# 510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
# DECISION SUMMARY

**A. 510(k) Number:**
k042272

**B. Purpose for Submission:**
New devices

**C. Measurand:**
Heterophile antibodies

**D. Type of Test:**
Qualitative chromatographic immunoassays

**E. Applicant:**
ACON Laboratories, Inc.

**F. Proprietary and Established Names:**
ACON® *Mononucleosis* Rapid Test Strip (Whole Blood/Serum/Plasma)
ACON® *Mononucleosis* Rapid Test Device (Whole Blood/Serum/Plasma)

**G. Regulatory Information:**
1. Regulation section:
   21 CFR § 866.5640:  Infectious Mononucleosis Immunological Test System
2. Classification:
   Class II
3. Product code:
   KTN – System, Test, Infectious Mononucleosis
4. Panel:
   Immunology (82)

**H. Intended Use:**
1. Intended use(s):
   The ACON® *Mononucleosis* Rapid Test Strip (Whole Blood/Serum/Plasma) is a rapid chromatographic immunoassay for the qualitative detection of heterophile antibodies specific to infectious *Mononucleosis* in human whole blood, serum or plasma to aid in the diagnosis of infectious *Mononucleosis* infection in adults at 18 years of age and older.  It is intended for healthcare professionals and professionals at point-of-care sites.

   The ACON® *Mononucleosis* Rapid Test Device (Whole Blood/Serum/Plasma) is a rapid chromatographic immunoassay for the qualitative detection of heterophile antibodies specific to infectious *Mononucleosis* in human whole blood, serum or plasma to aid in the diagnosis of infectious *Mononucleosis* infection in adults at 18 years of age and older.  It is intended for healthcare professionals and professionals at point-of-care sites.

2. Indication(s) for use:
   The ACON® *Mononucleosis* Rapid Test Strip (Whole Blood/Serum/Plasma) is a rapid chromatographic immunoassay for the qualitative detection of heterophile antibodies specific to infectious *Mononucleosis* in human whole blood, serum or plasma to aid in the diagnosis of infectious *Mononucleosis* infection in adults at 18 years of age and older.  It is intended for healthcare professionals and

professionals at point-of-care sites.

The ACON® *Mononucleosis* Rapid Test Device (Whole Blood/Serum/Plasma) is a rapid chromatographic immunoassay for the qualitative detection of heterophile antibodies specific to infectious *Mononucleosis* in human whole blood, serum or plasma to aid in the diagnosis of infectious *Mononucleosis* infection in adults at 18 years of age and older. It is intended for healthcare professionals and professionals at point-of-care sites.

3. Special conditions for use statement(s):
   For prescription use.
4. Special instrument requirements:
   None

## I. Device Description:

The Rapid Test Strip assay consists of tests strips with a test line coated with bovine erythrocyte extracted antigen, disposable sample tubes, disposable heparinized capillary tubes and dispensing bulb, positive and negative controls, sample buffer, procedure card, package insert and a workstation.

The Rapid Test Device assay consists of tests strips with a test line coated with bovine erythrocyte extracted antigen encased in a plastic housing, disposable sample droppers, disposable heparinized capillary tubes and dispensing bulb, positive and negative controls, sample buffer, procedure card, and a package insert.

## J. Substantial Equivalence Information:

1. Predicate device name(s):
   [Wyntek] Genzyme OSOM® Mono Test
2. Predicate 510(k) number(s):
   K972231
3. Comparison with predicate:

| Similarities – ACON Test *Strip* vs. Genzyme OSOM | | |
|---|---|---|
| Item | Device | Predicate |
| Intended Use | For the qualitative detection of heterophile antibodies to infectious mononucleosis to aid in the diagnosis of infectious mononucleosis infection | For the qualitative detection of heterophile antibodies to infectious mononucleosis to aid in the diagnosis of infectious mononucleosis infection |
| Capture antigen | Bovine erythrocyte extract | Bovine erythrocyte extract |
| Specimen types | Serum, plasma, whole blood | Serum, plasma, whole blood |
| Test method | Chromatographic membrane strip based immunoassay | Chromatographic membrane strip based immunoassay |

| Similarities – ACON Test _Strip_ vs. Genzyme OSOM | | |
|---|---|---|
| Item | Device | Predicate |
| Reaction vessel | Test tube | Test tube |
| Controls | External positive and negative controls; built in procedural control line | External positive and negative controls; built in procedural control line |
| Endpoint | Colored lines (5 minutes) | Colored lines (5 minutes) |
| **Differences** | | |
| Item | Device | Predicate |
| No significant differences noted. | | |


| Similarities – ACON Test _Device_ vs. Genzyme OSOM | | |
|---|---|---|
| Item | Device | Predicate |
| Intended Use | For the qualitative detection of heterophile antibodies to infectious mononucleosis to aid in the diagnosis of infectious mononucleosis infection | For the qualitative detection of heterophile antibodies to infectious mononucleosis to aid in the diagnosis of infectious mononucleosis infection |
| Capture antigen | Bovine erythrocyte extract | Bovine erythrocyte extract |
| Specimen types | Serum, plasma, whole blood | Serum, plasma, whole blood |
| Test method | Chromatographic membrane strip based immunoassay | Chromatographic membrane strip based immunoassay |
| Reaction vessel | Test tube | Test tube |
| Controls | External positive and negative controls; built in procedural control line | External positive and negative controls; built in procedural control line |
| Endpoint | Colored lines (5 minutes) | Colored lines (5 minutes) |
| **Differences** | | |
| Item | Device | Predicate |
| Reaction vessel | Strip holder frame | Test tube |

**K. Standard/Guidance Document Referenced (if applicable):**
   None referenced.

**L. Test Principle:**
   The ACON Mononucleosis Rapid Test Strip (Whole Blood/Serum/Plasma) is a qualitative membrane strip based immunoassay for the detection of infectious Mononucleosis (IM) heterophile antibodies in whole blood, serum or plasma. Bovine erythrocyte extracted antigen is coated on the test line region of the strip. Patient samples and controls along with sample buffer are placed in the bottom of sample

tubes and the strip is inserted. This mixture migrates chromatographically along the length of the test strip and interacts with the coated bovine erythrocyte extracted antigen. If the sample contains IM antibodies, a colored line will appear in the test line region indicating a positive result. If the sample does not contain IM heterophile antibodies, a colored line will not appear in this region indicating a negative result. To serve as a procedural control, a colored line will always appear at the control line region, indicating that proper volume of specimen has been added and membrane wicking has occurred. The test is interpreted after 5 minutes.

The ACON Mononucleosis Rapid Test Device (Whole Blood/Serum/Plasma) is a qualitative membrane strip based immunoassay for the detection of infectious Mononucleosis (IM) heterophile antibodies in whole blood, serum or plasma. Bovine erythrocyte extracted antigen is coated on the test line region of the strip. The device is placed on a clean, level surface. Patient samples and controls followed by sample buffer are dropped into the sample well of the device. This mixture migrates chromatographically along the length of the test device and interacts with the coated bovine erythrocyte extracted antigen. If the sample contains IM antibodies, a colored line will appear in the test line region indicating a positive result. If the sample does not contain IM heterophile antibodies, a colored line will not appear in this region indicating a negative result. To serve as a procedural control, a colored line will always appear at the control line region, indicating that proper volume of specimen has been added and membrane wicking has occurred. The test is interpreted after 5 minutes.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

   a. *Precision/Reproducibility:*
      Intra-lot (within-run) precision and lot-to-lot (between-run) were tested with three separately manufactured lots. Test standards at three levels (negative, low positive and moderate positive) were run in replicates of 10. Day-to-day (between-day) precision studies were also tested with three separately manufactured lots. Each day, test standards at each of the three antibody levels were run in triplicate after sample application. In order to track the test line intensity more precisely, a scanner was also used to determine the quantitative readings as optical density unit (ODU) of test line intensity right after the 5 minute visual reads were taken. These scanner data are used as references only.
      The visual read results for the intra-lot, lot-to-lot and day-to-day studies for both the ACON test strip and device were in agreement with the expected results for the negative and the two positive samples. They were also in agreement with the results from the scanner. CVs for the scanner results were all less than 0.2%.

   b. *Linearity/assay reportable range:*
      Not applicable as these are qualitative assays.

   c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
      None given.

   d. *Detection limit:*

To determine the analytical sensitivity of the ACON test strip and test device a strong positive specimen was diluted to the following concentrations: 1:2, 1:4, 1:8, 1:16, 1:32, 1:64, 1:128, 1:256, 1:512, and 1:1024 with negative plasma. Different diluted positive specimens were also tested using a slide agglutination method. The diluted positive samples were randomized and run blind-coded in replicates of 10. One operator ran the test while the other three readers interpreted the results at 5 minutes. A scanner was also used to obtain quantitative intensity readings. The detection level for the ACON test strip was 1:256 (scanner reading of 3.5 – 3.7 ODU) and for the test device it was 1:512 (scanner reading of 3.3 – 3.7 ODU).

e. *Analytical specificity:*

Crossreactivity Study:

To determine if the ACON test strip and test device cross react with other disease specimens closely related to IM - RF, HBsAg, HBeAg, HBcAb, HBeAb, HCV, TB, syphilis and HIV positive specimens were tested. These samples were tested in triplicate with visual interpretations take at the 5 minute read time and at 10 minutes after sample application. None of the specimens showed any cross-reactivity with the ACON test strip or device and the recommended read time of 5 minutes or at the extended 10 minutes.

Interference Study:

To determine if various potentially interfering chemical substances or if lipemic and icteric samples will interfere with the ACON test strip or test device, a two part study was conducted. Part I – Analytes suspected of possible interference were spiked at high concentrations into IM negative and IM positive sera. The analytes included acetaminophen, caffeine, aspirin, Gentistic, oxalic acid, creatine, methanol, ascorbic acid, albumin, hemoglobin, bilirubin, acetoacetic acid, and samples with hematocrits of 20, 40, and 60%. The samples were tested in triplicate on 3 lots with visual interpretations at 5 minutes and 10 minutes after sample application. All results were as expected with the negative sample testing negative and the positive sample testing positive. Part II – Five lipemic and 6 icteric plasma samples were subject to measurements of triglyceride/total cholesterol and total/direct bilirubin, respectively. Subsequently, lipemic, icteric and control plasma samples were used as diluents. An IM positive specimen was diluted to 1:256 for test strips and to 1:512 for test devices. These IM positive and negative lipemic and icteric plasma samples were tested with results interpreted at the 5 minute and 10 minute read times. None of the substances at the concentrations tested interfered with the expected test results at either the 5 minute read time or 10 minutes after sample application for either the Test Strip or Test Device.

f. *Assay cut-off:*

Establishment of the ACON Mono Test Strip or Test Device cut-off (positive versus negative) employed a study using serial diluted positive samples containing heterophile antibody specific to IM together with the comparison of a slide mono device. A strong positive sample was serially diluted and tested with the slide test and the ACON devices. Cut-off values were established by determining the positive result obtained with the lowest

dilution.  Validation of the cut-off was established by testing positive and negative samples (side by side with the slide test) and plotting the results by histogram.  The plot showed distinction between the positive and negative samples.

2. Comparison studies:
   a. *Method comparison with predicate device:*
      Two-hundred forty serum and 240 plasma specimens were provided to three testing sites.  One-hundred and thirty whole blood specimens were tested at two ACON sites.  Specimens were tested according to package insert instructions.  All sites followed the same clinical study protocol.

ACON *Mononucleosis* Rapid Test **<u>Strip</u>** versus Genzyme OSOM Mono Test – **Plasma**:

|  |  | Genzyme OSOM Mono Test | |
| --- | --- | --- | --- |
|  |  | + | - |
| ACON *Mononucleosis* | + | 59 | 0 |
| Rapid Test Strip | - | 1 | 180 |

Positive Percent Agreement = 59/60 = 98% (91%-99%)*
Negative Percent Agreement = 180/180 = >99%**
Overall Percent Agreement = 239/240 = >99%**
*Denotes 95% confidence interval
**Denotes a 97.5% confidence interval

ACON *Mononucleosis* Rapid Test **<u>Strip</u>** versus Genzyme OSOM Mono Test – **Serum**:

|  |  | Genzyme OSOM Mono Test | |
| --- | --- | --- | --- |
|  |  | + | - |
| ACON *Mononucleosis* | + | 73 | 0 |
| Rapid Test Strip | - | 0 | 167 |

Positive Percent Agreement = 59/60 = >99% **
Negative Percent Agreement = 167/167 = >99% **
Overall Percent Agreement = 240/240 = >99% **
** Denotes a 97.5% confidence interval

ACON *Mononucleosis* Rapid Test **<u>Strip</u>** versus Genzyme OSOM Mono Test – **Whole Blood**:

|  |  | Genzyme OSOM Mono Test | |
| --- | --- | --- | --- |
|  |  | + | - |
| ACON *Mononucleosis* | + | 49 | 0 |
| Rapid Test Strip | - | 2 | 80 |

Positive Percent Agreement = 49/51 = 96% (87%-99%)*
Negative Percent Agreement = 80/80 = >99% (95%-100%)**
Overall Percent Agreement = 129/131 = >99% (95%-99%)**
*Denotes 95% confidence interval
** Denotes a 97.5% confidence interval

ACON *Mononucleosis* Rapid Test **Strip** versus Genzyme OSOM Mono Test – **All Specimens**:

| | | Genzyme OSOM Mono Test | |
|---|---|---|---|
| | | + | - |
| ACON *Mononucleosis* | + | 181 | 0 |
| Rapid Test Strip | - | 3 | 427 |

Positive Percent Agreement = 181/184 = 98% (95%-99%)*
Negative Percent Agreement = 427/427 = >99% (99%-100%)**
Overall Percent Agreement = 608/611 = >99% (99%-99.9%)**
*Denotes 95% confidence interval
** Denotes a 97.5% confidence interval

ACON *Mononucleosis* Rapid Test **Device** versus Genzyme OSOM Mono Test – **Plasma**:

| | | Genzyme OSOM Mono Test | |
|---|---|---|---|
| | | + | - |
| ACON *Mononucleosis* | + | 59 | 0 |
| Rapid Test Strip | - | 1 | 180 |

Positive Percent Agreement = 59/60 = 98% (91%-99%)*
Negative Percent Agreement = 180/180 = >99% (98%-100%)**
Overall Percent Agreement = 239/240 = >99% (98%-99%)**
*Denotes 95% confidence interval
** Denotes a 97.5% confidence interval

ACON *Mononucleosis* Rapid Test **Device** versus Genzyme OSOM Mono Test – **Serum**:

| | | Genzyme OSOM Mono Test | |
|---|---|---|---|
| | | + | - |
| ACON *Mononucleosis* | + | 72 | 0 |
| Rapid Test Strip | - | 1 | 167 |

Positive Percent Agreement = 72/72 = 99% (93%-99%)*
Negative Percent Agreement = 167/167 = >99% (98%-100%)**
Overall Percent Agreement = 239/240 = >99% (98%-99%**
*Denotes 95% confidence interval
** Denotes a 97.5% confidence interval

ACON *Mononucleosis* Rapid Test **Device** versus Genzyme OSOM Mono Test – **Whole Blood**:

| | | Genzyme OSOM Mono Test | |
|---|---|---|---|
| | | + | - |
| ACON *Mononucleosis* | + | 50 | 0 |
| Rapid Test Strip | - | 1 | 80 |

Positive Percent Agreement = 50/51 = 98% (90%-99%)*
Negative Percent Agreement = 80/80 = >99% (96%-100%)**
Overall Percent Agreement = 130/131 = >99% (96%-99%)**
*Denotes 95% confidence interval

ACON *Mononucleosis* Rapid Test **<u>Device</u>** versus Genzyme OSOM Mono Test – **All Specimens**:

| | | Genzyme OSOM Mono Test | |
|---|---|---|---|
| | | + | - |
| ACON *Mononucleosis* | + | 181 | 0 |
| Rapid Test Strip | - | 3 | 427 |

Positive Percent Agreement = 181/184 = 98% (95%-99%)*
Negative Percent Agreement = 427/427 = >99% (99%-100%)**
Overall Percent Agreement = 608/611 = >99% (99%-99.9%)**
* Denotes 95% confidence interval
** Denotes a 97.5% confidence interval

b. *Matrix comparison:*
Both the new devices and the predicate device can be used in serum, plasma and whole blood. To determine the effect of different anticoagulants on the ACON test strip and test device specimens containing K2EDTA, Na2EDTA, sodium citrate, potassium citrate, sodium oxalate, sodium heparin, and potassium heparin were collected. Thirty-five positive whole blood specimens and 35 positive plasma specimens were prepared by adding a strong positive into the collected anticoagulant specimens. All samples were run in triplicate. Both the test strip and the test device gave the expected positive and negative results for each type of antigcoagulated plasma tested.

3. Clinical studies:
a. *Clinical Sensitivity:*
Not given
b. *Clinical specificity:*
Not given
c. Other clinical supportive data (when a. and b. are not applicable):
Not applicable.
4. Clinical cut-off**:**
See assay cut-off
5. Expected values/Reference range:
The incidence of EBV-associated infectious mononucleosis in the US has been estimated at 45 per 100,000 and is highest in adolescent and young adults, about 2 out of 1,000. No seasonal pattern of EBV infection occurs. The incubation period is 10 to 60 days, though 7 to 14 days is common for children and adolescents.

**N. Proposed Labeling:**
The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10. The components of the tests (positive and negative controls) contain human source materials. Human samples were tested in the studies to support a substantially equivalent determination.

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