K011668

JUL - 9 2001

Oridion

510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21CFR807.92

The assigned 510(k) number is

PRODUCT NAME

TRADE/PROPRIETARY NAME

BreathID™ System

COMMON NAME

^{13}C-Urea Breath Test for the Presence of *Helicobacter pylori*

CLASSIFICATION NAME

MSQ *Campylobacter pylori.*
The urea breath test was recently reclassified from LYR to MSQ

ESTABLISHMENT ADDRESS:

Oridion Medical 1987 Ltd.
7 HaMarpe St.
Har Hotzvim Science Based Industrial Park
POB 45025
91450 Jerusalem, Israel

ESTABLISHMENT REGISTRATION NUMBER

NUMBER: 8044004

DEVICE LISTING FDA FORM 2892:

B073773

Oridion

Table of comparison to legally marketed predicate devices:

Characteristics	**BreathID™ System**	**CLOtest® K882199**	**MERETEK UBT® Breath Test K952220**	**MERETEK UBT® Breath Test K K972352**
Test measurement device	Oridion BreathID™ Test Device	Visual observation of color change	Gas Isotope Ratio Mass Spectrometer	Gas Isotope Ratio Mass Spectrometer
Test Sample	Gas Sample continuously transported to test measurement device by Oridion nasal cannula Filterline K980324	Sample is biopsy specimen	Gas sample stored in specially designed breath collection bag	Gas sample stored in specially designed breath collection bag
^{13}C-Urea	Raw material supplier CIL, 75mg Tablet dissolved in water. Manufacturer and Packager CIL (NDA #21-314 submitted)	NA	Raw material supplier ISOTEC, 125mg powder (Pranactin®) (in a glass vial) dissolved in water. Manufacturer and Packager unknown	Raw material supplier ISOTEC, 125mg powder (Pranactin®) (in a glass vial) dissolved in water. Manufacturer and Packager unknown
Applicable pre and post-treatment	Yes	Yes	No	Yes

Characteristics	**BreathID™ System**	**CLOtest® K882199**	**MERETEK UBT® Breath Test K952220**	**MERETEK UBT® Breath Test K K972352**
Test Meal	Citrica 4.5 gr dissolved in water	NA	Ensure pudding	Ensure pudding
Test results time	10-30 minutes	NA	Sample must be sent to lab for measurement, could be hours to days	Sample must be sent to lab for measurement, could be hours to days
Breath collection	Continuous over test time of 10-30 minutes	NA	One sample before ingestion of ^{13}C-Urea and one sample after 30 minutes.	One sample before ingestion of ^{13}C-Urea and one sample after 30 minutes.
Cut off point	5.0 delta per mil above baseline (post dose minus pre dose)	NA	2.4 delta per mil above baseline (post dose minus pre dose)	2.4 delta per mil above baseline (post dose minus pre dose)
Intended use	See Below (page 16)	See Below (page 16)	See Below (page 16)	See Below (page 16)
Organism	*Hp* in vivo	*Hp* in tissue biopsy	*Hp* in vivo	*Hp* in vivo
Reagent	^{13}C-Urea	Urea	^{13}C-Urea	^{13}C-Urea
Result	$^{13}CO_2/^{12}CO_2$ ratio – Molecular Correlation Spectroscopy (MCS)	CO_2+NH_3 Color change	$^{13}CO_2+NH_3$ Gas Isotope Ratio Mass Spectrometer	$^{13}CO_2+NH_3$ Gas Isotope Ratio Mass Spectrometer

Oridion

Intended Use

- Oridion BreathID™ system

The intended use of the Oridion BreathID™ system is to non invasively measure, in a continuous manner, changes in the $^{13}CO_2/^{12}CO_2$ ratio of exhaled breath after drinking a test drink which includes ^{13}C enriched urea. The system measures urease associated with *Helicobacter pylori* infection in the stomach to aid in the initial diagnosis and post treatment monitoring of *Helicobacter pylori.*infection. The detection is accomplished by measuring changes in the ratio between $^{13}CO_2$ and $^{12}CO_2$ using Oridion proprietary (MCS) gas measurement technology. The level of change in the $^{13}CO_2/^{12}CO_2$ ratio may be indicative of a physiological or metabolic change in the patient's condition. The system is for use by trained operators under the supervision of physicians, nurses or other healthcare professionals.

- The Meretek UBT® Breath test (K972352)

The intended use of the Meretek test is for use in the qualitative detection of urease associated with *Helicobacter pylori* in the human stomach and as an aid in the initial diagnosis and post-treatment monitoring of *Helicobacter pylori* infection in adult patients. This test is essentially equivalent to the test described in Meretek K952220 except that the intended use labeling has been expanded to include post-treatment monitoring of *Helicobacter pylori.*

- Intended Use (Meretek)K952220

The intended use is to non invasively detect urease associated with *Helicobacter pylori* infection in the stomach, and to aid in the initial diagnosis and post treatment monitoring of *Helicobacter pylori.* infection.

- Intended Use (CLOtest®)

The intended use is to detect urease associated with *Helicobacter pylori* infection in the stomach, and to aid in the initial diagnosis and post treatment monitoring of *Helicobacter pylori.*infection.

Oridion

ORIDION BreathID™ SYSTEM DESCRIPTION

The BreathID™ system is a non-invasive breath test system for detecting urease associated with *Helicobacter pylori*. The system consists of:

1) A medical device (BreathID™ system) to measure and compute the ratio between $^{12}CO_2$ and $^{13}CO_2$ in the patient's exhalation.
2) A Test Kit.

Test Device

The BreathID™ system is based on Oridion's proprietary CO_2 measurement technology. The device will be used to measure and compute changes in the ratio between $^{12}CO_2$ and $^{13}CO_2$ in the patient's exhalation. The Oridion BreathID test device measurement is made by continuous sampling of the breath.

The CO_2 produced in normal breathing contains approximately 99% $^{12}CO_2$ and 1% $^{13}CO_2$ (^{12}C and ^{13}C are stable isotopes of carbon). The Oridion BreathID™ system measures the changes in ratio between $^{13}CO_2$ and $^{12}CO_2$ using our proprietary technology. The system is for use by trained operators under the supervision of physicians, nurses or other healthcare professionals.

Test Kit

Part of the BreathID™ system is the Test Kit (IDkit™). The Test Kit is used to perform the test for the presence of *Helicobacter pylori*. The drug in the Test Kit is ^{13}C-Urea. The nasal cannula device used in the kit is an Oridion Nasal Filterline.

The Test Kit consists of:

1) Oridion Nasal FilterLine™
2) A packaged tablet of ^{13}C-urea
3) A package of powdered Citrica
4) A drinking straw
5) Package insert

Oridion

CLINICAL STUDY SUMMARY

Dates: (Pivotal study)
September 1999-June 2000
Subjects:
315 subjects pre-therapy and 77 subjects post-therapy
Objective:

- To evaluate the sensitivity and specificity of the BreathID™ system to detect the presence of *Helicobacter pylori pre-treatment.*

Results:
Comparison of BreathID™ system results to endoscopic results – Pre-therapy
[1]Sensitivity 100%
Specificity 99.2%

Helicobacter pylori positive is defined as positive CLOtest® and positive histology; *Helicobacter pylori* negative is defined as negative CLOtest® and negative histology. 24 hr CLOtest® results were used to evaluate efficacy.

Comparison of BreathID™ system results to CLOtest® results – Pre-therapy
Relative Sensitivity 100%
Relative Specificity 99.2%

Comparison of BreathID™ system results to Histology results – Pre-therapy
Sensitivity 95.8%
Specificity 97.7%

Objective:

- To evaluate the sensitivity and specificity of the BreathID™ system to detect the presence of *Helicobacter pylori* post- treatment, and to evaluate the ability of Oridion's BreathID™ system to monitor the efficacy of treatment.

Results:
Comparison of BreathID™ system results to Endoscopic results - Post-therapy
Sensitivity 100%
Specificity 100%

Comparison of BreathID™ results to CLOtest® results – Post-therapy
Relative Sensitivity 100%
Relative Specificity 100%

Comparison of BreathID™ results to Histology results – Post-therapy
Sensitivity 100%
Specificity 95.2%

[1] The limits of the 95% 2 sided confidence interval are calculated using exact method

Oridion

Comparison of BreathID™ results to Meretek results – Post-therapy

Relative sensitivity 93.3%
Relative specificity 100%

Objective:

- To evaluate the sensitivity and specificity of the BreathID™ system to detect the presence of *Helicobacter pylori* with a "variable time" breath test procedure.

Results :

Clinical data demonstrated the equivalence of the standard test to the varying time tests regarding the diagnostic results.These results did not depend on clinical stage or on the specific medical center.

Analysis of the influence of PPI and H^2

This multi-site study had no exclusionary criteria for and was indifferent to PPI/H^2 therapy. No difference was noted between the predicate devices and the experimental device (BreathID™ system), regarding testing accuracy and concurrent therapy. Out of 317 diagnostic patients, 233 (73.5%) were using PPI/H^2. Amongst all *Helicobacter pylori*-positive test results (32), 61.5% were being therapeutically treated by PPI/H^2. Of these *Helicobacter pylori*-positive patients using PPI/H^2, 48.4% had taken the PPI/H^2 24 hours prior to testing, while 71.0% had taken their medication within 48 hours of testing.

Percentage of *Helicobacter pylori* Positive Pre-Therapy Patients According to Days without Medication

Drug/Days	0	1	2	3+	Total
H^2	33.3%	45.45%	33.3%	14.3%	25%
PPI	9.5%	8.75%	26.9%	15.6%	11.8%
None					26.5%

Conclusions:

There were no false negatives reported for any of the subjects taking PPI or H^2. The results for subjects taking either PPI or H^2 therapy (shown according to therapy) are shown in the tables above.

ADVERSE EVENTS:

There were only two adverse events in two subjects in this study, both of which were judged as mild. One adverse event was judged not to be related to the device, and possibly related to the procedure; and the other was judged as possibly related to the device and the procedure. Both subjects recovered without treatment.

Oridion

CUT-OFF POINT (THRESHOLD) DETERMINATION

The cut-off point (COP) is the level (threshold) used to discriminate between *H. pylori* infected and non-infected individuals. The threshold value (COP) for the BreathID™ System test is 5 DOB.

The threshold level of 5 DOB was confirmed to be the optimal Cut-off point (COP) for the BreathID System in a multi center study . The sensitivity and specificity achieved with this COP were found to be 100% and 99.2%, respectively, for pre-therapy patients and 95.5% and 100% for post-therapy patients.

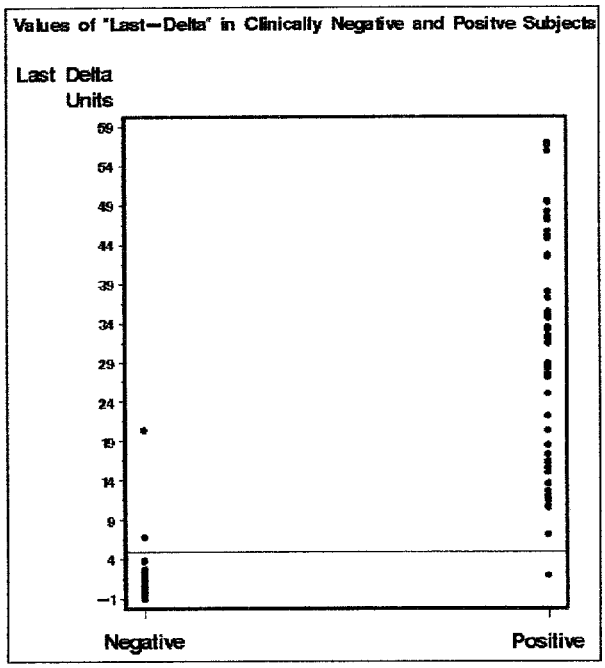

Figure 1 Cut-off point histogram

The histogram in Figure 1 shows graphically that the 5 DOB can distinguish very clearly between the infected (positive) and the uninfected (negative) populations.

Oridion

Reference Studies

In addition to the Pivotal study there were several reference studies (one still ongoing) that included 190 positive and 247 negative patients. The results reported were supportive of the conclusions reached in the pivotal study.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUL - 9 2001

Mr. Sandy Brown
Regulatory Affairs Manager
Oridion Medical 1987 Ltd.
7 HaMarpe Street
Har Hotzvim Industrial Park
P.O. Box 45025
Jerusalem, Israel

Re: K011668
Trade Name: Oridion BreathID™ System for *Helicobacter pylori*
Regulation Number: 866.3110
Regulatory Class: I
Product Code: MSQ
Dated: May 14, 2001
Received: May 17, 2001

Dear Mr. Brown:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments. You may, therefore, market the device, subject to the general controls provisions of the Federal Food, Drug, and Cosmetic Act (Act). The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, and labeling, and prohibitions against misbranding and adulteration.

In addition, we have determined that your product contains the following component subject to regulation as drugs: ^{13}C-enriched urea tablet-75mg.

Our substantially equivalent determination does not apply to the drug component (NDA 21-314) of your product. For information on applicable Agency requirements for marketing this product, we suggest you contact:

Mark Goldberger, M.D., M.P.H.
Director
Division of Special Pathogens and Immunologic Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Blvd.
Rockville, Maryland 20850

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval) it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, FDA will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, the Food and Drug Administration (FDA) may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under section 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification although we recommend that you first contact the Center for Drug Evaluation and Research before marketing your drug component[s]. An FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and permits your device to proceed to the market, but it does not mean that FDA approves your device. Therefore, you may not promote or in any way represent your device or its labeling as being approved by FDA. If you desire specific advice for your device on the labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), promotion, or advertising, please contact the Office of Compliance, Promotion and Advertising Policy Staff (HFZ-302) at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification"(21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll free number (800) 638-2041 or (301) 443-6597, or at its internet address "http://www.fda.gov/cdrh/dsmamain.html".

Sincerely yours,

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

Oridion

June 10, 2001

Indications For Use

510(k) Number (if known): K011668

Device Name: BreathID™ System

Indications For Use:

The BreathID™ System is used to diagnose and monitor *Helicobacter pylori* infection by measuring changes in the $^{13}CO_2/^{12}CO_2$ ratio in a patient's breath following the ingestion of ^{13}C urea.

The Oridion BreathID™ system continually and non-invasively measures changes in the $^{13}CO_2/^{12}CO_2$ exhaled breath, which may be indicative of increased urease production associated with active *Helicobacter pylori* infection in the stomach. The Oridion BreathID™ System is to be used as an aid for initial diagnosis and post treatment monitoring of *Helicobacter pylori* infection.

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use X OR Over-The-Counter Use _____
(Per 21 CFR 801.109)

(Optional Format 1-2-96)

Woody Dubois
(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K011668

Oridion Medical 1987 Ltd. • POB 45025 • Jerusalem 91450 Israel • Voice:+972 2 589-9115 • Fax:+972 2 582-8873