CLIA Waiver by Application Approval Determination

Decision Summary

A. Document Number

CW230008

B. Parent Document Number

K231151

C. CLIA Waiver Type:

Dual 510(k) and CLIA Waiver by Application (Dual Submission)

D. Applicant

Kenota Inc.

E. Proprietary and Established Names

Kenota 1 Total IgE
Kenota 1 (instrument)

F. Measurand (analyte)

Human Immunoglobulin E (IgE)

G. Sample Type(s)

Capillary fingerstick whole blood

H. Type of Test

Semi-quantitative, fluorescence lateral flow immunoassay

I. Test System Description

1. Overview

The Kenota 1 Total IgE measures total IgE in human capillary whole blood on the Kenota 1 instrument is intended for in vitro diagnostic use as an aid in the clinical diagnosis of IgE-mediated allergic disorders in conjunction with other clinical findings. The test is to be used in allergist/immunologist offices.

The Kenota 1 Total IgE consists of Kenota 1 Total IgE Cartridge and other test system components including: Kenota 1 instrument with Kenota 1 Developing Solution, Kenota 1 Total IgE External Controls, and Kenota 1 Sample Collection Kit specific to Kenota 1 Total IgE.

2. Test System Components

   Refer to K231151 for details.

3. Result Interpretation

   The Kenota 1 Total IgE test results are generated automatically by the instrument. No further calculation is needed by operators. The test results can be viewed, printed, and emailed by or to the ordering allergists / immunologists from the tablet screen on the Kenota 1 instrument.

   The test results are provided in the semi-quantitative categories to the ordering allergist / immunologist for interpretation as follows:

Semi-quantitative Category
Below LoQ (< 5 kU/L)
Very Low (5-34 kU/L)
Low (35-100 kU/L)
Medium (101-200 kU/L)
High (201-540 kU/L)
Very High (541-900 kU/L)
Above Measuring Range (> 900 kU/L)

   The results are intended to be used as an aid in the clinical diagnosis of IgE-mediated disorders in conjunction with other clinical findings.

J. Demonstrating "Simple"

The following demonstrates how the Kenota 1 Total IgE is simple per the *Guidance for Industry and FDA Staff: Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Wavier Applications for Manufacturers of In Vitro Diagnostic Devices*, issued January 30, 2008.

- The Kenota 1 Total IgE uses unprocessed fresh fingerstick (FS) whole blood samples directly collected using the Lithium-Heparin anticoagulant coated blood collectors.
- Untrained operators can conduct the test by performing four simple steps: 1) collect fingerstick specimen, 2) transfer sample to the cartridge with a fixed volume pipette, 3) run the test on the instrument, and 4) read the results automatically generated on the screen of the instrument.
- There is no reagent handling, all reagents are inside the single-use cartridge. The test cartridges are QR (Quick Response)-coded and can be inserted into the instrument only in one direction.

- The test does not require any operator intervention during the analysis step.
- Technical or specialized training is not required for troubleshooting or error code interpretation. If an error code is shown, simple on-screen instructions are provided to the operator.
- There are no required electronic or mechanical maintenance tasks. System Control Checks for temperature are built-in to ensure the instrument is operating within validated heating / cooling, humidity, and tilt specifications.
- Interpretation for categorizing test results is automated. Categories are displayed on the instrument screen and may be printed. No further calculation or interpretation by the operator is required.
- The instrument screen is designed for ease of use and features a color display that facilitates easy-to-read messages. Error messages are reported on a screen and there is no interpretation required by the operators. Error messages are unambiguous and include easy-to-interpret solutions.
- The Quick Reference Guide and Kenota 1 Quick Setup Guide are written at a 7th grade comprehension level. In addition, the instrument software includes an instructional video that the operator can follow. The instructional video demonstrates how to collect specimen, prepare a sample, add the sample to the cartridge, and load the cartridge into the instrument.

K. Demonstrating "Insignificant Risk of an Erroneous Result"- Failure Alerts and Fail-safe Mechanisms

1. Risk Analysis

   Risk analysis was performed using the Failure Modes and Effects Analysis (FMEA) Method. In addition, the recommendations in the Guidance for Industry and FDA Staff: Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices (issued February 26, 2020) and ISO 14971*:2012 - Medical Devices - Application of Risk Management to Medical Devices* were considered. Potential sources of error that could adversely affect system performance were identified and mitigated first through system design and then through additional cautions in the labeling. The identified risks which could result in erroneous test results were evaluated in flex studies which stressed the functional limits of the test.

2. Fail-Safe and Failure Alert Mechanisms

   a. Lockout features

      The Kenota 1 Total IgE Cartridge is shaped and marked with arrows to fit only into the proper location and orientation on the sleeve.

      The tablet screen displays an error code for 'no sample detected' if the cartridge is inserted into the sleeve and the drawer is closed before adding a sample syringe.

The sleeve prevents re-use of a cartridge by releasing the cartridge into a trash box within instrument (Kenota 1) after testing. The instrument software detects a used cartridge and displays an error message that a new cassette is required. The instrument firmware will invalidate a previously used cartridge.

If a cartridge is removed before the test has completed, the instrument will display an error code. Test validity is further supported by the external controls.

The instrument will not initiate a test if the drawer is not fully closed. The instrument will display message "sample detected close lid". If excessive time passes, the instrument will invalidate the cartridge.

If the drawer is opened during a test but the cartridge is not disturbed, the instrument will provide an audible sound and display a message to close the drawer.

If power is lost during a test run, the test is cancelled, and the tablet screen displays an error code. The instrument instructs the operator that the test cartridge is used and needs to be replaced.

The instrument has a lockout function if an operator attempts to use the instrument outside of the specified temperature, humidity, and tilt range.

b. Procedural Control

Operators are required to scan QR codes on the cartridge before loading the cartridge on the sleeve.

c. External Controls

Performance of the Kenota 1 Total IgE is checked with the Kenota 1 Total IgE external controls. The external controls are stabilized control materials used for checking the performance of the Kenota 1 Total IgE cartridge, Kenota 1 instrument, and intended users' operational procedures. Results of the external control session are not interpreted by the operator but by the Kenota 1 instrument. If the external control session fails, the Kenota 1 is automatically locked out and the operator is instructed to contact Kenota Support. An external control session is required when a new lot of Kenota 1 Total IgE Test Kit is used, or a new operator is qualified while a monthly (every 30 days) maintenance session is performed.

3. Flex Studies

Operational limits of the Kenota 1 Total IgE were tested in the following series of studies:

a. Flex study for temperature and relative humidity:

A study was performed to evaluate whether performing tests using an instrument and cartridges at a wide range of temperature and relative humidity (RH) conditions could

lead to erroneous results. If the room temperature and/or humidity conditions exceed, the instrument's limit (17–28°C, 10–90% RH) the instrument's failure alert check is triggered. The instruments and cartridges were exposed to seven test conditions (see Test condition 2 to 8 below) and the test was performed using two fresh venous whole blood samples (~ 45 kU/L and ~450 kU/L) in 10 replicates:

1) Control condition: 22°C, RH 37%
2) Test condition: 17°C, RH 6%
3) Test condition: 17°C, RH 88%
4) Test condition: 28°C, RH 11%
5) Test condition: 27°C, RH 86%
6) Test condition: 16°C, RH 32%
7) Test condition: 29°C, RH 22%
8) Test condition: 22°C, RH 96%

The test results were within ± 5% bias in Test Condition 2, 3), and 4 compared to Control condition 1 above. The run was not initiated when the instrument detected the room temperature and/or humidity conditions exceeding the instrument's limit (17–28°C, 10–90% RH) in Test condition 6, 7, and 8 above and the tablet screen displayed an error message (e.g., 'Room Temperature Too High'). This study demonstrates that the test reports valid results only when the testing room temperature and/or relative humidity conditions are within the instrument's operating specification (17–28°C, 10–90% RH) based on the instrument's failure alert check.

b. Flex study for instrument on vibrating surface:

A study was performed to evaluate whether performing tests using the instrument in environments subject to vibrations leads to erroneous results. A fresh venous whole blood sample (~ 200 kU/L) was tested in 24 replicates each on a surface with no/minimal environmental vibration and a surface with extreme environmental vibration. An unbalanced centrifuge was run at 3000 RPM. A vibration meter was used to detect the vibrations for 1 minute at specific locations that were measured at 0.33g on the top of the centrifuge, 0.09g on the table next to the centrifuge, 0.07g on the side of the instrument, and 0.16g on the top of the instrument. This study demonstrates the test is unaffected (within ±5% bias) by running a test on vibrating surface.

c. Flex study for instrument on tilted surface:

A study was performed to evaluate whether performing tests using the instrument in environments subject to tilted surface leads to erroneous results. If the tilted surface beyond its specification limit is detected, the instrument's failure alert check is triggered. A fresh venous whole blood sample (~ 175 kU/L) was tested in a control condition (no tilt / 0 degree, 24 replicates), slight tilt (2 degrees, 24 replicates), moderate tilt (4 degrees, 3 replicates), and high tilt (8 degrees, 3 replicates). The test results were within ±5% bias on front/back and left/right tilt at ±2 degrees. The run was not initiated when the instrument detected a front/back and left/right tilt at ±4 degrees and ±8 degrees, showing an error message "Tilt Error" on the tablet screen.

This study demonstrates that the test reports valid results only when the instrument is placed up to 2-degree tilted angle.

d. Flex study for sub-optimal lighting conditions:

A study was performed to evaluate test performance when operators perform testing under varying lighting conditions. A fresh venous whole blood sample was (~ 200 kU/L) tested in 48 replicates in each of the following conditions:

1) Control condition: office lighting (≅ 500 lux)
2) Test condition: direct sunlight (≅ 10000 lux)
3) Test condition: dark (≅ 5 lux)

The test results were within ±5% bias in Test condition 2 and 3 compared to Test condition 1 above. This study demonstrates that the test operators were able to perform the tests in various lighting conditions.

e. Flex study for mechanical impact on instrument:

A study was performed to evaluate whether mechanical impacts (100g object dropped five times from 30 cm) to the instrument could lead to biased results. A fresh venous whole blood sample (~ 220 kU/L) was tested in 24 replicates in each of the following conditions:

1) Control condition: no mechanical impact
2) Test condition: mechanical impact during run initialization failure alert checks
3) Test condition: mechanical impact during sample dispensing
4) Test condition: mechanical impact during cartridge imaging

The test results were within ±5% bias in Test condition 2, 3 and 4 compared to Control condition 1 above. This study demonstrates that the test is unaffected by mechanical impacts on the instrument during different stages of testing.

f. Flex study for samples with air bubbles:

A study was performed to determine the ability of the instrument's failure alert check to detect the presence of air bubbles in the sample after the instrument mixes the sample in the sample collection kit (SCK). Air bubbles introduced into the SKC syringe are typically resolved by the sample mixing performed by the instrument and unresolved bubbles are assessed by a failure alert check, preventing SCK with large bubbles from beginning a run. If air bubbles exceeding the size limit are detected by the instrument, the failure alert check is triggered. A fresh venous whole blood sample (~ 194 kU/L) was tested in 24 replicates with (Test condition) and without (Control condition) induced air bubbles. For the test condition, air bubbles were intentionally introduced until two sample syringes passed the run initialization failure alert checks (approximately 1–4 µL air bubble size). The test results were within ±5% bias in Test condition compared to Control condition. This study demonstrates that

accurate results can be obtained if operators introduce air bubbles in the test sample up to approximately 4 µL size.

g. Flex study for different cartridge positions within the sleeve:

A study was performed to determine if the test results are affected by the location within the stack of cartridges in the sleeve. Each sleeve holds up to 15 Kenota 1 Total IgE cartridges. A fresh venous whole blood sample (~ 200 kU/L) was used to evaluate using cartridges in three different location categories (Low: position 1-5, Middle: position 6-10, High: position 11-15). The sample was tested in 12 runs with 5 replicates per run that generated a total of 60 replicates per location category (e.g., 60 results from Low category). The average of test results was within ±5% bias in comparison by the location category (Low, Middle, and High). This study demonstrates that the test results are unaffected by different cartridge positions within the sleeve.

h. Flex study for delayed procedure between sample collection and initiation of testing:

A study was performed to determine whether a delayed procedure between the collection of a fresh fingerstick whole blood and the initiation of the test on the instrument could lead to erroneous results. A fresh FS whole blood sample (~ 230 kU/L) was tested using the instrument in 48 replicates for condition 1, 2 and 3 and in 24 replicates for condition 4 and 5 below:

1) Control condition: no delay
2) Test condition: 1 hour delay for FS whole blood in the blood collector (Minivette POCT lithium-heparin) before transferring to the sample collection kit (SCK) syringe
3) Test condition: 1 hour delay for FS whole blood in in the SCK syringe before adding the sample diluent
4) Test condition: 1 hour delay for FS whole blood sample in the SCK syringe after adding the sample diluent
5) Test condition: 2-hour delay for FS whole blood sample in the SCK syringe after adding the sample diluent

The test results were within ±5% bias in Test condition 2, 3, 4 and 5) compared to Control condition 1 above. This study demonstrates that accurate test results can be obtained if operators delay a procedure between sample collection and initiation of testing for up to one or two hours depending on procedures.

i. Flex study for samples prepared in variable volumes:

A study was performed to evaluate the instrument's ability to detect an incorrect volume of the test sample in the sample collection kit (SCK) when operators load incorrect test sample volumes in the SCK using two fresh venous whole blood samples (~ 40 kU/L and 410 kU/L). The directed test volume is 100 µL blood with 100 µL added Sample Diluent (total 200 µL Test sample volume in the SCK) loaded on the instrument. The test samples were loaded in the SCK and tested in five

replicates for Control condition 1, Test condition 2, and 3 and in three replicates for Test condition 4 and 5 below:

1) Control condition: 100 µL blood and 100 µL Sample Diluent
2) Test condition: 80 µL blood and 100 µL Sample Diluent
3) Test condition: 100 µL blood and 80 µL Sample Diluent
4) Test condition: 50 µL blood and 100 µL Sample Diluent
5) Test condition: 100 µL blood and 50 µL Sample Diluent
6) Test condition: 100 µL blood and 200 µL Sample Diluent

The test results were acceptable in Test condition 2 and 3 compared to Control condition 1 above. The testing was not initiated in Test condition 4 and 5 and the tablet screen showed an error message "SAMPLE VOLUME LOW". The testing was not initiated in Test condition 6 and the tablet screen showed an error message "SAMPLE VOLUME HIGH". This study demonstrates that reliable test results can be obtained if operators loaded a test sample volume down to 180 µL on the instrument.

j. Flex study for missed or misplaced SCK plunger:

A study was performed to evaluate if the samples pass the instrument's failure alert checks when the plunger in SCK misses or is misplaced for initiating a test run. The test was performed using a fresh venous whole blood sample in three replicates (syringes) in each of the following conditions:

1) Control condition: plunger in correct position in SCK
2) Test condition: missed plunger in SCK
3) Test condition: plunger not filled inserted to SCK (3.3 ± 0.2 mm above the directed level of the SCK syringe)
4) Test condition: plunger not filled inserted to SCK (3.8 ± 0.2 mm above the directed level of the SCK syringe)
5) Test condition: plunger inserted up-side-down in SCK

The sample passed failure alert checks under Control condition 1 and Test condition 3. The testing was not initiated under Test condition 2 and 5 with an error message "SAMPLE PLUNDGER NOT LOADED" on the tablet screen. The instrument drawer was not closed in Test condition 4. This study demonstrates that accurate test results can be obtained if operators misplace the plunger in SCK up to 3.3 ± 0.2 mm above the directed level of the SCK syringe.

k. Flex study for samples collected with soap residue:

A study was performed to evaluate whether the presence of soap residue on a patient's hands at the time of sample collection affects the test results. Five fresh fingerstick (FS) whole blood samples were collected from each of the five fingers on one hand that was not washed prior to the sample collection (Control condition) then pooled together for a FS whole blood sample at 283.1 kU/L. The donor's other hand was washed with soap by an operator (Test condition) then immediately five fresh

FS whole blood samples from each of the five fingers were collected and pooled together for a FS whole blood sample at 288.7 kU/L. Each condition was tested with 24 replicates. The test results were within ±5% bias in Test condition compared to Control condition. This study demonstrates that accurate test results can be obtained if operators collect FS whole blood from patients' fingers with soap residue.

l. Flex study for test cartridges loaded in an incorrect orientation:

A study was performed to determine if inserting the cartridge into the sleeve of the instrument in an incorrect orientation triggers the failure alert check. The cartridge has a laser barcode etched on its side and is used to identify the test and confirm the orientation of the cartridge before running the test. A fresh venous whole blood sample was tested in five replicates with cartridges placed backwards (Test condition 2), upside down (Test condition 3), and backwards with upside down (Test condition 4). The test conditions triggered the failure alert checks preventing the instrument from running the test for Test condition 2 with an error message "CARTRIDGE BARCODE MISSING", and Test condition 3 and 4 with an error message "CARTRIDGE UNSTACK FAILED". This study demonstrates that the test is not initiated if operators load test cartridges in an incorrect orientation in the sleeve of the instrument.

m. Flex study for sample stayed in tilted SCK before initiating test run:

A study was performed to determine if the samples pass the instrument's sample homogeneity failure alert checks when the collected samples stay in the SKC placed on a tilted angle before being added to the sleeve. The instrument has several run initialization checks for sample quality. SCKs with collected samples were tilted for 5 minutes prior to starting a test run. A sample was tested five times after the SKC is tilted on 1) a level surface (no tilt), 2) +10 degree tilt with SKC needle end up, and 3) -10 degree tilt with SKC needle end down. The sample passed failure alert checks under all three SKC tilt conditions above without displaying an error message on the instrument's tablet screen. This study demonstrates that samples pass the instrument's sample homogeneity failure alert checks when the sample stayed in tilted SCK up ±10 degrees.

L. Demonstrating "Insignificant Risk of an Erroneous Result" –Accuracy

To demonstrate that the Kenota 1 Total IgE poses an insignificant risk of erroneous results, the sponsor submitted a clinical study which was also used to support FDA clearance under K231151.

1. Comparision Study

a. Study Design

i. Study Sites and Duration

Clinical performance characteristics of the Kenota 1 Total IgE were evaluated in a multi-site prospective study between January 2023 and April 2023 in three U.S. sites located in Minnesota, North Carolina, and Virginia. The study was completed within two months at each site. All three sites consisted of allergy speciality care clinics and qualified as representative of CLIA waived intended use sites for the Kenota 1 Total IgE testing intended for capillary whole blood samples. For comparison, the venous blood specimen collected from the same patients at these CLIA waived sites by phlebotomists were transferred to a clnical laboratory (moderate complexity) for the comparator (ImmunoCAP Total IgE, K161899) testing intended for venous serum and plasma samples.

ii. Operators

There was a total of 11 operators representative of intended CLIA waived users across the three clinical testing sites. The operators consisted of administrative personnel, medical assistants, nurses, a graduate student, and patient service representatives. The test operators who participated in the study were untrained in the use of the Kenota 1 Total IgE and none were trained laboratory technicians. Upon completion of the study, the operators at each site were asked to complete an Operator Questionnaire that asked them to rate the ease of use of the test procedure.

iii. Instructions for Use

The operators were given the Quick Reference Guide (QRG) and Kenota 1 Quick Setup Guide (QSG). No other materials or instructions were provided, and the operators received no training in the use of the test system.

iv. Subjects and samples

The subjects were recruited as representative of the intended use population, for patients with eczema or atopy coming in for regular appointments to the allergy speciality care clinics. Individuals with skin damage, burns or scars at the site of venipuncture on both arms were excluded. Patients provided fresh fingerstick whole blood collected by a total of 11 untrained operators at three CLIA-waived sites in the U.S. using Minivette POCT lithium-heparin tubes

for the Kenota 1 Total IgE. The same patients provided venous whole blood collected by phlebotomists for the comparator at the same three CLIA-waived sites in the U.S. A total of 411 eligible subjects, aged 6 to 80 years, participated in the study. Of these 411 subjects, 15 subejcts did not participate in the study. Three hundred ninety six (396) subjects were tested with Kenota 1 Total IgE and 392 subejcts had valid results and four subjects had Invalid results. Percent of Invalid resuts was 1.0% (4/396) with 95% CI: (0.4%; 2.6%). Among 396 subjects, 39 subjects did not have venous whole blood for the comparative method. In the analysis of the clinical performance study data, there were 357 (=396-39) subjects with valid Kenota 1 Total IgE results and the comparative method results.

v. Comparative Method (CM)

ImmunoCAP Total IgE (K161899) from Phadia AB

b. Results and Analysis

i. Allowable Total Error (ATE)
A total of 357 samples were used for comparison study analysis. The semi-quantitative analysis for the Kenota 1 Total IgE result categories is summarized in the table below where cells in green color present allowable candidate test categories and the cells in the orange color present "erroneous" categories (Limits of Erroneous Results, LER) where a difference between the candidate category and the comparator values is more than ±1 category.

Kenota 1 Total IgE (kU/L)	ImmunoCAP Total IgE (kU/L)										
	<5	5-27.5	27.6-41.4 Near C1	41.5-80.3	80.4-121 Near C2	122-159	160-241 Near C3	242-431	432-649 Near C4	650-900	>900
<5	2										
5-34	8	95	12	2							
35-100		3	17	49	15	2					
101-200				1	19	24	10	1			
201-540						1	16	32	13	1	1
541-900								1	9	8	11
>900											4
Total	10	98	29	52	34	27	26	34	22	9	16
Percent in ATE	100.0% (10/10)	96.9% (95/98)	100.0% (29/29)	94.2% (49/52)	100.0% (34/34)	88.9% (24/27)	100.0% (26/26)	94.1% (32/34)	100.0% (22/22)	88.9% (8/9)	93.8% (15/16)
Percent in ATE	Low range 96.8% (183/189) 95%CI: (93.2%; 98.5%)				Middle range 96.6% (84/87) 95%CI: (90.3%; 98.8%)			High range 95.1% (77/81) 95%CI: (88.0%; 98.1%)			
Percent in ATE	96.4% (344/357) 95%CI: (93.9%; 97.9%)										
Percent in LER	0.0% (0/357) 95%CI: (0.0%; 1.1%)										

ii. Regression Analysis

In addition, of these 357 samples used for semi-quantitative analysis above, 339 samples were used for regression analysis based on the test results within the AMI of both the Kenota Total IgE test and the comparator. Results of a weighted Deming regression analysis for numeric values of the test samples are summarized in the table below.

	Sample Range (kU/L)	N	Slope (95% CI)	Intercept (95% CI)	(r)
Kenota 1 Total IgE vs. ImmunoCAP Total IgE	5.1–824.1	339	1.03 (1.00, 1.06)	1.10 (0.49, 1.66)	0.95

iii. Limits for Erroneous Results (LER)

See the table in the section for Allowable Total Error (ATE) above.

iv. Repeatability of fingerstick whole blood test results

An estimate of repeatability was determined using fresh fingerstick whole blood samples collected and tested by a total of 11 untrained operators at three CLIA-waived sites in the U.S. Refer to K231151 for details.

2. Operator Questionnaire

At the end of the study, each untrained operator who participated in the comparison study was given a questionnaire to provide feedback on the ease of use of the Kenota 1 Total IgE Test and the Kenota 1 (instrument). The questionnaire had 26 questions split into distinct critical tasks including testing preparation, procedures to follow, instrument use, and result interpretation. Based on the 11 operators' feedback, it was found to be easy to perform the test using the Quick Reference Guide instructions and the on-screen instructions of the instrument for 91% (10 out 11) untrained operators.

M. Labeling for Waived Devices

1. The labeling consists of:
   - Package Insert for Kenota 1 Total IgE
   - Quick Reference Guide (QRG) for Kenota 1 Total IgE
   - Kenota 1 Quick Setup Guide (QSG) for Kenota 1 instrument
   - Kenota 1 Operator's Manual (OM) for Kenota 1 instrument

2. The following elements are appropriately present:
   - The Quick Reference Guide (QRG) and Kenota 1 Quick Setup Guide (QSG) are written at no higher than a 7th grade reading level.
   - The QRG and QSG identify the test as CLIA waived.
   - The Kenota 1 Total IgE package insert contain a statement that a Certificate of Waiver is required to perform the test in a waived setting.
   - The QRG and QGS provide instructions for conducting quality control procedures.
   - The labeling is sufficient and satisfies the requirements of 21 CFR Part 809.10.

N. Conclusion:

The submitted information in this CLIA waiver application supports a CLIA waiver approval decision.