

From: [Valenti, Elizabeth](#)
To: [Kim M. Sullivan \(SULLIVAN@smarthealth.com\)](#)
Cc: [Houck, Christina M](#); [Valenti, Elizabeth](#)
Subject: IR, STN 125579/0
Date: Friday, November 13, 2015 4:35:40 PM

Dear Kim,

We are reviewing your BLA for STN 125579/0 for Rubber Panel T.R.U.E. TEST (Rubber Panel Thin-Layer Rapid Use Epicutaneous Patch Test) for “use as an 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.” After further review we have the following information request:

- 1) We have the following requests for additional analyses for STN 125579:
 - a. Table 12-1 (Summary of Adverse Event Characteristics (All Subjects)) from the pediatric Clinical Study Report for Study Mekos 07 29P1/2/3 401 (p. 52) indicates that 52 adverse events occurred in 35 of the 102 pediatric subjects enrolled in the trial. Please complete a separate table for Visits 3-5 (as shown below).
 - b. Table 2 (Summary of Adverse Reactions Reported Among Adult Subjects 18 Years of Age and Older, Appendix 4a, p. 6) does not specify the allergen(s) associated with the adverse reaction. Please provide a similar analysis of adverse events associated with the five Rubber Panel allergens for the adult subjects as what we requested above for the pediatric subjects.

Table __ : Visit __ : Adverse Events Within __ Days After Removal of T.R.U.E. Test Rubber Panel Allergens

	Black Rubber Mix N=	Carba mix N=	MBT N=	Mercapto mix N=	Thiuram mix N=	Neg Control N=
Adverse Events						
Erythema Mild Moderate Severe	n (%)					
Dermatitis Flare Mild Moderate Severe						
Hyperpigmentation Mild Moderate Severe						
Pruritus Mild Moderate Severe						
Scarring						

Mild Moderate Severe						
Urticaria Mild Moderate Severe						
Rash Mild Moderate Severe						
Delayed Reaction Mild Moderate Severe						
Sensitization (potential) Mild Moderate Severe						
Sensitization (probable) Mild Moderate Severe						
Infiltration/Skin thinning Mild Moderate Severe						

- 2) Section 9.5.1.2 (Safety Variables) of the pediatric Clinical Study Report of Study Mekos 07 29P1/2/3 401 indicates that subjects with adverse events associated with the investigational product were followed until they resolved or until the investigator determined they were “chronic” or “stable.” Please submit additional information regarding the outcome of the adverse events associated with patch testing from Line Listing 16.2.7.1 (Adverse events) in the Clinical Study Report (p.394).
- Subject 048 is documented as having “slight worsening of existing rash” at Visit 3, and a “reaction around panel 2.1 secondary to carba mix rx” Visit 4. There is no information for Visit 5. Please provide additional information regarding the outcome, and duration of follow up.
 - For all subjects with adverse events associated with the Rubber Panel allergens, please provide a table summarizing the outcome at their last follow up visit.
 - For all subjects with positive patch test reactions to the five Rubber Panel allergens, please submit the Case Report Forms and corresponding patch test site photographs.

- 3) Section 7.4.4, Manufacturing Process Flow, submitted on August 27, 2015 in response to Question #6, lists a storage condition of (b) (4) for the allergen (b) (4) and the finished rubber panel. Stability study of the rubber panel was conducted at 25°C/(b) (4) RH and the recommended storage condition for the panel is (b) (4) 25°C in your submission. Please clearly state the storage conditions for the allergen (b) (4) and the finished Rubber Panel.
- 4) Please indicate the chemical assays and tests used for determining rubber panel allergens during the stability studies.
- 5) The batch records submitted on October 21, 2105 in Appendix 1b are in Danish. Please submit the records in English.

Please let me know if you have any questions.

Thank you, Betsy

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