Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research

MEMORANDUM

To:	Craig Zinderman, MD, MPH Associate Director for Medical Policy Office of Biostatistics and Epidemiology (OBE) Center for Biologics Evaluation and Research (CBER)
From:	Meghna Alimchandani, MD Deputy Director, Division of Epidemiology (DE), OBE, CBER
Subject:	Safety and Utilization Review for the Pediatric Advisory Committee
Applicant:	SmartPractice Denmark ApS
Product:	Rubber Panel Thin-Layer Rapid Use Epicutaneous Patch Test (Rubber Panel T.R.U.E. TEST)
STN:	125579/13
Indication:	Indicated for use as an aid in the diagnosis of allergic contact dermatitis (ACD) in persons 6 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.
Meeting Date:	Pediatric Advisory Committee Meeting, September 2021

Contents

1 INTRODUCTION

1.1 Objective

This memorandum for the Pediatric Advisory Committee (PAC) presents a comprehensive review of the postmarketing pediatric safety covering a period including 18 months following the approval in accordance with Section 505B (i) (1) of the Food and Drug Cosmetic Act [21 U.S.C. §355c]. The trigger for this pediatric postmarketing safety review was the initial approval of Rubber Panel Thin-layer Rapid Use Epicutaneous Patch Test (Rubber Panel T.R.U.E. TEST), BLA 125579/0 on March 3, 2017 for use in persons 6 years of age and older.

This memorandum documents the Food and Drug Administration's (FDA's) complete evaluation, including review of adverse event (AE) reports in passive surveillance data, periodic safety reports from the manufacturer, data mining, and a review of the published literature.

1.2 Product Description

Rubber Panel Thin-layer Rapid Use Epicutaneous Patch Test (Rubber Panel T.R.U.E. TEST), is a ready-to-use allergen patch test system consisting of 5 allergen and allergen mix patches and a negative control.

Rubber Panel T.R.U.E. TEST is indicated for use as an aid in the diagnosis of allergic contact dermatitis (ACD) in persons 6 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.

1.3 Regulatory History

- March 3, 2017: Approval of original BLA 125579/0 for use in persons 6 years of age and older. This approval is the trigger for the presentation to the 2021 PAC. Of note, this product (b) (4) .

2 MATERIALS REVIEWED

- FDA Adverse Event Reporting System (FAERS)
- Manufacturer's Submissions
  - Rubber Panel T.R.U.E. TEST U.S. package insert; revised 11/2016
  - Applicant response to information request regarding dose distribution data, received April 26, 2021
  - Pharmacovigilance Plan, dated 2015
  - Periodic safety reports
- FDA Documents
  - STN 125579/0 Rubber Panel T.R.U.E. TEST Approval Letter, dated March 3, 2017
- Publications (see Literature Search in Section 7)

3 LABEL CHANGES IN REVIEW PERIOD

There were no safety-related labeling changes during the PAC review period.

4 PRODUCT UTILIZATION DATA

In a response to a request for distribution data[1], as per the sponsor, Rubber Panel T.R.U.E. TEST (b) (4) . Additionally, Rubber Panel T.R.U.E. TEST is (b) (4) .

5 PHARMACOVIGILANCE PLAN AND POSTMARKETING STUDIES

5.1 Pharmacovigilance Plan

The manufacturer's current Pharmacovigilance Plan (PVP) is dated 2015.
An important identified risk is sensitization. An important potential risk is anaphylactic reaction. Missing information includes use of Rubber Panel T.R.U.E. TEST during pregnancy or in nursing mothers.

The above risks are common to the product class, and both sensitization and acute allergic reactions are labeled under *Warnings and Precautions* section of the package insert.

The safety risks for Rubber Panel T.R.U.E. TEST are monitored with routine safety surveillance, including review of adverse event reports submitted to FDA, manufacturer submitted periodic safety reports, published literature, and data mining. There are no postmarketing requirement (PMR) safety-related studies under Food and Drug Administration Amendments Act (FDAAA) of 2007 or Risk Evaluation and Mitigation Strategy (REMS) for this product. There are no outstanding postmarketing commitment (PMC) safety-related studies for Rubber Panel T.R.U.E. TEST (please see section 5.2).

5.2 Postmarketing Studies

Pediatric Research Equity Act (PREA) studies:

- FDA granted a waiver for the pediatric study requirement for ages birth to 6 years because necessary studies are impossible or highly impracticable. This is because contact dermatitis due to rubber allergens is uncommon in patients less than 6 years of age.
- Applicant has fulfilled the pediatric study requirement for ages 6 to 17 years. To support licensure of the Rubber Panel T.R.U.E. TEST in pediatric subjects 6 years of age and older, the applicant submitted data from an open-label, single-site Phase 3 trial of T.R.U.E. TEST panels 1.1, 2.1, and 3.1 in 102 pediatric subjects (6 through 17 years of age) under the original BLA 125579/0.

[1] This information was provided by the manufacturer for FDA review. Distribution data is protected as confidential commercial information and may require redaction from this review.

6 ADVERSE EVENT REVIEW

6.1 Methods

FAERS stores postmarketing AE and medication error reports submitted to FDA for all approved drug and therapeutic biologic products. These reports originate from a variety of sources, including healthcare providers, consumers, and manufacturers. Spontaneous surveillance systems such as FAERS are subject to many limitations, including variable report quality and accuracy, inadequate data regarding the numbers of doses administered, and lack of direct and unbiased comparison groups. Reports in FAERS may not be medically confirmed and are not verified by FDA. FDA does not receive reports for every AE or medication error that occurs with a product. Many factors can influence whether or not an event will be reported, such as the time a product has been marketed and publicity about an event. Also, there is no certainty that the reported event was actually due to the product. FDA does not require that a causal relationship between a product and event be proven.

6.2 Results

Rubber Panel T.R.U.E. TEST (b) (4) and no individual case safety reports have been submitted to FAERS.

6.3 Periodic safety reports

The manufacturer's postmarketing periodic safety reports for Rubber Panel T.R.U.E. TEST were reviewed. No new safety issues were identified, and no actions were taken by the sponsor for safety reasons.

7 LITERATURE REVIEW

A search of the US National Library of Medicine's PubMed.gov database on May 6, 2021, for peer-reviewed literature, with the search term "Rubber Panel T.R.U.E. TEST" or "Rubber Panel Thin-layer Rapid Use Epicutaneous Patch Test" and "safety" limited by human species, and dates from March 3, 2017 (PAC trigger) to date of search May 6, 2021, did not retrieve any publications pertaining to safety.

8 CONCLUSION

This postmarketing pediatric safety review was triggered by the March 3, 2017 approval of BLA 125579/0 for use in persons 6 years of age and older. Rubber Panel T.R.U.E. TEST (b) (4) and there are no passive surveillance adverse event reports. Review of the sponsor's periodic safety reports, and the published literature does not indicate any new safety concerns.

9 RECOMMENDATIONS

FDA recommends continued routine safety monitoring of Rubber Panel T.R.U.E. TEST.