

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION  
DECISION SUMMARY  
INSTRUMENT ONLY TEMPLATE**

**A. 510(k) Number:**

k112910

**B. Purpose for Submission:**

This submission is for modification of the OPTIGEN® Allergen-Specific IgE Assay System. The modified version is the AP 720S™ Semi-Automated Instrument that provides a semi-automated option for processing the assay. In the existing device, all test operations are manual; in the semi-automated processor, the instrument automates the manual steps.

**C. Manufacturer and Instrument Name:**

Hitachi Chemical Diagnostics, Inc., AP 720S™ Semi-Automated Instrument

**D. Type of Test or Tests Performed:**

Allergen Specific anti-IgE antibodies assays

**E. System Descriptions:**

1. Device Description:

The AP 720S™ Semi-Automated Instrument is a modification of its predecessor product OPTIGEN® Allergen Specific IgE Assay, cleared under k051677. The difference between the two systems is that the modification includes a semi-automated processor for customer convenience; the predecessor product requires manual operation. The AP 720S™ Semi-Automated instrument runs OPTIGEN® Allergen Specific IgE Assay, a solid phase *in vitro* test used for the semi quantitative measurement of circulating allergen-specific IgE antibodies to allergen in human serum. The instrument re-hydrates the device, aspirates the serum sample, incubates for 2 hours, washes, aspirates the conjugate, incubates for 2 hours, washes and aspirates the photoreagents. The device is then manually removed from the instrument and read in the same CLA-1 Luminometer as the manual assay. The AP 720S™ Semi-Automated Instrument comes with AP 720S™ Instruction Manual, AP 720S™ LCD Panel Guide and AP 720S™ Quick Start.

2. Principles of Operation:

The AP 720S™ Semi-automated Instrument is a software controlled system that

includes a processor to automate the manual steps of the assay, from device re-hydration step to addition of Photoreagents into the device.

3. Modes of Operation:

Semi-automated; the software-controlled processor controls assay protocol steps to control the in vitro diagnostic assay workflow. The Operator loads and checks that the Wash Buffer Bottle, Deionized Water Bottle, and Antibody Reservoir are filled, and that the Waste Bottle is emptied prior to the Auto-Run. Operator also fills the Photoreagent Reservoir with Photoreagent mixture and loads the required number of empty Sample Cups into the Sample/Reagent Rack. Following this, the Operator transfers the correct volume of each prepared sample into the Sample Cups, and installs the Sample/Reagent Rack. The instrument is set to “start mode” and the processor software controls the OPTIGEN® Allergen Specific IgE assay workflow.

4. Specimen Identification:

The operator uses Manual keyboard entry and enters patient sample identification manually into the instrument at the time of assay.

5. Specimen Sampling and Handling:

Specimen sampling and handling is performed manually; Sample handling instructions are described in the Package Insert. Operator loads the filled sample cups into the Sample/Reagent Rack and starts the AP 720S™ Semi-Automated instrument run.

6. Calibration:

The AP 720S™ processor does not require calibration.

7. Quality Control:

The device contains a Positive Procedural Control as well as a Negative Blanking Control. These controls ensure the reagents are added in the correct order and filled to the proper levels.

8. Software:

FDA has reviewed applicant’s Hazard Analysis and Software Development processes for this line of product types:

Yes   X   or No

**F. Regulatory Information:**

1. Regulation section:

21 CFR § 866.5750, Radioallergosorbent (RAST) immunological test system

2. Classification:

Class II

3. Product code:

DHB - System, Test, Radioallergosorbent (RAST), Immunological

4. Panel:

Immunology (82)

**G. Intended Use:**

1. Indication(s) for Use:

The AP 720S™ Semi-Automated Instrument is a semi-automated processor for use with the OPTIGEN® Assay. The OPTIGEN® Assay is an *in vitro* diagnostic test for use in the semi-quantitative determination of circulating allergen-specific IgE concentrations in human serum. It is intended to aid in the clinical diagnosis of IgE mediated allergic disorders in conjunction with other clinical findings. The device is designed for use in clinical laboratories.

2. Special Conditions for Use Statement(s):

For Prescription Use Only. In addition, the CLA-I Luminometer is used to read the results of the test with the AP 720STM Semi-automated Instrument.

**H. Substantial Equivalence Information:**

1. Predicate Device Name(s) and 510(k) numbers:

OPTIGEN® Allergen Specific IgE Assay, k051677

2. Comparison with Predicate Device:

Similarities		
Item	Device	Predicate
Intended Use/ Indications for Use	The OPTIGEN® assay is an <i>in vitro</i> semi-	Same

Similarities		
Item	Device	Predicate
	quantitative test, which provides a measurement of the circulating allergen specific IgE antibodies in human serum.	
Sample Type	Serum	Same
Methodology	Immunoassay	Same
Reagent Packaging	Kit with all required reagents	Same
Testing Environment	Professional use	Same
Throughput	Approx. 5 hours	Same
Processing temperature	18-30°C	Same
Reader	CLA-1 Luminometer	Same

Differences		
Item	Device	Predicate
Sample Processing	The AP 720S™ Semi-automated Instrument is a semi-automated processor for the OPTIGEN® assay.	Manual
Consumables	Device plugs	Device tips and sample cups

**I. Special Control/Guidance Document Referenced (if applicable):**

CLSI EP05-A2 — Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline - Second Edition

EP06-A — Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

**J. Performance Characteristics:**

1. Analytical Performance:

*a. Method comparison:*

Three validation experiments were performed using the OPTIGEN® Universal Panel 20 (k051677) at two testing sites to confirm that the performance of the OPTIGEN® allergen specific IgE assay with the manual method (k051677) and the AP 720S™ Semi-Automated Instrument is equivalent. The validation studies were done using 25 patient serum samples on 20 allergens resulting in 500 test results. As per assay instructions,

samples that had net IU below LoD were considered “class-0” (no antibodies detected,) and samples having net IU of 27-65 were considered “class-I” (low levels of antibodies detected). The three studies included:

- Study-1: Manual Assay (K051677) to AP 720S™ Semi-Automated Instrument.
- Study-2: AP 720S™ Semi-Automated Instrument to AP 720S™ Semi-Automated Instrument.
- Study-3: AP 720S™ Semi-Automated Instrument day-to-day.

The semi-quantitative results were dichotomized, and following positive and negative agreement rates were obtained.

Study	Positive percent agreement	Negative percent agreement	+/- 1 class
1	≥ 85%	≥ 90%	≥90%
2	≥ 85%	≥ 90%	≥90%
3	≥ 85%	≥ 90%	≥90%

In addition, per class comparison was done between the manual and semi-automated methods with all sera and all allergens (using CLA class) as taken from the AP 720S™ validation; the results are summarized in the table below:

		Manual					
		CLA-1	0	1	2	3	4
Semi-automated	0	205	20	1	0	0	226
	1	4	35	24	1	0	64
	2	0	10	44	6	2	62
	3	0	0	3	18	10	31
	4	0	0	0	6	111	117
	Total	209	65	72	31	123	

Almost all disagreements were within 1 category. Only 4/500 differed by 2 categories and none differed by 3 or more categories.

*b. Precision/Reproducibility:*

Assay precision was assessed for both the OPTIGEN® manual and the semi-automated methods, according to CLSI EP5-A2. The studies, including within-run and between-run were performed for 2 allergens (Mugwort and Egg White). Three to four samples, representing CLA “class-0” (20-25% below cut-off), “Low class-1” (20-25% above cut-off), “High class-1” (50 to 65 net LUs) and “class-2” (66 to 142 net LUs) were tested in replicates of 2, twice per day for 10 days (total n=40).

The results from within-run and between-run studies in manual and semi-automated methods were similar and are summarized below:

Within-run

		AP720S™ Semi automated			Manual		
		Mean LUs	SD	%CV	Mean LUs	SD	%CV
Mugwort	Class 0	26.4	5.8	22.1	20.7	7.1	34.5
	Low Class 1	41.9	11.6	27.6	38.2	7.8	20.3
	Class 2	124.3	21.4	17.2	112.3	18.1	16.1
Egg White	Class 0	20.7	7.4	35.9	19.7	7.4	37.6
	Low Class 1	42.9	6.4	15.0	39.1	10.9	27.8
	High Class 1	58.6	11.7	19.9	55.2	12.1	21.9
	Class 2	100.2	17.8	17.8	102.4	20.6	20.2

Between-run

		AP720S™ Semi-automated			Manual		
		Mean LUs	SD	%CV	Mean LUs	SD	%CV
Mugwort	Class 0	26.4	3.5	13.2	20.7	6.1	29.5
	Low Class 1	41.9	0.0	0.0	38.2	7.1	18.5
	Class 2	124.3	17.9	14.4	112.3	1.7	1.5
Egg White	Class 0	20.7	4.2	20.4	19.7	0.0	0.0
	Low Class 1	42.9	3.5	8.1	39.1	9.0	23.0
	High Class 1	58.6	8.2	13.9	55.2	3.0	5.4
	Class 2	100.2	0.0	0.0	102.4	14.3	14.0

c. *Linearity:*

Linearity was determined following CLSI Standard EP6-A using the OPTIGEN® manual and AP 720STM Semi-Automated Instrument methods. The CLA-1 reader having a range from 0 to 300 Light Units (LU) was used for both reads. Two allergens including Aspergillus and Timothy were used to demonstrate linearity of the continuous LU signal, and the results are tabulated below:

AP 720S™ Linearity Summary

Allergen	Regression Equation	R <sup>2</sup>	95% CI Slope	95% CI Intercept
Aspergillus	y = 1.04x + 2.61	0.99	0.95 – 1.12	-12.1-17.4
Timothy	y = 1.04x – 3.68	0.99	0.96 – 1.12	-17.5 – 10.2

Manual Linearity Summary

Allergen	Regression Equation	R <sup>2</sup>	95% CI Slope	95% CI Intercept
Aspergillus	y = 1.05x + 5.62	0.99	0.96 – 1.13	-9.1 - 20.4
Timothy	y = 1.00x + 3.56	0.99	0.90 – 1.10	-14.8 – 22.0

d. *Carryover:*

Not applicable

e. *Interfering Substances:*

Not applicable

2. Other Supportive Instrument Performance Data Not Covered Above:

*Limit of Detection (LoD):* LoD was determined for the OPTIGEN® Allergen Specific Assay with AP720S™ Semi-Automated Instrument using 20 allergens. The methods used were in alignment with CLSI EP17-A. The LoD for each allergen was determined by running 10 low “class-1” sera. Each serum was run over 10 different days. For each allergen, the criterion for use of a serum to calculate the LoD was that the mean LU for the runs for that allergen had to fall between 1 and 46 LU (halfway point for Class 1), and there had to be no more than one zero value among the 20 values obtained. Results showed that the LoD was not uniform across allergens and instead was a range from 11.6 LUs to 28.2 LUs.

**K. Proposed Labeling:**

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

**L. Conclusion:**

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.