

Proposed BreathTek™ UBT package insert **(Revised 5/9/01)**

I. Intended Use

The BreathTek™ UBT Collection Kit is intended 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. The test may be used for monitoring treatment if used at least four weeks following completion of therapy. For these purposes, the system utilizes a Gas Isotope Ratio Mass Spectrometer ("GIRMS") for the measurement of the ratio of $^{13}\text{CO}_2$ to $^{12}\text{CO}_2$ in breath samples.

For administration by health care professionals. To be administered under a physician's supervision.

II. Summary and Explanation

Since the isolation of the spiral urease-producing *Helicobacter pylori* (*H. pylori*) in 1983 by Warren and Marshall¹, a significant body of evidence has accumulated indicating that the bacteria is an important pathogen in the upper GI tract of humans.^{2,3} The causal relationship between *H. pylori* and chronic active gastritis, duodenal ulcer, and gastric ulcer is well documented.^{4,5}

Methods available for detecting **current** infection of the human stomach by *H. pylori* are generally divided into two general types: *Invasive* and *Non-invasive*. Invasive methods are so called because they include, as a first step, an esophagogastroduodenoscopy ("EGD") with collection of gastric biopsies. These biopsies are then examined by one or more detection methods: histological examination of stained tissue, microbiological culture of the organism, or direct detection of urease activity in the tissue (for example, the CLOtest®). Biopsy based methods are expensive, entail some patient risk and discomfort, and may give false negative results due to sampling errors when colonization of the gastric mucosa is patchy.⁶

The non-invasive, non-radioactive method for detecting **current** *H. pylori* infection is based on the BreathTek™ UBT which is described in the next section.

Several serological tests that detect serum antibodies to *H. pylori* are commercially available. A positive result with these tests cannot distinguish between **current** infection or past exposure to infection and, therefore, is not a conclusive indicator of current gastrointestinal colonization by *H. pylori*.

III. Principle of the BreathTek™ UBT for *H. pylori*

Description of the Pranactin-Citric™ Diagnostic Drug Component

The diagnostic drug component of the kit is ^{13}C -urea, a synthetic urea contained in a granulated powder (Pranactin-Citric™) for reconstitution with potable water to provide a clear solution for oral administration. The carbon in the drug component is predominantly Carbon-13, a stable, naturally occurring, non-radioactive isotope of carbon; the relative abundance of Carbon-13 is greater than or equal to 99%.

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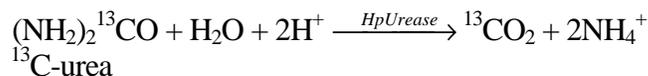
Each three (3) gram dose of Pranactin-Citric™ is supplied in a polyethylene-lined foil pouch and contains 75 mg of ¹³C-Urea, citric acid⁹, aspartame and mannitol.

¹³C-urea is the diamide of ¹³C-carbonic acid and is highly soluble in water (1 gram per mL at 25°C). It has the following chemical formula: ¹³CH₄N₂O.

An average adult body normally contains about 9.0 grams of urea which is a product of protein metabolism. Urea in the body is referred to as natural isotopic abundance urea since it is composed of 98.9% ¹²C-urea and 1.1% ¹³C-urea.

Principle of the Test

In the BreathTek™ UBT for *H. pylori*, 3 g of reconstituted Pranactin-Citric™ containing 75 mg of ¹³C-urea is ingested by the patient. In the presence of urease associated with gastric *H. pylori*, ¹³C-urea is decomposed to ¹³CO₂ and NH₄⁺ according to the following equation:



The ¹³CO₂ is absorbed in the blood, then exhaled in the breath. This results in an increase in the ratio of ¹³CO₂ to ¹²CO₂ in a TEST breath sample compared to a BASELINE sample taken before the Pranactin-Citric™ solution was consumed. Analysis of the breath samples is performed by Gas Isotope Ratio Mass Spectrometry ("GIRMS") at Meretek's clinical laboratory or at other qualified laboratories licensed by Meretek Diagnostics, Inc.

The BreathTek™ UBT can detect very low levels of *H. pylori* colonization and, by assessing the entire gastric mucosa, avoids the risk of sampling errors inherent in biopsy based methods. In the absence of gastric *H. pylori*, the ¹³C-urea does not produce ¹³CO₂ in the stomach. The ratio of ¹³CO₂ to ¹²CO₂ in the TEST breath sample remains essentially the same as the BASELINE.

IV. Warnings and Precautions

1. For *in vitro* diagnostic use only. The Pranactin-Citric™ drug solution is taken orally as part of the diagnostic procedure.
2. Phenylketonurics: Contains Phenylalanine, 75 mg per dosage unit. (For reference, 12 ounces of typical diet cola soft drinks contain approximately 80 mg of phenylalanine.)
3. A negative result does not rule out the possibility of *Helicobacter pylori* infection. False negative results do occur with this procedure. If clinical signs are suggestive of *H. pylori* infection, retest with a new sample or an alternate method.
4. Antimicrobials, proton pump inhibitors, and bismuth preparations are known to suppress *H. pylori* and ingestion of these within two weeks prior to performing the BreathTek™ UBT may give false negative results.

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5. A false positive test may occur due to urease associated with other gastric spiral organisms observed in humans such as *Helicobacter heilmannii*.
6. Premature TEST breath collection time can lead to a false negative diagnosis for a patient with a marginally positive BreathTek™ UBT result.
7. A false positive test could occur in patients who have achlorhydria.⁷
8. If particulate matter is visible in the reconstituted Pranactin-Citric™ solution after thorough mixing, the solution should not be used.

V. Shelf Life and Storage

The BreathTek™ UBT Collection Kit should be stored at 15°-30°C (59°-86°F). Pranactin-Citric™ has an expiration date. Do not use beyond the expiration date stated on the label.

VI. Patient Preparation

1. Remind the patient that Pranactin-Citric™ contains phenylalanine. Phenylketonurics restrict dietary phenylalanine.
2. The patient should have fasted at least one hour before administering the BreathTek™ UBT.
3. The patient should not have taken antimicrobials, proton pump inhibitors, or bismuth preparations within two weeks prior to administering the BreathTek™ UBT.

VII. Procedure

Materials

Materials provided:

Each single-patient BreathTek™ UBT Collection Kit contains:

- ◆ One plastic drinking cup
- ◆ Three plastic straws
- ◆ One clear plastic specimen return box containing:

Pranactin-Citric™ powder (3 g)

Four (4) bar-coded 10 mL breath sample tubes

A set of three self-adhesive bar-code stickers. All bar-codes should bear the same number.

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Materials needed but not provided

- ◆ A timer capable of timing an interval up to fifteen (15) minutes.
- ◆ Scissors for opening the Pranactin-Citric™ pouch.
- ◆ Test request forms and specimen return envelopes are supplied with the kits or are provided separately by your Meretek licensed testing laboratory.

Note: A Gas Isotope Ratio Mass Spectrometer and related analytical equipment are required for analysis of breath samples. Breath sample analyses are performed at Meretek's clinical laboratory or qualified laboratories licensed by Meretek Diagnostics, Inc.

Step-By-Step Procedure

Time intervals listed in the following step-by-step-procedure are critical. They are highlighted by the timer icon: ⌚

1. Verify that the patient has been prepared for the test as specified in Section VI.
2. Open the BreathTek™ UBT Collection Kit, which should contain all the materials listed above. Open the clear plastic specimen return box at the arrows indicated by “PULL”. Fold back the sides of the plastic box and place on a flat surface so that the four (4) bar coded tubes are presented in a vertical, upright position. Remove the self-adhesive label containing the three (3) peel-off bar-code stickers. Place one peel-off bar-code sticker on the **Lab Copy** of the test request form and one on the **Physician Copy** of the test request form. An extra bar-code sticker is provided if needed. There are two blue-labeled BASELINE sample tubes and two pink-labeled TEST sample tubes.

The contents of each clear plastic specimen return box are bar-coded to maintain positive patient identification. Verify that the bar-codes on the test request form and tubes match. To avoid confusion, be sure to keep these items patient-specific.

3. Complete all areas of the test request form.
4. Collect two BASELINE breath samples according to the following procedure:
 - a. Remove the collection tube stopper.
 - b. Insert a new straw to within about 0.5 inch of the bottom of the tube.
 - c. Instruct the patient to take a deep breath, pause momentarily, then blow **gently** through the straw into the bottom of the tube for about 3 to 5 seconds. *The tube should be held in a near-vertical position during this process.*

While the patient is blowing through the straw, slowly withdraw the tube and immediately

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replace the stopper. *Seat the stopper completely within the rim of the tube and press it down with a slight twisting motion to its original position. Avoid pressing too hard on the stopper as it could break the glass tube.*

Note: Using this procedure, condensed moisture on the inside of the tube indicates the tube has been adequately filled. However, there must be no saliva or sputum in the tube. If mouth fluids accumulate in the tube, discard the tube using biohazard precautions.

5. ⌚ Prepare the Pranactin-Citric™ solution *no more than sixty (60) minutes before administering it to the patient. Urea slowly decomposes in water.*
 - a. Remove the Pranactin-Citric™ pouch from the specimen return box. Tap the upright packet of Pranactin-Citric™ to settle the contents in the bottom half.
 - b. With scissors, cut off the top of the packet and carefully empty the contents into the drinking cup provided, making sure to transfer all of the contents by tapping.
 - c. Add potable water to the **FILL LINE** indicated on the outside of the container.
 - d. Replace the lid securely and swirl up to *two minutes* to dissolve the packet contents; typically, only one minute is required for complete dissolution. *The resulting solution should be clear with no particulate matter. If particulate matter is present after thorough mixing, the solution should not be used.*
6. Instruct the patient to drink all of the solution with a new straw, without stopping. Advise the patient NOT to ‘rinse’ the inside of his/her mouth with the solution before swallowing. *Discard the straw as it must not be used for breath collection.*
 - ⌚ Set the timer for 15 minutes.
7. The patient should sit quietly and should not eat, drink or smoke during the 15-minute interval. When fifteen (15) minutes have elapsed, collect two TEST breath specimens by the procedure described in Step 4 above.
8. Review the test request form for accuracy and completeness, and retain the **Physician Copy** for your records. Verify that the bar-code number on the test request form matches the bar-code number on all breath specimen tubes.
9. Fold the **Lab Copy** of the test request form and put it into the specimen return box or specimen return envelope, as directed by your testing laboratory. Close the specimen return box and put it into the specimen return envelope. Store the specimens at 15°-30°C (59°-86 °F) until shipment.
10. ⌚ Send the return envelope to the Meretek clinical laboratory, or other qualified laboratory licensed by Meretek, within three (3) days after the breath samples were collected.

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VIII. Quality Control

The Meretek clinical laboratory and other qualified laboratories licensed by Meretek to perform the BreathTek™ UBT analyses follow written policies and procedures for a comprehensive Quality Assurance (QA) program which is designed to monitor and evaluate the overall quality of the total testing process (pre-analytic, analytic and post-analytic).

As part of the QA program, the analytical Quality Control system includes provisions for the detection of persistent and sporadic errors. Persistent analytical errors, which span multiple samples and controls, are detected by analysis of periodically placed control gases in the patient breath sample runs. Control rules with high error detection capability are applied to the control data to accept or reject whole runs or portions of runs. Sporadic errors, which occur unpredictably on individual specimens, are detected by quality criteria applied to each sample tube measurement.

Quality checks are also performed on the final results. For example:

- ◆ Each specimen tube must contain at least 1.5 volume percent CO₂ to assure the tube contains adequate breath for analysis. If not, the result is rejected.
- ◆ The relative abundance of the BASELINE sample must be within the interval: -27.0 to -17.0 delta per mil. Fasting samples outside this range are highly unlikely and new (backup) specimens should be tested.
- ◆ Quality criteria are applied to BreathTek™ UBT results to assure that BASELINE and TEST specimens were collected properly. The DOB result must be greater than -1.0.

In the event that failure of quality criteria on both specimen pairs which have been submitted for analysis precludes reporting a valid test result, you will be notified as soon as possible. The notification on the report form will include the nature of the quality failure (e.g., empty sample tube) and the recommended remedial action.

IX. Test Results

The Test Method

The ratio of ¹³CO₂ to ¹²CO₂ in breath samples is determined by Gas Isotope Ratio Mass Spectrometry ("GIRMS") at the Meretek clinical laboratory or qualified laboratory licensed by Meretek Diagnostics, Inc.

Calculation of Results

The result of the BreathTek™ UBT for *H. pylori* is provided as the Delta Over Baseline. No calculations are required by the customer. Delta Over Baseline is the difference between the ratio (¹³CO₂/¹²CO₂) in the TEST specimen and the corresponding ratio in the BASELINE sample.

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Determination of the Cutoff Point

The cutoff point is the level of BreathTek™ UBT result used to discriminate between *H. pylori* infected and uninfected individuals. For the BreathTek™ UBT, the Delta Over Baseline cutoff point was determined to be 2.4 in a controlled study of 26 infected and 23 uninfected adult volunteers. Test subjects were judged to be in acceptable health based on the results of a medical history and physical examination and demonstrated no uncontrolled clinically significant abnormality other than, for some, symptoms of peptic ulcer. The previous version of the Meretek urea breath test, the Meretek UBT®, was used as the reference standard. The cutoff point was calculated by determining the BreathTek™ UBT result level at which negative and positive subjects were best distinguished by co-optimization of relative sensitivity and specificity. The 2.4 cutoff point for the BreathTek™ UBT was verified in an independent study by retrospective analysis of Clinical Field Trial data collected on 145 *H. pylori* negative and 105 *H. pylori* positive test subjects, again using the original Meretek UBT® as reference. Asymptomatic subjects and those with dyspepsia were included in the validation study. Figure 1a shows graphically the BreathTek™ UBT Delta Over Baseline cutoff point which distinguishes *H. pylori* positive and negative subjects.

For the Meretek UBT® Breath Test, the Delta Over Baseline cutoff point was determined to be 2.4 in a controlled study of 66 infected and 53 uninfected asymptomatic, apparently healthy volunteers. Histological examination of biopsy tissue was used as the reference standard. The cutoff point was evaluated by determining the Meretek UBT® Breath Test result level at which histologically negative and positive subjects were best distinguished. Figure 1b shows graphically the Meretek UBT® Breath Test Delta Over Baseline cutoff point which distinguishes histologically positive and negative subjects. Note that in Figures 1a and 1b, the Delta Over Baseline scales are logarithmic.

Figure 1a. Cutoff for BreathTek™ UBT

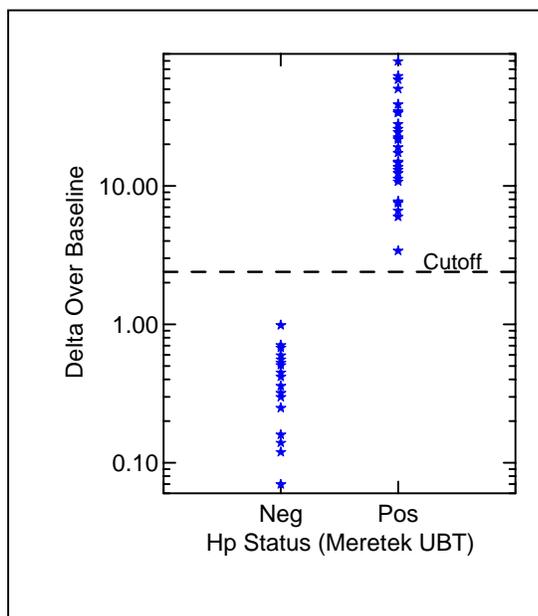
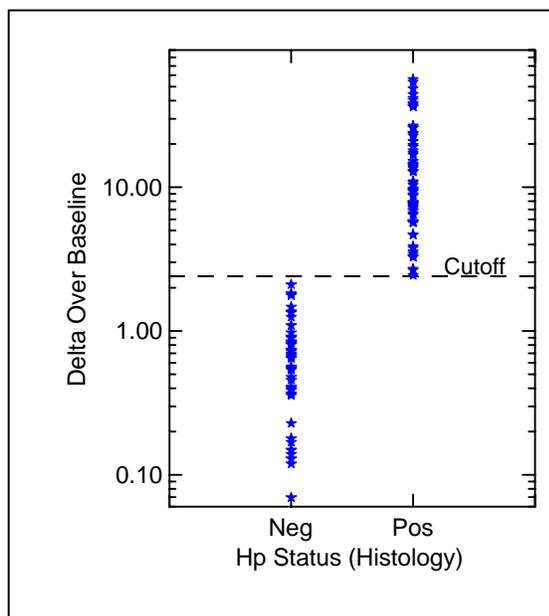


Figure 1b. Cutoff for Meretek UBT®



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Interpretation of Results

A BreathTek™ UBT result greater than or equal to 2.4 Delta Over Baseline is interpreted as diagnostically positive indicating the presence of urease associated with *H. pylori*. A BreathTek™ UBT result less than 2.4 Delta Over Baseline is interpreted as diagnostically negative indicating the absence of urease associated with *H. pylori*.

The 2.4 Delta Over Baseline cutoff point applies to both initial diagnosis and post-treatment monitoring of *H. pylori* infection.

X. Limitations of the Test

1. The BreathTek™ UBT should not be used until four weeks or more after the end of treatment for the eradication of *H. pylori*, as earlier post-treatment assessment may give false negative results.
2. The performance characteristics for persons under the age of 18 have not been established for this test.
3. The specimen integrity due to storage of breath samples in collection tubes under ambient conditions has not been determined beyond 20 days.
4. A correlation between the number of *H. pylori* organisms in the stomach and the BreathTek™ UBT result has not been established.
5. The predicate device (Meretek UBT®) was standardized in asymptomatic healthy volunteers and subsequently validated in clinical trials limited to patients with documented duodenal ulcer disease.

XI. Expected Values

Delta Over Baseline values for the BreathTek™ UBT were determined in a controlled clinical study of 26 infected and 23 uninfected adult volunteers. The Meretek UBT® Breath Test was used as the reference method in the diagnosis of infection. The range of BreathTek™ UBT Delta Over Baseline values for the *uninfected* group was determined to be 0.0 to 1.0. A histogram for the distribution of Delta Over Baseline values from the uninfected subjects is shown in Figure 2a.

Values for the Meretek UBT® Breath Test were determined in a controlled clinical study of 66 infected and 53 uninfected asymptomatic, apparently healthy volunteers. Histological examination of biopsy tissue was used as the reference method in the determination of infection in this study. The range of Meretek UBT® Delta Over Baseline values for the uninfected group was determined to be 0.0 to 2.2. A histogram for the distribution of Delta Over Baseline values from the uninfected subjects is shown in Figure 2b.

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Figure 2a. BreathTek™ Expected Values

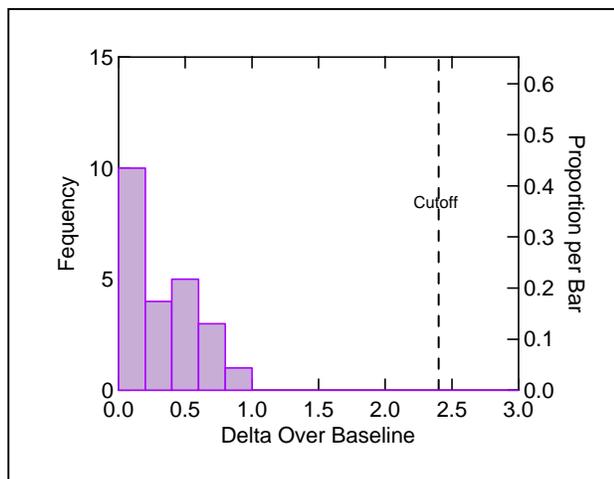
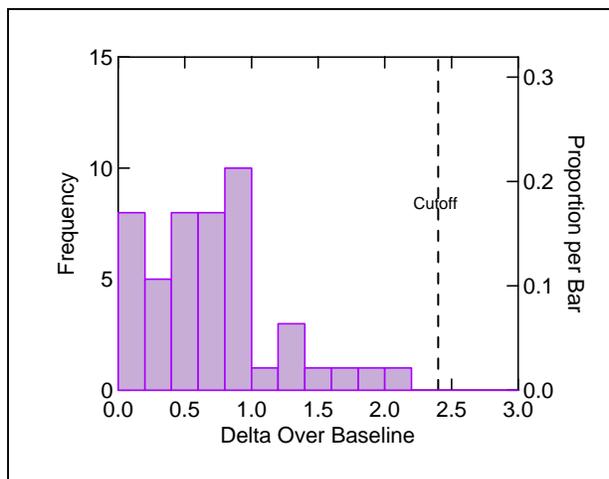


Figure 2b. Meretek UBT® Expected Values



XII. Performance Characteristics

Imprecision of the GIRMS Analytical System

Experimental Design

The experimental design of the GIRMS system imprecision study conformed to the general recommendations of the NCCLS Guideline EP5-A (User Evaluation of Precision Performance of Clinical Chemistry Devices). On each of nineteen test days, each of the three levels of test gases were analyzed three (3) times each. Whenever possible these test specimens were analyzed along with the daily run of patient samples.

Results

For each control level, a nested, one-way analysis of variance was performed to estimate:

- ◆ Within-run imprecision, S_{wr}
- ◆ Day-to-day imprecision, S_{dd} (corrected)
- ◆ Total imprecision, S_t (with Satterthwaite correction)

Statistical results are summarized in Table 1. In the table, each entry represents the standard deviation followed in parentheses by the percent coefficient of variation.

Table 1. Nested Analysis of Variance Results

| Imprecision Component | Level 1 Mean = -26.3 | Level 2 Mean = -16.7 | Level 3 Mean = 119.8 |
|------------------------------|---------------------------------|---------------------------------|---------------------------------|
| Within-run | 0.14 (0.54) | 0.10 (0.63) | 0.15 (0.13) |
| Day-to-Day | 0.00 (0.00) | 0.09 (0.55) | 0.08 (0.07) |
| Total | 0.14 (0.54) | 0.14 (0.84) | 0.17 (0.14) |

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Method Comparisons in Clinical Trials

A. Comparison of the BreathTek™ UBT with the Meretek UBT®

Experimental Design

The method comparison data presented here were collected from a prospective, cross-over clinical field trial designed to validate the BreathTek™ UBT test procedure and to examine the effect of pre-test fasting time on test performance. The study included 252 adult test subjects from Houston and Galveston, Texas. Subjects were judged to be in acceptable health based on the results of a medical history and physical examination and demonstrated no uncontrolled clinically significant abnormality other than, for some, symptoms of dyspepsia.

Test subjects were tested for *H. pylori* infection using the Meretek UBT® Breath Test according to established procedure and with the BreathTek™ UBT under differing conditions of pre-test fasting times. Otherwise, no special instructions were given to subjects beyond those listed in the step-by-step procedures for administration of the Meretek UBT® and BreathTek™ UBT. To minimize potential bias due to test order, the sequence of urea breath tests administered to each subject was randomized. All breath tests were administered to a given individual within fourteen (14) days of one another, most often, and at a minimum, on successive days.

Results

It was demonstrated in the field trial that the BreathTek™ UBT may be administered at any time beyond one hour after consuming solid and/or liquid food.

Method comparison results are presented in a two-way contingency table below (Table 2).

Point estimates of *Percent Agreement* of the BreathTek™ UBT with Meretek UBT® positive and negative results are listed below the contingency table. The comparative method for determining the true diagnosis was the predictive device (Meretek UBT®) rather than endoscopic methods. The exact binomial distribution was used to calculate the lower and upper limits of the 95% confidence intervals of the performance statistics. The confidence intervals are entered in parentheses following the point estimate of the statistic.

Table 2. Comparison of BreathTek™ UBT (≥ 1-hour fast) with Meretek UBT®

| Meretek UBT® | BreathTek™ UBT Results | | |
|--------------|------------------------|----------|-------|
| | positive | negative | Total |
| positive | 105 | 1 | 106 |
| negative | 1 | 145 | 146 |
| Total | 106 | 146 | 252 |

Percent Agreement with Meretek UBT® positive subjects: 99.1 % [95% CI: (94.9, 100.0)]

Percent Agreement with Meretek UBT® negative subjects: 99.3 % [95% CI: (96.2, 100.0)]

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B. Comparison of the Meretek UBT® with endoscopic methods

Experimental Design

The method comparison data presented here were collected from two (2) independent double blind clinical field trials which involved treatment of *H. pylori* infection. The studies included 499 adult patients with duodenal ulcer disease at 75 clinical sites in the United States. Patients were tested for *H. pylori* infection initially (using histopathology, microbiological culture, CLOtest®, and the Meretek UBT®), and at various post-treatment intervals throughout the study (using histopathology, microbiological culture, and the Meretek UBT®). In these clinical trials patients were treated with various combinations of clarithromycin, omeprazole and placebo. Note, however, that there is no evidence that differing treatment regimens affect the performance of the Meretek UBT®.

1. Histopathology

Biopsy specimens, fixed with 10% buffered formalin, were cut into 4-mm sections, stained with Genta stain and examined by an experienced pathologist.

2. Microbiologic culture

Culture was performed using fresh blood-based media, both selective and non-selective, at 37°C in 12% CO₂ in air with 98% humidity. *H. pylori* were identified by Gram stain, typical colony morphology, and biochemical properties (production of oxidase, catalase, and urease).

3. CLOtest® (Delta West, Limited, Bently, West Australia)

A biopsy specimen was tested for urease activity with the CLOtest® according to the instructions in its package insert.

4. The Meretek UBT® Breath Test for *H. pylori*

The diagnostic Meretek UBT® Breath Test was performed in accordance with procedures described in its package insert.

Results

Method comparison results are presented in two-way contingency tables. In tables 3, 4, and 5, the Meretek UBT® Breath Test results are compared with the CLOtest®, histology, and with the combined endoscopic method results (CLOtest®, histology and culture) for the initial patient visit.⁸ In table 6, the Meretek UBT® Breath Test results are compared with the combined endoscopic method results (histology and culture) for the post-treatment visits which occurred four weeks or more after end of treatment.

The exact binomial distribution was used to calculate the lower and upper limits of the 95% confidence intervals of the performance statistics. The confidence intervals are entered in parentheses following the point estimate of the statistic.

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Performance Characteristics for Initial Diagnosis

Table 3. Comparison with CLOtest® for Initial Visit

| CLOtest® | Meretek UBT® Results | | |
|--------------|----------------------|----------|-------|
| | positive | negative | Total |
| positive | 397 | 31 | 428 |
| negative | 1 | 16 | 17 |
| Total | 398 | 47 | 445 |

Relative sensitivity: 92.8 % [95% CI: (90, 95)]

Relative specificity: 94.1 % [95% CI: (71,100)]

Table 4. Comparison with Histology for Initial Visit

| Histology | Meretek UBT® Results | | |
|--------------|----------------------|----------|-------|
| | positive | negative | Total |
| positive | 394 | 20 | 414 |
| negative | 3 | 27 | 30 |
| Total | 397 | 47 | 444 |

Relative Sensitivity: 95.2 % [95% CI: (93, 97)]

Relative Specificity: 90.0 % [95% CI: (74, 98)]

Table 5. Comparison with combined endoscopic methods for Initial Visit

Combined endoscopic methods used were CLOtest®, histology, and culture per DAIDP guidelines⁸ for pre-treatment diagnosis.

| Endoscopy | Meretek UBT® Results | | |
|--------------|----------------------|----------|-------|
| | positive | negative | Total |
| positive | 395 | 20 | 415 |
| negative | 3 | 26 | 29 |
| Total | 398 | 46 | 444 |

Sensitivity: 95.2 % [95% CI: (93, 97)]

Specificity: 89.7 % [95% CI: (73, 98)]

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Performance Characteristics for Post-Treatment Monitoring

Table 6. Comparison with combined endoscopic methods* for Post-Treatment Visits (four weeks or more after End of Treatment (EOT))

| Meretek UBT® Breath Test results | | | | | | | | |
|----------------------------------|------------------------|-----|------------------------|-----|-------------------------|-----|------------------------|-----|
| | 1 Month EOT | | 3 Months EOT | | 6 Months EOT | | 1-6 Months Combined | |
| Endoscopy | pos | neg | pos | neg | pos | neg | pos | neg |
| positive | 187 | 6 | 123 | 8 | 91 | 5 | 401 | 19 |
| negative | 5 | 97 | 4 | 87 | 2 | 80 | 11 | 264 |
| Sensitivity (95% CI) | 96.9 (93,99) | | 93.9 (88,97) | | 94.8 (88,98) | | 95.5 (93,97) | |
| Specificity (95% CI) | 95.1 (89,98) | | 95.6 (89,99) | | 97.6 (92,100) | | 96.0 (93,98) | |

*Combined endoscopic methods used were histology and culture per DAIDP guidelines⁸ for post-treatment monitoring.

Please note that the post-treatment performance characteristics at 1, 3 and 6 months after therapy are not statistically different. Therefore, the single best estimates of sensitivity and specificity are presented in the 1-6 Months Combined column.

Negative Predictive Value (NPV) for Post-Treatment Monitoring

Given the post-treatment sensitivity (95.5%) and specificity (96.0%) observed in these studies, and assuming a treatment efficacy of 90% (10% prevalence of residual *H. pylori* infection), the NPV of the Meretek UBT® is greater than 99%. When efficacy of treatment drops to 50%, the NPV is still greater than 95%.

XIII. Bibliography

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XIV. Name and Place of Business

The BreathTek™ UBT for *H. pylori* Collection Kit is manufactured for Meretek Diagnostics, Inc., Nashville, TN 37211.

XV. Labeling Revision Information

Revision: 09May01

Part Number: 2207

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6 SIMPLE, BREATHTAKING STEPS

Directly detect an ACTIVE H. pylori infection



One

*Collect baseline
breath sample*



Two

*Prepare the
Pranactin-Citric™
solution*



Three

*Patient drinks
Pranactin-Citric™
solution*



Four

*Collect second
breath sample
after 15 minutes*



Five

*Send breath
tubes to your
testing
laboratory*



Six

*Receive patient
results and treat
accordingly*