

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

k034057

B. Analyte:

Total IgE

C. Type of Test:

Semi-quantitative immunoassay on test strip

D. Applicant:

Adiatec S.A.

E. Proprietary and Established Names:

Proprietary name: Lacrytest; Common name: IgE immunoassay

F. Regulatory Information:

1. Regulation section:
21 CFR § 866.5510 Immunoglobulins A, G, M, D, E immunological test system
2. Classification:
Class II
3. Product Code:
DGC – IgE antigen, antiserum, control
4. Panel:
Immunology (82)

G. Intended Use:

Lacrytest is a rapid immunoassay for the detection of total IgE in tears. Semi-quantitative detection of total IgE in tears (< 2.5 kIU/liter, 2.5 - 10 kIU/liter, 10 - 40 kIU/liter, and > 40 kIU/liter) indicates local IgE production associated with allergic conjunctivitis. This test is used in the physician office and professional clinical laboratories.

1. Indication(s) for use:
Local (in tears of the eye) IgE production associated with allergic conjunctivitis
2. Special condition for use statement(s):
For prescription use only.
3. Special instrument Requirements:
None

H. Device Description:

Ready-to-use test strip containing reagents to capture and visualize total IgE in tears.

I. Substantial Equivalence Information:

1. Predicate device name(s):
Pharmacia Unicap total IgE assay
2. Predicate K number(s):
k964152
3. Comparison with predicate

Similarities		
Item	Device	Predicate
Antigen Capture material	Anti-human IgE	Anti-human IgE
Differences		
Item	Device	Predicate
Visualization of immobilized IgE	Gold-labeled anti-human IgE	Enzyme labeled anti-human IgE + substrate + chromogenic reagent
Sample matrix	Tears	Serum or plasma
Separation of bound and free analyte	Chromatographic separation on solid phase	Mechanical separation after absorption on solid phase
Instrument required	No	UniCap 100
Analytical assessment	Qualitative/semi-quantitative in 4 concentrations (< 2.5 kIU/liter, 2.5 - 10 kIU/liter, 10 - 40 kIU/liter, and > 40 kIU/liter)	Quantitative

J. Standard/Guidance Document Referenced (if applicable):

None referenced

K. Test Principle:

The device is an immunoassay with all reagents embedded on a test strip that performs without the use of instruments. Total IgE in human tears is bound by anti-human IgE immobilized on test strips in the IgE reactive field of the test strip. Visualization of captured IgE is indicated by colloidal gold labeled anti-human IgE. Excess labeled antibodies are captured by antibodies in the control field. A control line appears in the control field and determines when enough tears have been collected. The presence of IgE in the sample is visualized by the appearance of a dark red line in the reactive field and the control field. Absence of a line in the control field, regardless of the presence of line in the reactive field, indicates an invalid assay result. The area on the support identifying the reactive field and control field are on

the back surface of the support in two colors. A sample with IgE in the normal reference range lacks a line in the reactive field but has a line in the control field. The presence of lines in the reactive and control fields indicates a sample with elevated total IgE levels. The device provides a qualitative/semi-quantitative measure of total IgE in tears when the intensity of color on the test strip is visually observed. Four possible categories of results are possible: negative; < 2.5 kUI/l, 2.5-10 kUI/l, 10-40 kIU/liter, and > 40 kUI/l.

L. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

For precision, the sponsor lists the following intra-run and inter-run precision on 3 samples

intra-run	Sample 1	Sample 2	Sample 3
number of determinations	30	30	30
total IgE levels KUI/L	5	20	50
ranges (intensities)	0-1	2-3	3-3
mean value (intensity)	1	2	3
variance %	7	3	0

inter-run	Sample 1	Sample 2	Sample 3
number of determinations	30	30	30
total IgE levels KUI/L	5	20	50
ranges (intensities)	0-1	2-3	3-3
mean value (intensity)	1	2	3
variance %	10	4	0

No description is given on the precision studies.

b. Linearity/assay reportable range:

None provided

c. Traceability (controls, calibrators, or method):

Correspondence to concentrations of the WHO Third International standard reference preparation is asserted. Artificial tear samples with defined amounts of added IgE (2, 7.5, 30 and 50 kIU/l) were tested in multiple replicates by three professional lab technicians. A single manufacturing lot of test strips was used for the test. The lab testers were blinded to the IgE concentration of the samples. For samples with 2 kIU/l, 7.5 kIU/l, and 50 kIU/l, the accuracy was 100%. For a sample with 30 kIU/l, the accuracy was 93%. Since the accuracy (comparison to target value) is above 90% for each semi-

quantitative range, it can be concluded that semi-quantitative measurement using the strips corresponds with the WHO IgE reference preparation concentrations and imply correspondence with other commercially available total IgE assays using this standard.

d. Detection limit:

Three different dilutions of a control serum from an IgE assay from a different manufacturer were prepared in tears without detectable levels of IgE. One dilution contained an expected value of 2 kIU/l, one dilution contained an expected value of 2.5 kIU/l, and one dilution contained an expected value of 3 kIU/l. Additionally, a human serum sample was diluted with a pool of tears to give an expected value of 2.5 kIU/l. Twenty replicates of each dilution were tested with the assay test strips. For the sample with an expected value of 2 kIU/l, 19 of 20 replicates (95%) tested negative with the test strips. Samples with an expected value of 2.5 kIU/l or 3 kIU/l tested negative from 2 to 9 out of 20 replicates (i.e. from 10% to 45% of 20 replicates tested negative). The claimed detection limit is 2.5 kIU/l.

e. Analytical specificity:

No information provided

f. Assay cut-off:

No information provided

2. Comparison studies:

a. Method comparison with predicate device:

One hundred and sixty-five samples were tested in the proposed and predicate assay for total IgE levels using the tear matrix. A single lot of the proposed assay was used. Testers were blinded to the clinical status and results of the other test method. The following table summarizes results:

Lacrytest	Pharmacia UniCAP		total
	Positive > 2.5 kIU/l	Negative < 2.5 kIU/l	
Positive	89	1	90
negative	8	67	75
Total	97	68	165

Exact binomial
95% Conf. limit

observed
agreement= 0.945 0.899 to 0.975
expected
agreement= 0.508
Kappa = 0.889
std error = 0.0776

P(kappa=0)= $p < 0.001$

The probability that the observed agreement is significantly higher than chance agreement is < 0.001 . This indicates significantly better agreement between test results of the proposed and predicate assay than chance agreement. The probability that observed agreement is equivalent with perfect agreement (kappa = 1) was 0.076. Since the probability is not less than 0.05, then it can be concluded that agreement is equivalent with perfect agreement.

Among 68 samples tested in both assays, agreement of negative results in both assays was 98.5%. Among 25 samples with values between 2.5 and 10 kIU/l, agreement in both assays was 85.7%. Among 18 samples with values between 10 and 40 kIU/l, agreement was 76%. Among 44 samples with values greater than 40 kIU/l, agreement was 90.9%. Agreement of positive results in both assays is estimated to be 82% (exact binomial confidence interval 73% - 89.6%), the numerical average of agreement in the 4 categories.

To compare test results of physicians at the point-of-care with test results of professional lab technicians, 3 sites tested samples. At each site a physician tested 5 negative and 5 positive samples. At each site 3 lab technicians also tested the same positive and negative samples. Negative samples were randomly selected subjects visiting a physician office without allergy symptoms. Positive samples were randomly selected patients visiting a physician's office with clinical evidence of seasonal allergy, acute allergy, or periodic allergy. A quality control material prepared from a sample of the WHO standard reference material (75/502) was provided to each site. The agreement of test results among negative samples when tested by physician vs lab technician was 93%, 93%, and 87% at each of the three sites. The agreement of test results among positive samples

when tested by physician vs lab technician was 83%, 89%, and 100% at each of the test sites. The approximate agreement of physician test result with lab technician test result for all samples was 90%.

b. Matrix comparison:

No information comparing IgE concentrations from serum and tears was provided

3. Clinical studies:

a. Clinical sensitivity:

No information provided

b. Clinical specificity:

No information provided

c. Other clinical supportive data (when a and b are not applicable):

4. Clinical cut-off:

No information provided

5. Expected values/Reference range:

One hundred patient samples were randomly collected from subjects visiting a physician. Patients were absent allergy symptoms, allergy history, and ocular inflammation. Of the 100 subjects, 87 subjects had results less than 2.5 kIU/l. Thirteen patients had concentrations from 2.5 to 10 kIU/l. From this data, 85% of normal subjects had truly negative test results. The exact binomial 95% confidence interval for the normal subjects is 76.5 – 91.4%. Therefore, it can be concluded that approximately 90% of normal subjects will have negative test results.

M. Conclusion:

Based on information included in the file, the Lacrytest can be recommended as substantially equivalent to the predicate device, Pharmacia Unicap total IgE assay, regulated under 21 CFR 866.5510, Immunoglobulins A, G, M, D, E, immunoglobulin test system (class II, product code - DGC IgE antigen, antiserum, control).