510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

K173777

B. Purpose for Submission:

To expand the indications for use of the BreathID Hp Lab System to include use with pediatric patients ages 3-17 years old.

C. Measurand:

Changes in the $^{13}CO_2/^{12}CO_2$ ratio of exhaled breath following ingestion of ^{13}C urea

D. Type of Test:

H. pylori ^{13}C-Urea Breath Test

E. Applicant:

Exalenz Bioscience Ltd.

F. Proprietary and Established Names:

Exalenz BreathID Hp Lab System

G. Regulatory Information:

1. Regulation section:

   866.3110

2. Classification:

   Class I

3. Product code:

   MSQ, JJQ

4. Panel:

   83 Microbiology

H. Intended Use:

1. Intended use(s):

   The Exalenz BreathID Hp Lab System is intended for use to non-invasively measure changes in the $^{13}CO_2/^{12}CO_2$ ratio of exhaled breath, which may be indicative of increased urease production associated with active *Helicobacter pylori* (*H. pylori*) infection in the stomach.

   The Exalenz BreathID Hp Lab System is indicated for use as an aid in the initial diagnosis and post treatment monitoring of *H. pylori* infection in adult patients and pediatric patients ages 3-17 years old. The Exalenz BreathID Hp Lab System consists of the appropriate IDkit Hp kit, and the BreathID Hp device, Auto Sampler and Lab Application.

   To be administered by trained personnel as ordered by a licensed healthcare practitioner.

2. Indication(s) for use:

   The Exalenz BreathID Hp Lab System is intended for use to non-invasively measure changes in the $^{13}CO_2/^{12}CO_2$ ratio of exhaled breath, which may be indicative of increased urease production associated with active *Helicobacter pylori* (*H. pylori*) infection in the stomach.

   The Exalenz BreathID Hp Lab System is indicated for use as an aid in the initial diagnosis and post treatment monitoring of *H. pylori* infection in adult patients and pediatric patients ages 3-17 years old. The Exalenz BreathID Hp Lab System consists of the appropriate IDkit Hp kit, and the BreathID Hp device, Auto Sampler and Lab Application.

   To be administered by trained personnel as ordered by a licensed healthcare practitioner.

3. Special conditions for use statement(s):

   Prescription use only

4. Special instrument requirements:

   For use with the Exalenz BreathID Hp Lab System

I. Device Description:

The BreathID Hp Lab System is a non-invasive breath test system for detecting the presence of *Helicobacter pylori* (*H. pylori*). The system consists of the BreathID Hp device which is an electro-optical medical device with embedded software that measures and computes the changes in ratio between $^{13}CO_2$ and $^{12}CO_2$ concentrations in the patient's exhalation, an Auto Sampler, a Lab Application, and the IDkit Hp Two test kit.

The IDkit Hp Two kit consists of:

- Two Breath Sample Bags (Baseline and Post Ingestion) with bar code labels
- One large Sample Transport Bag
- One 75mg ^{13}C-urea tablet
- One 4.3g package of powdered Citrica (citric acid)
- One drinking straw
- Package Insert (Instructions for Use)
- Quick User Guide

The BreathID Hp Lab System measures and computes the ratio between $^{13}CO_2$ and $^{12}CO_2$ in the patient's exhaled breath before and after the ingestion of ^{13}C-urea. The change in the $^{13}CO_2$ / $^{12}CO_2$ ratio before and after ingestion of ^{13}C-urea is used to compute the Delta over Baseline (DOB).

The ^{13}C measurement method for the BreathID Hp Lab system uses Molecular Correlation Spectroscopy (MCS) technology. MCS technology is based on the concept of optical absorption of specific radiation emitted from CO_2 discharge lamps.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Exalenz BreathID Hp Lab System

2. Predicate 510(k) number(s):
   K162150

3. Comparison with predicate:

Similarities		
Item	Device **BreathID Hp Lab System (K173777)**	Predicate **BreathID Hp Lab System (K162150)**
Indications	Initial diagnosis and post treatment monitoring for *H. pylori* infection	Same
System Hardware Components	• BreathID Hp device • Auto Sampler • IDkit Hp Two test kit • PC	Same
System Software Components	• BreathID Hp Lab embedded SW • BreathID Hp Lab Application • Auto Sampler embedded SW	Same
Test Sample	Human breath exhaled into breath sample bags	Same
Sample Collection Method	Two breath sample bags: for baseline and post ingestion	Same

Similarities		
Item	Device **BreathID Hp Lab System (K173777)**	Predicate **BreathID Hp Lab System (K162150)**
Organism	*Helicobacter pylori*	Same
Reagent	^{13}C Urea (NDA 21-314)	Same
Test Duration	15 – 20 minutes	Same
Detection Method	Measuring levels of $^{13}CO_2$ and $^{12}CO_2$ using MCS	Same
Test Output (Reported Result)	DOB of the $^{13}CO_2$ / $^{12}CO_2$ ratio before and after ingestion of ^{13}C Urea	Same
Cut-off Point	5.0 DOB per mil (post dose minus pre dose)	Same

Differences		
Item	Device **BreathID Hp Lab System (K173777)**	Predicate **BreathID Hp Lab System (K162150)**
Intended Use Population	Adult and Pediatric	Adult

K. Standard/Guidance Document Referenced (if applicable):

Not applicable

L. Test Principle:

The Exalenz BreathID Hp Lab System is a non-invasive diagnostic test that analyzes a breath sample before and after ingestion of ^{13}C- urea; it is used to identify those patients with *H. pylori* infection. The Exalenz BreathID Hp Lab System breath test is performed as follows: a 75 mg ^{13}C-urea tablet and 4.3 g Citrica Powder are dissolved in water, and the resulting solution is ingested by the patient. The Citrica creates an acidic environment in the stomach and delays the transfer of the ingested solution to the duodenum. These two characteristics facilitate the decomposition of the urea by *H. pylori*, if present. In the presence of gastric *H. pylori* urease, ^{13}C-urea is decomposed to $^{13}CO_2$ and NH_3 according to the following equation:

$$2\ {}^{13}\text{C-urea} + 2\ H_2O \xrightarrow{\textit{H. pylori}\ \text{urease}} 2\ {}^{13}CO_2 + 2\ NH_3$$

In *H. pylori* infected patients, *H. pylori* urease cleaves the urea immediately after the ^{13}C-urea solution is ingested. The resulting $^{13}CO_2$ is rapidly absorbed into the blood and then exhaled in the breath. The BreathID Hp Lab System measures and computes the ratio between $^{13}CO_2$ and $^{12}CO_2$ in the patient's exhaled breath before and after the ingestion of ^{13}C-urea. The change in the $^{13}CO_2$ / $^{12}CO_2$ ratio before and after ingestion of ^{13}C-urea is used to compute the Delta over Baseline (DOB). In *H. pylori*-negative patients, ^{13}C-urea is not converted to $^{13}CO_2$ in the stomach because there are no human enzymes that

metabolize urea in the stomach.

The BreathID Hp Lab System consists of the BreathID Hp Device, an Auto Sampler, the computer based BreathID Hp Lab application with a Work Station, and the IDkit:Hp Two test kit. The system enables sample collection into breath sample bags, instead of using a nasal cannula. Breath sample bag collection enables off site and deferred testing. The BreathID Hp Lab System with the IDkit:Hp Two test kit enables testing of multiple breath sample bags sequentially using the Auto Sampler. A maximum of ten pairs of bags (Baseline and Post Ingestion) can be attached to the Auto Sampler in 20 ports, for measurement on the BreathID Hp Device. The Lab Application controls the automated process and presents the results.

Patients first fill a Baseline Breath Sample Bag prior to ingestion of the ^{13}C-urea test solution, and then fill a Post-Ingestion Breath Sample Bag 15 minutes after ingestion. The bags are color-coded to reduce the risk of mixing-up the patient samples collected before and after consuming the test drink. One DOB measurement detecting the change in the $^{13}CO_2/^{12}CO_2$ ratio is sufficient since the Post-Ingestion Breath Sample Bag contains breath collected 15 minutes after consumption of the test drink. Immediately following the conclusion of the test, the system prints a summary of the test results.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Precision and reproducibility studies were demonstrated in a previous submission for the same device. See K162150 (section M1a).

   b. Linearity/assay reportable range:

   Not applicable

   c. Traceability, Stability, Expected values (controls, calibrators, or methods):

   See K162150 (section M1c).

   d. Detection limit:

   Not applicable

   e. Analytical specificity:

   See K162150 (section M1e).

f. Assay cut-off:

The cut-off value is 5.0 Delta Over Baseline (DOB) for both adult and pediatric populations. Values below 5.0 DOB are interpreted as negative and values greater than or equal to 5.0 are interpreted as positive.

2. Comparison studies:

a. Method comparison with predicate device:

Not applicable

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical Sensitivity:

See K162150 (section M3a) for clinical sensitivity determined in an adult population.

b. Clinical specificity:

See K162150 (section M3a) for clinical specificity determined in an adult population.

c. Other clinical supportive data (when a. and b. are not applicable):

The clinical sensitivity and specificity of the BreathID Hp Lab System for pre- and post-therapy *H. pylori* diagnosis was previously established in a clinical study with adult patients in comparison to esophagogastroduodenoscopy biopsy testing (K162150). No major changes to instrumentation, software, assay cut-off, drug formulation, or drug dosing were made for use in the pediatric population. Therefore, the BreathID Hp Lab System test was evaluated in a limited number of pediatric subject with the primary goal of evaluating safety in this population. Supported by existing clinical performance in the adult population, device performance was assessed in a limited clinical study in a pediatric population as described below.

Pediatric population study:
A multi-center, non-randomized, open label study was conducted with the primary goal of evaluating the safety of the standard dose of the ^{13}C-urea and citric acid solution in a pediatric population, and a secondary goal of evaluating performance of the BreathID Hp Lab System compared to stool antigen testing in this population using IDkit Hp Two kit breath collection and the same 5 DOB diagnostic cutoff. The study tested the ^{13}C-urea drug using the BreathID Hp Lab System in symptomatic children ages 3-17 who were suspected of *H. pylori* infection and who were scheduled to undergo both a breath test and an FDA cleared *H. pylori* stool antigen

test. The study was not powered to assess effectiveness in pediatric subjects, and the standard reference method (i.e., composite results based on samples from endoscopy) was not used as the comparator.

The study was conducted at six geographically diverse clinical sites of differing sizes representing clinical laboratory as well as point of care settings in the US and Israel. Local site personnel were trained on administering the breath test. To represent point of care and clinical laboratory settings, the bagged sample analysis was performed either on site or at a central laboratory using a BreathID Hp Lab System. FDA cleared *H. pylori* stool antigen testing was analyzed at a central laboratory. All adverse events associated with the breath test were recorded.

A total of 54 subjects were screened for study enrollment, and one subject was excluded prior to participating in any study related procedure. Fifty-three subjects were enrolled and were followed for the safety assessment. Forty-two subjects completed the full study protocol requirements and provided evaluable results for both the BreathID Hp Lab System and the stool antigen test. Of the total enrolled subjects, 57% (30/53) were female, 43% (23/53) were male, and 77% (41/53) were less than 12 years old.

Results

Among the 53 pediatric subjects followed for the safety assessment, one adverse event of vomiting was experienced by one subject (1.89%) and resolved on the same day. No reportable major safety concerns were observed due to adverse events during the study.

For the 42 subjects with evaluable test results, the positive percent agreement (PPA) between the BreathID Hp Lab System and the stool antigen test was 93.3% (14/15) [95% CI: 70.19, 98.82], and the negative percent agreement (NPA) was 100% (27/27) [95% CI: 87.55, 100]. See Table 1.

Table 1. Comparison of BreathID Hp Lab System results to FDA-cleared H. *pylori* stool antigen test results

		Stool Antigen Test Results		
		Positive	**Negative**	**Grand Total**
BreathID Hp Lab System results using IDkit Hp Two	**Positive**	14	0	14
	Negative	1	27	28
	Grand Total	15	27	42

			95% CI	
PPA	93.33%	(14/15)	70.19%	98.82%
NPA	100.00%	(27/27)	87.55%	100%

4. Clinical cut-off**:**

   Not applicable

5. Expected values/Reference range:

   Not applicable

N. Instrument Name:

Exalenz BreathID Hp Lab System

O. System Descriptions:

1. Modes of Operation:

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes ___X____ or No _____

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

   Yes ___X____ or No _____

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes ___X____ or No _____

3. Specimen Identification:

   Specimens IDs can be entered manually or through a barcode reader.

4. Specimen Sampling and Handling:
   Specimens for the BreathID Hp Lab System consist of breath exhaled through the mouth into the breath collection bags (IDkit Hp Two test kit) before and after ingesting the ^{13}C-urea solution. Breath specimens collected in bags can be measured up to 14 days from the time of collection.

   The Exalenz BreathID Hp Lab System Auto Sampler, BreathIDLab Application, and Work Station permit the automated consecutive batch measurement of up to 10 pairs of breath bags (before and after ingestion of ^{13}C- urea) for a total of 20 bags.

5. Calibration:

   Calibration is performed by the instrument using five gas samples of known concentration and isotope ratio to adjust the absorption cell calibration curves. Calibration is intended to attain identical isotope ratios over the collection range of CO_2 concentrations to ensure accurate readings in both negative and positive samples. The device uses these five concentrations to determine the systematic error of the system and to ensure that the estimated systematic error is below a specified value. If the systematic error is not below the specified value, the device prompts the user to contact Exalenz for repair or replacement.

6. Quality Control:

   To ensure correct functioning of the system, the BreathID Hp Lab System will automatically perform a self test using an internal SystemTest cartridge after 75 tests are completed. This procedure confirms that the system is functional and is performing within specifications.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Not applicable

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable.

R. Conclusion:

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