DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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October 31, 2016

EXALENZ BIOSCIENCE LTD.
C/O ORNA OZ
BIOMEDICAL STRATEGY LTD.
155 BIALIK ST.
RAMAT-GAN, IL 5252346

Re: K162150
Trade/Device Name: BreathID Hp Lab System
Regulation Number: 21 CFR 866.3110
Regulation Name: *Campylobacter fetus* serological reagents
Regulatory Class: I
Product Code: MSQ, JJQ
Dated: July 28, 2016
Received: August 2, 2016

Dear Ms. Oz:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and 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, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Ribhi Shawar -S

For Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K162150

Device Name
BreathID® Hp Lab system

Indications for Use *(Describe)*
The Exalenz BreathID® Hp Lab System is intended for use to non-invasively measure changes in the 13CO2/12CO2 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. The Exalenz BreathID® Hp Lab System consists of the IDkit:Hp™ kits, and the BreathID® Hp device, Auto Sampler and Lab Application.
To be administered by trained personnel as ordered by a licensed healthcare practitioner.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(K) SUMMARY

510(K) Number K162150

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Date Prepared:
July, 2016

Trade Name:
BreathID® Hp Lab System

Classification Name:
Test, urea (breath or blood)

Product Code:
MSQ, JJQ

Device Class:
I

Regulation Number:
866.3110

Panel:

Microbiology

Predicate Device:

Exalenz BreathID® Hp System [Exalenz Bioscience Ltd.] cleared under K130524

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 an electro-optical medical device with embedded software designed to measure and compute 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 a test kit. The IDkit Hp™ Two kit consists of:

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

Using bags for breath collection along with the Auto Sampler enables off site and deferred testing as well as testing of multiple breath sample bags sequentially in a batch.

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 both the current and the cleared versions of the BreathID® Hp systems 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.

Intended Use / Indication 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. The Exalenz BreathID® Hp Lab System consists of the IDkit Hp™ kits, and the BreathID® Hp device, Auto Sampler and Lab Application.

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

Substantial Equivalence:

The following table summarizes the data on the Exalenz BreathID® Hp Lab System (subject of this 510(k) submission) and compares to the Exalenz BreathID® Hp System cleared under K130524 (the predicate).

	BreathID® Hp Lab System	**BreathID® Hp System**
510(k) Number	**K162150**	**K130524**
Product Code/Class	MSQ/Class I	Same
Regulation	*Campylobacter fetus* serological reagents, 866.3110	Same
Manufacturer	Exalenz Bioscience Ltd.	Same
Intended 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. The Exalenz BreathID® Hp Lab System consists of the IDkit Hp™ kits, and the BreathID® Hp device, Auto Sampler and Lab Application. To be administered by trained personnel as ordered by a licensed healthcare practitioner.	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. The Exalenz BreathID® Hp System consists of the IDkit Hp™ and the BreathID® Hp test device. The device is for use by trained health care professionals. To be administered under a physician's supervision.

	BreathID® Hp Lab System	BreathID® Hp System
System Hardware Components	• BreathID® Hp Lab device • Auto Sampler • IDkit Hp™ Two	• BreathID® Hp device • IDkit:Hp™ One
System Software Components	• BreathID® Hp Lab device embedded SW • BreathID® Hp Lab Application • Auto Sampler embedded SW	• BreathID® Hp device embedded SW
Test Sample	Human breath exhaled into breath sample bags	Human breath collected using a nasal cannula
Sample Collection Method	Two breath sample bags: for baseline and for post ingestion	Continual collection over the test duration through a nasal cannula
Organism	*Helicobacter pylori*	Same
Reagent	^{13}C Urea (NDA 21-314)	Same
Test Duration	15-20 minutes	10-30 minutes
Indications	Initial diagnosis and post treatment monitoring	Same
Detection Method	Measuring levels of $^{13}CO_2$ and $^{12}CO_2$ using Molecular Correlation Spectroscopy (MCS)	Same
Test Output (Reported Result)	Delta Over Baseline (DOB) of the $^{13}CO_2$ / $^{12}CO_2$ ratio (before and after ingestion of ^{13}C Urea) and positive/negative determination for *H. pylori* infection	Same
Cut-off Point	5.0 DOB per mil (post dose minus pre dose)	Same

Comparison of Intended Use:

The intended use and indications for use of the BreathID® Hp Lab System are substantially equivalent to those of its predicate; both are indicated for the initial diagnosis and post treatment monitoring of *H. pylori* infection in adult patients, and both are prescription devices. The BreathID® Hp Lab System uses breath bags for collection of the breath sample, unlike its predicate. These differences, however, have

no effect on the fundamental intended use or indications for use of the system nor do they alter the system diagnostic characteristics or raise any new safety issues.

Ingested Drug:

The ingested drug product used in the BreathID® Hp Lab System IDkit Hp™ Two kit, (13C-Urea tablet, 75mg and Citrica powder, 4g), was originally approved in NDA 21-314. The identical drug product with identical preparation and administration is used in the cleared predicate device BreathID® Hp System kit.

Comparison of Technological Characteristics:

The BreathID® Hp Lab System shares with its predicate device the same underlying technology, the same test substrate, and the same diagnostic capabilities. Both the subject and predicate systems use the MCS technology (Molecular Correlation Spectroscopy) and measure the ratio of $^{13}CO_2/^{12}CO_2$ in exhaled breath prior to and after administration of the test substrate (^{13}C-Urea). The MCS technology measures the light absorbance by an infrared spectrometry, which is correlative to CO_2 concentration in the breath sample. The output result in both systems is the Delta Over Baseline (DOB) and a positive/negative determination is based on the same assay cut-off (≥5 DOB).

Like its predicate device, the BreathID® Hp Lab System includes an analyzer device with embedded SW and a test kit. In addition, unlike its predicate, the subject system also includes the Auto Sampler with its embedded SW and the BreathID® Lab Application with its Work Station. These components directly relate to the use of breath bags in the subject system, are designed for the convenience of the operator and are commonly used in other FDA cleared *H. pylori* breath test devices that collect breath into bags (K011668, K130524).

The subject system uses breath bags, hence the breath is exhaled through the mouth into the bag, unlike the nasal cannula used in the predicate device, which transfers breath exhaled from the nose. Yet, as demonstrated in the analytical and clinical testing, the underlying technology similarly applies to both systems as well as the diagnostic specifications (*i.e.,* the light absorbance similarly correlates to the concentration of $^{13}CO_2$ and $^{12}CO_2$ regardless of the breath source, and the same cut-off and accuracies apply to both systems). It is also important to note that the actual measurement by the predicate device (*i.e.,* the BreathID® Hp System) is performed in an intermittent fashion, at timed intervals, despite the continuous transfer of the breath sample through the nasal cannula. Consequently, the absorbance measurement of the two discrete breath collection bags in the subject BreathID® Hp Lab System may be considered substantially equivalent to the intermittent measurement of the light absorbance in the predicate device. Finally, any additional differences between the

subject and predicate systems were evaluated in the performance testing, as briefly described below, all demonstrating comparable safety and efficacy characteristics of the BreathID® Hp Lab System, subject of this 510(k) submission, and its predicate, the BreathID® Hp System.

Summary of Performance Testing:

Exalenz has performed extensive and well-executed verification and validation for demonstration of substantial equivalence of the BreathID® Hp Lab System to the cleared BreathID® Hp System. The following key verification and validation tests were used to establish substantial equivalence:

- Analytical Studies (Bench)
  - Precision testing

    The precision/repeatability testing was conducted using the complete BreathID® Hp Lab System, hence evaluating all system components concomitantly. The reproducibility testing was conducted in two parts: The first part tested the precision/repeatability and reproducibility of the entire System while a dedicated, additional, test focused on the reproducibility of the Auto Sampler. The testing evaluated variability across different operators, test devices, sites, and days.
  - Carry over testing

    Cary over testing was designed in compliance with the recommendations of the CLSI EP-10 standard and successfully demonstrated that there was no sample carry over for the BreathID Hp Lab System.
  - Specimen storage conditions

    Testing successfully demonstrated that the Breath Sample Bags maintain their performance characteristic when under their end limits storage conditions of temperature and relative humidity and for the maximal allowed storage time of 14 days.
  - System operating conditions

    Auto Sampler: Testing successfully demonstrated that the Auto Sampler operates according to its specifications while operating within the defined environmental conditions.
- Software Verification and Validation

  Software testing was conducted to evaluate the performance of the subject system and to verify that it performs according to its specifications. Verifications involved functionality testing, timing analysis, integration with the hardware, and error detection and handling. Verification was achieved by design reviews, code walkthroughs, functional testing of sub-components and integration testing with the hardware. Additionally, the software was extensively verified at the system level.

- Clinical Validation

  A multi-center, non-randomized, open label validation study was completed to confirm the safety and efficacy of the BreathID® Hp Lab System, when used together with the IDkit Hp™ Two kit, for initial diagnosis and post-treatment monitoring of *H. pylori* infection versus composite biopsy results (histology and RUT). The clinical study was conducted in compliance with its protocol and in accordance with the ethical principles under Investigational Review Board (IRB) approval consistent with Good Clinical Practice (GCP) and with applicable regulatory requirements. All endpoints in the protocol were met. The study evaluated 179 adult initial diagnosis patients and 68 post–treatment patients who were positive for infection and who had completed eradication therapy at least six weeks prior to participation in the study. For the initial diagnosis cohort, the sensitivity in comparison to composite biopsy results was 100% [95% CI (90.60; 100.00)] and specificity was 97.9% [95% CI (93.97; 99.28)]. For the post-treatment cohort, the sensitivity was 92.3% [95% CI (66.69; 98.63)] and the specificity was 100% [95% CI (93.47; 100.00)]. Therefore, the study demonstrated that breath samples can be successfully collected in the Exalenz breath sample bags and accurately tested using the BreathID® Hp Lab System. There were no reportable major safety concerns due to adverse events. It can thus be concluded that the BreathID® Hp Lab System can successfully be used for initial diagnosis and post-eradication monitoring, similar to the predicate device.

The results of analytical and clinical studies demonstrate that the BreathID® Hp Lab System performs according to its specifications and to the requirements established for devices for the detection of *H. pylori* without raising new questions regarding their safety or efficacy.

Conclusion:

The Exalenz BreathID® Hp Lab System has been demonstrated to be as safe and effective as its predicate device, the cleared Exalenz BreathID® Hp System (K130524), for its intended use, and it is substantially equivalent to its predicate device without raising new safety and/or effectiveness issues.