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

A. 510(k) Number:

K173772

B. Purpose for Submission:

To expand the indications for use of the BreathID Hp 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 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 System is intended for use to continually and 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 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 System consists of the appropriate IDkit Hp kit, and the BreathID Hp device.

   The device is for use by trained health care professionals. To be administered under a physician's supervision.

2. Indication(s) for use:

   The Exalenz BreathID Hp System is intended for use to continually and 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 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 System consists of the appropriate IDkit Hp kit, and the BreathID Hp device.

   The device is for use by trained health care professionals. To be administered under a physician's supervision.

3. Special conditions for use statement(s):

   Prescription use only

4. Special instrument requirements:

   For use with the Exalenz BreathID Hp System

I. Device Description:

The BreathID Hp 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, and the IDkit Hp One test kit.

The IDkit Hp One kit consists of:

- One IDcircuit nasal cannula
- One 75mg ^{13}C-urea tablet
- One 4.3g package of powdered Citrica (citric acid)
- One drinking straw
- Package Insert (Instructions for Use)

The BreathID Hp System continually measures and computes the ratio between $^{13}CO_2$ and $^{12}CO_2$ in the patient's exhaled breath collected using a nasal cannula 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 system is based on 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 System

2. Predicate 510(k) number(s):
   K130524

3. Comparison with predicate:

Similarities		
Item	Device **BreathID Hp System (K173772)**	Predicate **BreathID Hp System (K130524)**
Indications	Initial diagnosis and post treatment monitoring for *H. pylori* infection	Same
System Hardware Components	• BreathID Hp device • IDkit Hp One test kit • PC	Same
System Software Components	• BreathID Hp device embedded SW	Same
Test Sample	Human breath collected using a nasal cannula	Same
Sample Collection Method	Continual collection over the test duration through a nasal cannula	Same
Organism	*Helicobacter pylori*	Same
Reagent	^{13}C Urea (NDA 21-314)	Same
Test Duration	10 - 20 minutes	Same

Similarities		
Item	Device **BreathID Hp System (K173772)**	Predicate **BreathID Hp System (K130524)**
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 System**	Predicate **BreathID Hp 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 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 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 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 test begins with the collection of a baseline breath sample prior to ingestion of the ^{13}C-urea test solution. The patient breathes normally while the BreathID Hp System collects

samples through the IDcircuit nasal cannula. The IDcircuit extracts moisture and patient secretions from the breath samples to provide accurate CO_2 readings, and the device measures the $^{13}CO_2$ / $^{12}CO_2$ ratio of the baseline measurement. The patient then ingests the ^{13}C -urea test drink. While the patient continues to breathe normally, the BreathID Hp System continually and non-invasively samples the patient's breath via the cannula and measures the changes in the $^{13}CO_2$ / $^{12}CO_2$ ratio versus the baseline sample. These changes are displayed as a graph on the display screen while the test continues. The graph shows multiple points that allow the physician to identify the change in the DOB of the $^{13}CO_2$ / $^{12}CO_2$ ratio in response to the administered ^{13}C-urea. Once the BreathID Hp System has collected enough data to determine whether or not the graph passes the assay cut-off threshold unambiguously, it automatically ends the test and prints out the 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 K130524 (section J1b).

   b. *Linearity/assay reportable range:*

      Not applicable

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

      Not applicable

   d. *Detection limit:*

      Not applicable

   e. *Analytical specificity:*

      Not applicable

   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 DOB 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 K011668 for clinical sensitivity determined in an adult population.

   b. *Clinical specificity:*

      See K011668 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 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 (K011668). 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 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 System compared to stool antigen testing in this population using IDkit Hp One kit breath collection and the same 5 DOB diagnostic cutoff. The study tested the ^{13}C-urea drug using the BreathID Hp 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 and experience levels in the US and Israel. Local site personnel were trained on

administering the breath test. 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-one of the enrolled subjects completed the full study protocol requirements and provided evaluable results for both the BreathID Hp 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 41 subjects with evaluable test results, the positive percent agreement (PPA) between the BreathID Hp 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% (26/26) [95% CI: 87.1, 100]. See Table 1.

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

		Stool Antigen Test Results		
		Positive	**Negative**	**Grand Total**
BreathID Hp System results using IDkit Hp One	**Positive**	14	0	14
	Negative	1	26	27
	Grand Total	15	26	41

			95% CI	
PPA	93.33%	(14/15)	70.19%	98.82%
NPA	100.00%	(26/26)	87.13%	100%

4. Clinical cut-off**:**

   Not applicable

5. Expected values/Reference range:

   Not applicable

N. Instrument Name:

Exalenz BreathID Hp 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 are entered manually.

4. Specimen Sampling and Handling:
   Specimens for the BreathID Hp System consist of breath acquired through a nasal cannula.

5. Calibration:
   Calibration is performed by the instrument by diluting pre-dose patient breath or operator breath into five different concentrations within an absolute maximum concentration range. 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 the manufacturer for repair or replacement.

6. Quality Control:
   To ensure correct functioning of the BreathID Hp System in the field, a self test is required every 25 breath tests. BreathID Hp System will automatically perform a self test after 25 tests are completed, during the baseline measurement phase of the next patient test. This procedure confirms that the BreathID Hp 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.