

Mid-cycle Meeting Summary SmartPractice STN#125579/0

Application type and number: Biological Licensure Application (BLA), Original Submission (OS), STN 125579/0

Product name: Rubber Panel T.R.U.E. TEST, Rubber Panel Thin-Layer Rapid Use Epicutaneous Patch Test

Proposed Indication: Aid in the diagnosis of allergic contact dermatitis in persons six years of age and older whose history suggests sensitivity to one or more of the five substances included on the Rubber Panel T.R.U.E. TEST

Applicant: SmartPractice Denmark ApS

Meeting date & time: December 7, 2015 1:00PM-2:30PM

Committee Chair: CDR Elizabeth J. Valenti, M.P.H., RAC (U.S.), REHS/RS

RPM: Christina Houck

CBER/FDA Attendees:

Meghna Alimchandani, M.D., Medical Officer, DE/OBE

Lokesh Bhattacharyya, Ph.D., Chief, LACBRP/DBSQ

Karen Campbell, M.S., CMC/Lot Release Reviewer, DBSQ/OCBQ

Rana Chattopadhyay, Ph.D., Regulatory Project Manager, DVRPA/OVRR

Richard Heath Coats, Biologist, DMPQ/OCBQ

CAPT Jon Daugherty, Ph.D., Regulatory Review Branch I Chief, DVRPA/OVRR

Oluchi Elekwachi, Advertising and Promotional Labeling Reviewer, DCM/OCBQ

Marion Gruber, Ph.D., Director, OVRR

Patricia Holobaugh, Ph.D., Bioresearch Monitoring Branch Chief, DIS/OCBQ

Dale Horne, Ph.D., Vaccine Evaluation Branch Chief, DB/OBE

Christina Houck, Regulatory Project Manager, DVRPA/OVRR

Kristine T. Khuc, Pharm.D., Advertising and Promotional Labeling Reviewer, DCM/OCBQ

Taruna Khurana, Ph.D., Product Reviewer, DVRPA/OVRR

Colonious King, BiMo Reviewer, DIS/OCBQ

Joohee Lee, M.D., Clinical Reviewer, DVRPA/OVRR

Loris McVittie, Ph.D., Deputy Director, DVRPA/OVRR

Laurie P. Norwood, Deputy Director, DMPQ/OCBQ

Edward Patten, Associate Director for Manufacturing Science, OCBQ

Ronald L. Rabin, M.D., Laboratory of Immunobiochemistry Chief, DBPAP/OVRR

Roshan Ramanathan, M.D., Clinical Team Leader, DVRPA/OVRR

Carolyn Renshaw, Manufacturing Review Branch I Chief, DMPQ/OCBQ

Jeff Roberts, M.D., Clinical Branch Chief, DVRPA/OVRR

Patricia Rohan, M.D., Epidemiology Reviewer, DE/OBE

Lisa Stockbridge, Ph.D., Advertising and Promotional Labeling Branch Chief, DCM/OCBQ

Wellington Sun, M.D., Director, DVRPA/OVRR

Deborah Trout, Manufacturing Team Leader, DMPQ/OCBQ

CDR Elizabeth J. Valenti, M.P.H., RAC (U.S.), REHS/RS, Chair, DVRPA/OVRR

Lihan Yan, Ph.D., Statistical Team Leader, DB/OBE

Review Committee

Name, Certifications/Degree	Review Role	Module Assignment
Reviewer: Elizabeth J. Valenti, M.P.H. BC: Jon Daugherty, Ph.D	Chair	
Reviewer: Christina Houck, B.S. BC: Jon Daugherty, Ph.D	Regulatory Project Manager	
Reviewer: Jennifer Bridgewater, M.P.H. DD: Jay Slater, M.D.	Regulatory Coordinator	
Reviewer: Joohee Lee, M.D. BC: Jeff Roberts, M.D.	Clinical	
Reviewer: Solomon Ghideon, Ph.D. BC: Dale Horne, Ph.D.	Biostatistics	
Reviewer: Patricia Rohan, M.D. BC: Christopher Jankosky, M.D., M.P.H.	Pharmacovigilance/ Epidemiology	
Reviewer: Taruna Khurana, Ph.D. BC: Jon Daugherty, Ph.D.	CMC/Product	
Reviewer: Al Del-Grosso, Ph.D. DD: William McCormick, Ph.D.	CMC	
Reviewer: Richard Heath Coats BC: Carolyn Renshaw	CMC/Facility	
Reviewer: Karen Campbell, M.S. DD: William McCormick, Ph.D.	CMC/Lot Release	
Reviewer: Colonious King BC: Patricia Holobaugh, M.S.	Bioresearch Monitoring	
Reviewers: Oluchi Elekwachi, Pharm.D., M.P.H. Kristine T. Khuc, Pharm.D. BC: Lisa Stockbridge, Ph.D.	APLB/Promotional Labeling	

Background

BLA STN#125579/0 (originally STN#103738/5031) was submitted by SmartPractice on January 5, 2006. The proposed indication is to aid in the diagnosis of allergic contact dermatitis in persons six years of age and older whose history suggests sensitivity to one or more of the five substances included on the Rubber Panel T.R.U.E. TEST.

A Complete Response (CR) Letter was issued on June 30, 2006 and SmartPractice responded on August 14, 2006. A second CR Letter was issued on February 12, 2007. SmartPractice submitted an Incomplete Response on May 20, 2012. On June 11, 2012 an email was sent explaining the CR issues and providing additional information. The sponsor changed the company name from Mekos Laboratories AS to SmartPractice Denmark ApS during the review process. This change was accepted on February 28, 2013, STN 103738/5098. On June 7, 2013, SmartPractice was advised that upon receipt of the response to the next CR Letter, the supplement would be converted to a new BLA; however, the CR review clock (6 months) would still apply. SmartPractice responded to

the second CR Letter on August 19, 2014. The original PAS, STN 103738/5031, was converted to a BLA, STN 125579/0, in November 2014. A third CR Letter was issued on January 12, 2015. SmartPractice responded to the third CR Letter on August 25, 2015 and it was received on August 27, 2015. The review goal date is February 26, 2016. This is a non-PDUFA product.

The data to support this BLA is from approval of those allergens on the original T.R.U.E. TEST product, for adults, and a pediatric study conducted on the first 28 allergens from the original T.R.U.E. TEST (not yet approved for the legacy product).

Report and Discuss:

1. Reviewer Reports

- 1.1 **Clinical**/Joohee Lee - The clinical review is currently ongoing and no substantive issues that would impact approval or the review timeline have been identified. CBER discussed the study design and pediatric safety and efficacy data from Mekos Study 07 29P1/2/3 401, "Clinical Evaluation of T.R.U.E. TEST Panel 1.1, 2.1, and 3.1 in Children and Adolescents." The open-label study design of the Mekos protocol was agreed upon in 2007, based on the standards for safety and effectiveness defined by CBER at that time. In addition, the adult data with the allergens contained in the Rubber Panel T.R.U.E. TEST support the use of the licensed T.R.U.E. TEST product (which includes the rubber allergens) in adults 18 years of age and older. Based on the regulatory history of this product, the Mekos pediatric study was considered supportive of licensure of the Rubber Panel T.R.U.E. TEST.
- 1.2 **Statistical**/Ghideon Solomon/Lihan Yan - The statistical review is currently ongoing and no substantive issues have been identified.
- 1.3 **Epidemiology**/Patricia Rohan - The Pharmacovigilance Plan (PVP) has been reviewed and no significant safety issues were identified that would require post-marketing activities beyond routine surveillance.
- 1.4 **BiMo**/Colonious King - The Bioresearch Monitoring (BiMo) review is currently ongoing and no substantive issues have been identified. BiMo issued a clinical investigator inspection assignment for protocol 07 29P1/2/3 401, "Clinical Evaluation of T.R.U.E. TEST Panel 1.1, 2.1, and 3.1 in Children and Adolescents." The inspection is still pending receipt of the Establishment Inspection Report (EIR).
- 1.5 **Labeling**/Oluchi Elekwachi - A labeling review was completed in November 2014 and labeling comments will be added to the PI.
- 1.6 **Product/CMC**/Taruna Khurana - The CMC review is currently ongoing and no substantive issues have been identified. An Information Request (IR) was sent to the sponsor on November 13, 2015 for clarification regarding the storage conditions for

the allergen (b) (4) and the finished Rubber Panel, and for the chemical assays and tests used for determining rubber panel allergens during the stability studies.

1.7 **CMC/Al Del-Grosso/Lokesh Bhattacharyya** - The quality control review is currently ongoing and no substantive issues were identified. In-support testing is being planned for two patch components – tentatively Carba Mix ((b) (4)) and Thiuram Mix ((b) (4)). Reagents and consumables are being ordered and standards from sponsor should not be required. An IR will need to be sent to have the analytical methods and validations for the five component assays sent to this license file, including the finished product assays and validations for Carba Mix, Black Rubber Mix, Mercaptobenzothiazole, Mercapto Mix and Thiuram Mix. This will ensure all of the information is in one place under this BLA.

1.8 **CMC Lot Release/Karen Campbell** - The primary review of the Lot Release Protocol (LRP) template has been completed. The review of the Lot Testing Plan is ongoing. Two lots for in-support testing have been received.

1.9 **CMC/Facility/Richard Heath Coats** - The primary review is currently ongoing and no substantive issues were identified. The sponsor indicates no facility or equipment changes have been made since original submission. The Environmental Assessment is currently under review. An IR will need to be sent requesting details on the firm's project plan to come into compliance with QSR regulations since the gap analysis has been completed, and to request clarification in regard to temperature and humidity controls, and the vision system used to inspect final product.

2. Will Discipline Review (DR) Letters be issued? **Information requests will be sent to the sponsor as needed. This is a non-PDUFA product so DR Letters will not be issued.**
3. If the application will be discussed at an Advisory Committee, potential issues for presentation. **This application will not be presented to the APAC.**
4. Determine whether Postmarketing Commitments (PMCs), Postmarketing Requirements (PMRs) or a Risk Evaluation Mitigation Strategy (REMS) are needed. **N/A**
5. National Drug Code (NDC) assignments to product/packaging. **The NDC is provided on the product packaging.**
6. Proper naming convention. **Rubber Panel Thin-Layer Rapid Use Epicutaneous Patch Test**
7. Status of inspections (GMP, BiMo, GLP) including issues identified that could prevent approval. **The review is currently ongoing, however, at this time, no issues have been identified that could prevent approval.**

Confirm

8. Components Information Table was obtained and notification to the Data Abstraction Team (DAT) if discrepancies were found per *SOPP 8401.5: Processing Animal, Biological, Chemical Component Information Submitted in Marketing Applications and Supplements*. If not complete, indicate date it will be completed. **N/A**
9. New facility information is included in the application, requiring implementation of regulatory job aid *JA 910.01: Facility Data Entry*. If not complete, indicate date it will be completed. **Facility information is up-to-date in RMS-BLA.**
10. Status of decisions regarding lot release requirements, such as submitting samples and test protocols and the lot release testing plan. **As previously noted, the review of the lot release protocol is complete and the lot testing plan is currently ongoing.**
11. Unique ingredient identifier (UNII) code process has been initiated. See regulatory job aid *JA 900.01: Unique Ingredient Identifier (UNII) Code* for additional information. **Process initiated December 2, 2015.**
12. PeRC presentation date is set, and the clinical reviewer has addressed waiver/deferral/assessment of the PREA decision. **PeRC is scheduled for January 6, 2016. PeRC forms will be submitted two weeks in advance of scheduled PeRC meeting.**
13. Reach agreement on information to be included in the Mid-cycle communication with the applicant (see section below). The Mid-cycle communication is only for applications that qualify under the PDUFA V Program. **N/A**

Review

14. Major target and mile stone dates from RMS/BLA for this review cycle.
 - Submitted: August 27, 2015
 - Received: August 27, 2015
 - Committee Assignment: September 15, 2015
 - First Committee Meeting: NA
 - Filing Meeting: NA
 - Filing Action: NA
 - Deficiencies Identified: NA
 - VRPAC Determination: September 22, 2015
 - PeRC Determination: January 6, 2016
 - First Draft Reviews Due: December 7, 2015
 - Final Reviews Due: January 27, 2016
 - Action Due: February 26, 2016
 - Action Packing for Posting Due: February 26, 2016

MEETINGS

First Committee Meeting: NA

Filing Meeting: NA

Monthly Team Meetings: TBD

Mid-Cycle Review Meeting: December 7, 2015

PeRC: January 6, 2016

VRBPAC: N/A

Labeling Meetings: December 9, 2015

15. The status of the review for each discipline, inspection, EIR. If any primary reviews have not met the target date, provide the date the review will be completed. Include any consult disciplines. **Discussed above (#1 in the Report and Discuss section).**
16. Discuss pending dates of targets and milestones (e.g. PeRC, labeling discussion). **Discussed above (#14 in the Review section).**
17. Establish a labeling review plan and agree on future labeling meeting activities. **The labeling meeting is scheduled for December 9, 2015.**

Action items:

- Reviews 508 Compliant
- Calendars up to date
- Upload Notifications