Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes of the Dermatologic and Ophthalmic Drugs Advisory Committee Meeting
June 17, 2008

Topic: On June 17, 2008, the committee will discussed biologic licensing application (BLA) 125261, ustekinumab, a human monoclonal antibody, Centocor, Inc., proposed for the treatment of moderate to severe psoriasis.

These summary minutes for the June 17, 2008 Dermatologic and Ophthalmic Drugs Advisory Committee meeting were approved on July 1, 2008.

I certify that I attended the June 17, 2008 Dermatologic and Ophthalmic Drugs Advisory Committee meeting and that these minutes accurately reflect what transpired.

_____-*s*-_____
Yvette Waples, Pharm.D.
(Designated Federal Official)

_____-*s*-_____
Michael Bigby, M.D.
(Chair)

Summary Minutes of the Dermatologic and Ophthalmic Drugs Advisory Committee Meeting
June 17, 2008

The following is the final report of the Dermatologic and Ophthalmic Drugs Advisory Committee meeting held on June 17, 2008. A verbatim transcript will be available in approximately two weeks, sent to the Division and posted on the FDA website at http://www.fda.gov/ohrms/dockets/ac/cder08.html#DermatologicOphthalmicDrugs

All external requests for the meeting transcripts should be submitted to the CDER Freedom of Information Office.

The Dermatologic and Ophthalmic Drugs Advisory Committee of the Food and Drug Administration met on June 17, 2008 at the Hilton Washington DC/Silver Spring, Silver Spring, Maryland. Michael Bigby, M.D, chaired the meeting. There were approximately 140 in attendance.

Attendance:

Dermatologic and Ophthalmic Drugs Advisory Committee Members present (voting):
Michael Bigby M.D. (Chair); Mary A. Majumder, Ph.D.; Bruce H, Thiers, M.D.

Dermatologic and Ophthalmic Drugs Advisory Committee Members absent:
Marijean M. Miller, M.D.; Robert Skinner, M.D.

Dermatologic and Ophthalmic Drugs Advisory Committee Temporary Voting Members:
Lynn A. Drake, M.D.; Robert Katz, MD; Eileen Ringel, M.D.; Tor Shwayder, M.D.; Robert Stern, M.D.

Drug Safety and Risk Management Advisory Committee Voting Member:
Susan R. Heckbert, M.D., Ph.D.

Drug Safety and Risk Management Advisory Committee Temporary Voting Members:
Stephanie Crawford, Ph.D., M.P.H.; Arthur Levin, M.P.H.

Industry Representative (non-voting):
Ellen Strahlman, M.D., M.H.Sc

FDA Participants (non-voting):
Julie Beitz, M.D.; Susan J. Walker, M.D., FAAD; Mark Avigan, M.D.; Iyasu Solomon, M.D.; Brenda Carr, M.D.

Open Public Hearing Speaker:
Ellen Clements; Bernadette Dougherty; Daniel Farrington; Alan Menter, M.D. (President, International Psoriasis Council); Michael Paranzino (President Psoriasis Cure Now)

On June 17, 2008, the committee will discussed biologic licensing application (BLA) 125261, ustekinumab, a human monoclonal antibody, Centocor, Inc., proposed for the treatment of moderate to severe psoriasis.

Michael Bigby M.D., (Chair) called the meeting to order at 8:00 a.m. The Committee members and the FDA participants introduced themselves. The conflict of interest statement was read into the record by Yvette Waples, Pharm.D., Designated Federal Official (DFO). The agenda for the meeting was as follows:

8:00 a.m.	Call to Order and Opening Remarks	**Michael Bigby, M.D.** Chair Dermatologic and Ophthalmic Drugs Advisory Committee
	Introduction of Committee	
	Conflict of Interest Statement	**Yvette Waples, Pharm.D.** Designated Federal Official
8:15 a.m.	FDA Introductory Remarks	**Susan Walker, M.D., FAAD** Director Division of Dermatology and Dental Products, CDER, FDA
FDA PRESENTATION		
8:20 a.m.	Ustekinumab: Mechanism of Action	**Laurie Graham, MS** CMC Reviewer, Division of Monoclonal Antibodies
INDUSTRY PRESENTATION		
8:30 a.m.	Introduction	**Stella S. Jones, Ph.D** Centocor R&D, Inc.
	Moderate to Severe Psoriasis Clinical Background	**Alexa Boer Kimball, M.D., MPH** Massachusetts General Hospital
	Efficacy of Ustekinumab	**Cynthia Guzzo, M.D.** Centocor R&D, Inc.
	Safety of Ustekinumab	**Newman Yeilding, M.D.** Centocor R&D, Inc.
	Risk Management Plan	**Peter E. Callegari, M.D.** Centocor R&D, Inc.
	Unmet Need in Systemic Psoriasis Treatment	**Mark Lebwohl, M.D.** Mount Sinai School of Medicine
10:00 a.m.	Questions/Clarifications	

10:15 a.m. **BREAK**

FDA PRESENTATION

10:30 a.m.	Efficacy of Ustekinumab	**Kathleen Fritsch, PhD** Division of Biometrics III
	What is the Optimal Starting Dose of Ustekinumab	**Pravin Jadhav, Ph.D.** Division of Pharmacology and Biopharmaceutics, CDER, FDA
	Nonclinical Evaluation of Ustekinumab	**Jiaqin Yao, Ph.D.** Division of Dermatology and Dental Products
	Ustekinumab in the Treatment of Psoriasis: Selected Safety Concerns	**Brenda Carr, M.D.** Medical Officer, Division of Dermatology and Dental Products
	Usetekinumab Safety Concerns: The Way Forward	**Rizwan Ahmed, M.D.** Medical Officer, Division of Dermatology and Dental Products

11: 30 p.m. Questions/Clarifications

12: 15 p.m. **LUNCH**

1:15 a.m. **OPEN PUBLIC HEARING**

2: 00 p.m. Panel Discussion/Questions

3:35 p.m. **BREAK**

3:50 p.m. Panel Discussion/Questions

5:30 p.m. **ADJOURNMENT**

Questions to the Committee:

Please discuss the efficacy of ustekinumab:

1. Has the applicant provided sufficient information to demonstrate efficacy of ustekinumab in the treatment of plaque psoriasis?

(See transcript for complete discussion)

Yes: 11 **No: 0** **Abstain: 0**

2. The applicant has proposed “dosing every 12 weeks”. Has the applicant provided sufficient information to support this dosing schedule?
(See transcript for complete discussion)

Yes: 11 **No: 0** **Abstain: 0**

3. Please discuss the alternative weight-based dosing paradigms. Which dosing regimen do you recommend?
(See transcript for complete discussion)

The committee also voted on *dosing regimen recommendation of two dose or three dose paradigm?*

Two available doses: 7 **Three available doses: 3** **Abstain: 1**

The majority of the committee voted for the two available doses due to the fact the 45 mg and 90mg dose was studied by the sponsor.

For the members who voted for a third dose (67.5 mg) felt the population weighing between 70kg-100kg would have increase risk of side effects and toxicity if given the 90mg dose. In addition, it would be more optimal for their weight range.

4. Has the applicant provided sufficient information to inform patients/physicians regarding when/how to stop treatment with ustekinumab?
(See transcript for complete discussion)

Yes: 1 **No: 10** **Abstain: 0**

Please discuss the safety of ustekinumab:

5. Discuss the critical safety concerns with ustekinumab and the sufficiency of the database to characterize them.
(See transcript for complete discussion)

Have a sufficient number of subjects been studied?

Yes: 0 **No: 10** **Abstain: 1**

Have subjects been followed for a sufficient length of time?

Yes: 0 **No: 11** **Abstain: 0**

6. Discuss the potential for malignancy demonstrated by this class of compounds, including the findings from animal studies that indicated an increased carcinogenic risk with inhibition of IL-12/IL23.
(See transcript for complete discussion)

Are the members concerned with the potential malignancy demonstrated by this class of compounds, including the findings from animal studies that indicated an increased carcinogenic risk with inhibition of IL-12/IL23?

Yes: 11 **No: 0** **Abstain: 0**

Is it important to communicate these findings to prescribers?

Yes: 11 **No: 0** **Abstain: 0**

Are additional animal studies needed?

Yes: 1 **No: 9** **Abstain: 1**

Please discuss the relative benefits and risks for the use of ustekinumab in patients with moderate to severe plaque psoriasis:

7. Do the benefits of ustekinumab therapy in adult patients with moderate to severe psoriasis outweigh the risks?
(See transcript for complete discussion)

Yes: 9 **No: 1** **Abstain: 1**

8. Do you recommend approval of ustekinumab for the treatment of adult patients with moderate to severe plaque psoriasis?
(See transcript for complete discussion)

Yes: 11 **No: 0** **Abstain: 0**

a) If the answer is **no,** what additional premarketing studies do you suggest?
i) completion of the pivotal trials extensions prior to approval **N/A**

ii) new randomized clinical trials **N/A**

iii) other studies **N/A**

b) If the answer is **yes,**
i) describe the recommended dosing regimen and the length of treatment

ii) should the product be labeled for patient self administration or only for prescriber administration?

Self administration: 4 **Prescriber administration only: 7** **Abstain: 0**

iii) are the applicant's risk assessment proposals (PSOLAR, 5 year extension of pivotal trials) sufficient to characterize the long term safety of ustekinumab? Please discuss these options:

a) increasing sample size of PSOLAR…. Is this sufficient?

Yes: 0 **No: 11** **Abstain: 0**

b) epidemiologic study (observational)

c) mandatory registry/restricted distribution

d) disease-based registry

The last three (b, c, and d) were combined. FDA wanted members to answer how rigorous a study should we be demanding of the sponsor to collect the available data.

The meeting was adjourned at approximately 5:30 p.m. on June 17, 2008.