1. SYNOPSIS

Name of Sponsor / Company: Laboratorios LETI, S.L.Unipersonal	
Name of Finished Product:	Prick Test *Alternaria alternata* LETI at 10, 1, 0.1 and 0.01 mg/ml Positive control (histamine dihydrochloride {10 mg/ml}) Negative control (glycerinated phenol saline solution)
Name of Investigational product substance(s):	Experimental product: *Alternaria alternata* allergen extract Control product: Histamine dihydrochloride (10 mg/ml) Glycerinated phenol saline solution
Name of Non Investigational product substance:	Standardized PRICK TEST *Alternaria alternata* 30 HEP/ml (D.02949.02.1)
Title of the study: Biological standardization of *Alternaria alternata* allergen extract to determine the biological activity in HEP units.	
Study centres: 2 sites in Spain	
Study period:	First site initiated: 21st of February 2014 First patient first visit: 21st of February 2014 Last patient last visit: 26th of November 2014
Study phase: II	
Objectives: The objective of this study is to determine the biological activity of a *Alternaria alternata* allergen extract in histamine equivalent prick (HEP) units, in order to be used as in-house reference preparation (IHRP).	
Methodology: Titrated Skin Prick test biological study. Four concentrations of *Alternaria alternata* allergen extract, together with a positive and negative control, were tested in every patient in duplicate on the volar surface of the forearm. The tests were performed at the study sites and all patients remained in the medical rooms under observation at least 30 minutes after the application of the Titrated Skin Prick test.	
Number of patients (planned and analysed): A total number of 30 patients were enrolled and received the study medication. The wheal data of 26 patients were analysed (PP population), since 1	

<table>
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<tr><td>Name of Finished Product:</td><td>Prick Test Alternaria alternata LETI at 10, 1, 0.1 and 0.01 mg/ml
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Negative control (glycerinated phenol saline solution)</td></tr>
<tr><td>Name of Investigational product substance(s):</td><td><u>Experimental product:</u>
Alternaria alternata allergen extract
<u>Control product:</u>
Histamine dihydrochloride (10 mg/ml)
Glycerinated phenol saline solution</td></tr>
<tr><td colspan="2">out of the 30 subjects voluntarily left the study after signing and 3 subjects did not meet eligibility criteria (n=1) or did not meet the Nordic Guidelines(1) statistical criteria for analysis (n=2).</td></tr>
<tr><td colspan="2">Duration of study: The clinical trial consisted of 1 or 2 site visits per patient of approximately 30 minutes, depending on the possibility to assess eligibility criteria during visit 1.</td></tr>
<tr><td colspan="2">Criteria for evaluation: Wheal size area (mm^2) on the skin at the site of the puncture during the immediate phase.</td></tr>
<tr><td colspan="2">Dose response result: 3.96 mg of Alternaria alternata allergen extract is equivalent to 10 HEP.</td></tr>
<tr><td colspan="2">Safety results: No adverse events were reported in the clinical trial.</td></tr>
<tr><td colspan="2">Conclusion: The biological activity of the Alternaria alternata allergen extract is equivalent to 10 HEP = 3.96 mg. The administration of the study medication by prick testing was well tolerated and safe.</td></tr>
<tr><td colspan="2">Date of report: 24th Aug 2015</td></tr>
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