA)

**Craig Hitchman, RPh**  
Academy Director, Fagron North America

Diphenylcyclopropenone

**A. J. Day, PharmD, RPh , PCCA**  
**Gerald McEvoy, PharmD**  
Assistant Vice President, Drug Information  
American Society of Health-System  
Pharmacists (ASHP)

**OPEN PUBLIC HEARING SESSION**

Committee Discussion and Vote

Squaric Acid Dibutyl Ester

Diphenylcyclopropanone

**BREAK**

**FDA PRESENTATIONS**

**SECTION 503A BULK DRUG SUBSTANCES**

Cantharidin

**Patricia Brown, MD, FAAD**

Medical Officer, Division of Dermatology and  
Dental Products (DDDP), ODE III  
OND, CDER, FDA

Clarifying Questions from the Committee

Piracetam

**Kenneth Bergmann, MD**

Medical Officer  
Division of Neurology Products  
ODE I, OND, CDER, FDA

Clarifying Questions from the Committee

**NOMINATOR PRESENTATIONS**

Cantharidin

**A. J. Day, PharmD, RPh**  
PCCA

Piracetam

**OPEN PUBLIC HEARING SESSION**

Committee Discussion and Vote

Cantharidin

Piracetam

**ADJOURNMENT**

**Voting Questions for PCAC Regarding Whether to Include Certain Drugs on the  
Withdrawn or Removed List, and How to Describe Certain Entries**

*General Discussion: Committee members asked whether a vote to include the products below on the Withdrawn or Removed List meant that these products would NOT be available to any patients. The FDA clarified that there is an expanded access IND program in place and that if a physician wishes to treat a patient with a product NOT included on the 503A listing, the product could be made available to the provider and patient under the provisions of the program, upon filing of an IND. Dr. Sumathi Nambiar, Division Director of the CDER Division of Anti-Infective Products, provided an overview of the processes involved in the request and approval of an expanded access IND. She noted that FDA response to these types of INDs is very speedy and often takes hours rather than days to approve. Additionally, if the IND process is used, the*

*identified patient would be provided an informed consent document, which would describe the benefits and risks of the product.*

*Several on the committee asked whether the Withdrawn or Removed list was a static list or would/could it be added to or subtracted from over time. The FDA confirmed that the list will be updated and revised, and presented to the committee as drug products are newly withdrawn from the market. Similarly, the public could submit a Citizen's Petition requesting that any drug product or a specific formulation of any drug product be removed from the list. FDA also clarified that several of the proposed bulk drugs are limited to only certain product formulations, such as an injectable formulation; in those cases where a specific formulation is stated, other formulations of the drug product may not be compounded.*

**Vote options : YES, NO, or ABSTAIN were selected by committee members for each question.**

1. FDA is proposing that "*Alatrofloxacin mesylate: All drug products containing alatrofloxacin mesylate*" be added to the Withdrawn or Removed List. Do you agree?  
Yes: 12            No: 0
2. FDA is proposing that "*Aminopyrine: All drug products containing aminopyrine*" be added to the Withdrawn or Removed List. Do you agree?  
Yes: 12            No: 0
3. FDA is proposing that "*Astemizole: All drug products containing astemizole*" be added to the Withdrawn or Removed List. Do you agree?  
Yes: 12            No: 0
4. FDA is proposing that the current listing of "*Bromfenac sodium: All drug products containing bromfenac sodium*" on the Withdrawn or Removed List be modified to "*Bromfenac sodium: All drug products containing bromfenac sodium (except ophthalmic solutions).*" Do you agree?  
Yes: 12            No: 0
5. FDA is proposing that "*Cerivastatin sodium: All drug products containing cerivastatin sodium*" be added to the Withdrawn or Removed List. Do you agree?  
Yes: 11            No: 0
6. FDA is proposing that "*Cisapride: All drug products containing cisapride*" be added to the Withdrawn or Removed List. Do you agree?  
Yes: 12            No: 0
7. FDA is proposing that "*Esmolol hydrochloride: All parenteral drug products containing esmolol HCl that supply 250 mg/milliliter (mL) of concentrated esmolol per 10-mL ampule*" be added to the Withdrawn or Removed List. Do you agree?  
Yes: 12            No: 0
8. FDA is proposing that "*Etretinate: All drug products containing etretinate*" be added to the Withdrawn or Removed List. Do you agree?  
Yes: 11            No: 1
9. FDA is proposing that "*Gatifloxacin: All drug products containing gatifloxacin (except ophthalmic solutions)*" be added to the Withdrawn or Removed List. Do you agree?  
Yes: 12            No: 0

**10.** FDA is proposing that “*Grepafloxacin: All drug products containing grepafloxacin*” be added to the Withdrawn or Removed List. Do you agree?

Yes: 12          No: 0

**11.** FDA is proposing that “*Methoxyflurane: All drug products containing methoxyflurane*” be added to the Withdrawn or Removed List. Do you agree?

Yes: 11          No: 0

**12.** FDA is proposing that “*Novobiocin sodium: All drug products containing novobiocin sodium*” be added to the Withdrawn or Removed List. Do you agree?

Yes: 12          No: 0

**13.** FDA is proposing that “*Pemoline: All drug products containing pemoline*” be added to the Withdrawn or Removed List. Do you agree?

Yes: 11          No: 0

**14.** FDA is proposing that “*Pergolide mesylate: All drug products containing pergolide mesylate*” be added to the Withdrawn or Removed List. Do you agree?

Yes: 11          No: 0

**15.** FDA is proposing that “*Phenylpropanolamine (PPA): All drug products containing PPA* be added to the Withdrawn or Removed List. Do you agree?

Yes: 12          No: 0

**16.** FDA is proposing that “*Polyethylene glycol (PEG) 3350, sodium chloride, sodium bicarbonate, potassium chloride, and bisacodyl: All drug products containing PEG 3350, sodium chloride, sodium bicarbonate, and potassium chloride for oral solution, and 10 mg or more of bisacodyl delayed-release tablet*” be added to the Withdrawn or Removed List. Do you agree?

Yes: 12          No: 0

**17.** FDA is proposing that “*Propoxyphene: All drug products containing propoxyphene*” be added to the Withdrawn or Removed List. Do you agree?

Yes: 12          No: 0

**18.** FDA is proposing that “*Rapacuronium bromide: All drug products containing rapacuronium bromide*” be added to the Withdrawn or Removed List. Do you agree?

Yes: 12          No: 0

**19.** FDA is proposing that “*Rofecoxib: All drug products containing rofecoxib*” be added to the Withdrawn or Removed List. Do you agree?

Yes: 12          No: 0



20. FDA is proposing that “*Sibutramine hydrochloride: All drug products containing sibutramine hydrochloride*” be added to the Withdrawn or Removed List.

Yes: 12          No: 0

21. FDA is proposing that “*Tegaserod maleate: All drug products containing tegaserod maleate*” be added to the Withdrawn or Removed List. Do you agree?

Yes: 12          No: 0

22. FDA is proposing that “*Troglitazone: All drug products containing troglitazone*” be added to the Withdrawn or Removed List. Do you agree?

Yes: 12          No: 0

23. FDA is proposing that “*Trovafloxacin mesylate: All drug products containing trovafloxacin mesylate*” be added to the Withdrawn or Removed List. Do you agree?

Yes: 12          No: 0

24. FDA is proposing that “*Valdecoxib: All drug products containing valdecoxib*” be added to the Withdrawn or Removed List. Do you agree?

Yes: 12          No: 0

25. FDA is now proposing that the current entry of “*Adenosine phosphate: All drug products containing adenosine phosphate*” on the list of drug products that have been withdrawn or removed from the market because such drug products or components of such drug products have been found to be unsafe or not effective, codified at 21 CFR 216.24 be updated to state “*All drug products containing adenosine 5'-monophosphate (AMP), adenosine 5'-diphosphate (ADP), and adenosine 5'-triphosphate (ATP).*” Do you agree?

Yes: 12          No: 0

26. FDA is proposing that “*Chloramphenicol: All oral drug products containing chloramphenicol*” be added to the Withdrawn or Removed List. Do you agree?

Yes: 9            No: 2

27. FDA is proposing that “*Oxycodone hydrochloride: All extended-release drug products containing oxycodone hydrochloride that have not been determined by FDA to have abuse-deterrent properties*” be added to the Withdrawn or Removed List. Do you agree?

Yes: 11          No: 0

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

#### **General Committee Discussion on the Criteria:**

*A member raised concern that the impact of allowing 503A bulk drug substances (BDSs) to be compounded and provided to the public was to move back to the standards of safety and efficacy that existed prior to the implementation of the current safety/efficacy standards, e.g., before 1966 for efficacy and 1938 for safety. A committee member pointed out that other than Texas and Michigan, no other states have voluntary AE reporting programs for compounded drug products, making it difficult to assess safety of compounded drug products. Another member noted that many dermatologic preparations have a long and extended history of human use and that this history of use would serve well as support for safety and efficacy of the product. A member asked whether a long historical use of a product would override concerns about either a lack of, or unfavorable known safety or efficacy issues. The Agency noted that information for any one criteria would not override the necessity to balance all four of the criteria when making a decision about inclusion on the list.*

*Several members questioned why the nominated BDS's had no USP or NF monographs, particularly those which have been in use for a long time. Others responded that generally, monographs are created only after a commercial drug product is approved by the FDA for marketing; USP and the sponsor reach out to each other and begin the process of monograph preparation. FDA noted that USP will likely develop monographs for the new BDSs added to the 503A listing and thus the action of placing a BDS on the 503A list needs careful and critical review.*

**Vote options: YES, NO, or ABSTAIN were selected by committee members for each question.**

1. FDA is proposing that thymol iodide 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 thymol iodide be placed on the list?

Yes: 9            No: 2

*Committee Discussion: The committee noted that none of the thymol iodide trials that were included in the BDS nomination packages were publications of well-controlled, randomized trials, but instead were mostly case series or retrospective studies. The trials were neither comparative nor head-to-head, and none seemed to demonstrate efficacy of thymol iodide as an anti-microbial with antiseptic properties. The FDA noted that adding a BDS to the 503A listing does not connote to the public that the drug product compounded with this BDS is safe and effective for human use. Finally, many members recommended that the label of thymol iodide drug products include information that the compounded product be limited to topical or non-systemic use.*

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

Yes: 0            No: 12

*Committee Discussion: One committee member stated that as far as he knew, silver protein mild (SPM) has not been used routinely for ophthalmic purposes for at least 20 years. Furthermore, although one of the supportive references described the use of SPM during cataract surgery, the reference was over 30 years old and cataract surgery has greatly evolved since the date of the article. Most of the committee members stated that for SPM, they did not believe that any of the four proposed criteria for placing a BDS on the 503A listing were met.*

**February 24, 2015: Questions to the Committee (cont.)**

3. FDA is proposing that squaric acid dibutyl ester be placed on the 503A bulk list. Should squaric acid dibutyl ester be placed on the list?

Yes: 10      No: 0

4. FDA is proposing that diphenylcyclopropanone be placed on the 503A bulk list. Should diphenylcyclopropanone be placed on the list?

Yes: 9      No: 1

5. FDA is proposing that cantharidin be placed on the 503A bulk list. Should cantharidin be placed on the list?

Yes: 8      No: 2

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

Yes: 1      No: 9

*Please see the transcript for complete details of the committee discussion.*

*The meeting was adjourned at approximately 12:20 p.m.*