DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

May 13, 2016

Bone Index Finland, Ltd.
% Dr. Janne Karjalainen
CTO
Microkatu 1
Kuopio 70211
FINLAND

Re: K152020
Trade/Device Name: Bindex, BI-100
Regulation Number: 21 CFR 892.1180
Regulation Name: Bone sonometer
Regulatory Class: II
Product Code: MUA
Dated: April 25, 2016
Received: May 6, 2016

Dear Dr. Karjalainen:

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 Part 801); 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 regulation (21 CFR Part 801), 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,

For

Robert Ochs, Ph.D.
Director
Division of Radiological Health
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)*
K152020

Device Name
Bindex BI-100

Indications for Use *(Describe)*
Bindex measures apparent cortical bone thickness at the proximal tibia and can be used in conjunction with other clinical risk factors or patient characteristics as an aid to the physician in the diagnosis of osteoporosis and other medical conditions leading to reduced bone strength and in the determination of fracture risk.

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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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510(k) Summary

I. SUBMITTER

Bone Index Finland, Ltd.
Microkatu 1
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Phone: +358 45 896 2650
Contact Person: Janne Karjalainen
Date Prepared: Jun 30, 2015

II. DEVICE

Name of Device: Bindex, Model BI-100
Common or Usual Name: Bone sonometer
Classification Name: Bone sonometer (21 CFR 892.1180)
Regulatory Class: II
Product Code: MUA

III. PREDICATE DEVICE

BeamMed MiniOmni bone sonometer, K110646.

This predicate has not been subject to a design-related recall.

IV. DEVICE DESCRIPTION

The Bindex system includes ultrasound pulser, transducer and software. Bindex is connected to the USB port of a computer and controlled with computer software. Bindex is used for measurement of cortical bone thickness and it provides Density Index (DI), a parameter which estimates bone mineral density at the hip as measured with DXA. For measurements, gel is applied on skin and ultrasound transducer is manually placed on the measurement location. Standardized measurement location is at proximal (1/3 length) of tibia. Transducer is manually oriented perpendicularly to the surface of the cortical bone to achieve accepted measurement. Measurement is repeated five times at each measurement location. Finally, transducer is disinfected by wiping gel off with disinfective solution moistened cloth or tissue.

The associated accessories include:

- Measurement stick
- Ultrasound gel (optional)

V. INDICATIONS FOR USE

Bindex measures apparent cortical bone thickness at the proximal tibia and can be used in conjunction with other clinical risk factors or patient characteristics as an aid to the physician in the diagnosis of osteoporosis and other medical conditions leading to reduced bone strength and in the determination of fracture risk.

Indications for use discussion

The Indications for Use statement for the Bindex is not identical to the predicate device; however; the differences do not alter the intended diagnostic use of the device nor do they affect the safety of the device relative to the predicate. Both the subject and predicate devices have the same intended use for the diagnosis of osteoporosis.

Effectiveness discussion

As stated in the indications for use with the predicate, osteoporosis classification is based on T-score threshold (-2.5 standard deviations from young adult mean) determined for the speed of sound as measured with the predicate device. Osteoporosis is defined by the world health organization as T-score equal or less than -2.5 standard deviations from young adult average as measured with DXA (Bone mineral density at lumbar spine, proximal femur or femoral neck). It has been well established that the WHO definition of osteoporosis cannot be applied with any other measurement than axial DXA (Krieg et al. 2008, International society for clinical densitometry (ISCD) official positions) and stated also in FDA's Guidance for Industry and staff 'Class II Special Controls Guidance Document: Bone Sonometers'. The ISCD recommends the use of 90% sensitivity and specificity thresholds determined in comparison study with DXA. For an ultrasound device to be effective in the task of diagnosing osteoporosis, these thresholds have to be determined and applied. For Bindex, these

thresholds have been determined in Finnish Caucasian female population at age 50 to 90 years and found to be feasible for American Caucasian population.

VI. COMPARISON OF TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICE

The predicate and subject devices are based on ultrasound technology. Both devices send ultrasound waves to living tissues and receive them after they have interacted with bone tissue. Both devices use transducers placed on the skin with ultrasound gel to be able to transmit the ultrasound wave to tissues. The predicate device is detects ultrasound waves transmitted along the cortical bone whereas the subject device is based on detecting waves reflected from the tissue. At high level, the subject and predicate devices are based on the following same technological elements:

- Ultrasound pulser/receiver unit – generates voltage pulse which is transmitted to the transducer and receives waves transmitted/reflected from bone tissue.
- Ultrasound transducer – transfers electrical voltage change to mechanical wave and vice versa.
- Computer software – used for analyses of detected ultrasound waves
- Connected to computer by universal serial bus (USB)

The predicate and subject devices are further compared in table 1.

Table 1. Device comparison table.

#	Item	MiniOmni (Predicate)	Bindex BI-100 (subject)
1	Indications for use	The BeamMed MiniOmni Ultrasound Bone Sonometer is a non-invasive device that is designed for the quantitative measurement of the signal velocity of ultrasound waves ("Speed of Sound" or "SOS" in m/s) propagating at multiple skeletal sites (i.e., the distal one-third of the radius, the proximal third phalanx and the fifth metatarsal). SOS provides an estimate of skeletal fragility. The output is also expressed as a T-score and a Z-score, and can be used in conjunction with other clinical risk factors as an aid to the physician in the diagnosis of osteoporosis and other medical conditions leading to reduced bone strength and, ultimately, in the determination of fracture risk. Multiple skeletal site testing provided clinicians with alternatives if one site is	Bindex measures apparent cortical bone thickness at the proximal tibia and can be used in conjunction with other clinical risk factors or patient characteristics as an aid to the physician in the diagnosis of osteoporosis and other medical conditions leading to reduced bone strength and in the determination of fracture risk.

		not accessible and with additional skeletal information (i.e., from bones with different combinations of cortical and cancellous material and from weight bearing and non-weight bearing sites) that assists in diagnosing osteoporosis and risk fracture. The SOS measured by MiniOmni has a precision error low enough in comparison With the expected annual change in a patient's measurement to make it suitable for monitoring bone changes which occur in the early years following menopause (i.e., age range approximately 50-65 years).	
2	Measurement mode	Speed of Sound (SOS)	Cortical Thickness (Ct.Th.).
3	Probe compatibility	Four proprietary multitransducer probes; Centre frequency = 1.25MHz	One transducer, centre frequency = 3.0 MHz (nominal)
4	Electrical safety	Complies with lEC 60601 -1: 1998 including Amendments 1 and 2; IEC 60601-2-37:2001 including Amendments 1 and 2; and IEC 60601-1:2005	IEC 60601-2-37:2001 including Amendments 1 and 2; and IEC 60601-1:2005
5	Electromagnetic compatibility	Complies with IEC 60601-1-2:2007	Complies with IEC 60601-1-2:2007
6	Power supply	Medical grade power supply	PC USB port powered.
7	Operating Environment	Temperature: +10˚C to +35˚C Humidity: 30% to 75% RH, non-condensing Atmospheric Pressure: 700 to 1060 Pc	Temperature: +10˚C to +40˚C Humidity: 5% to 85% RH, non-condensing Atmospheric Pressure: 600 to 1060 Pc
8	Storage Environment	Temperature: +0 ˚C to 50 ˚C Humidity: 30% to 75%, non-condensing	Temperature: +10˚C to +40˚C Humidity: 5% to 85% RH, non-condensing
9	Calibration	Calibration free; Daily System Quality Verification (SQV) with Phantom is required.	Calibration before each use.

VII. PERFORMANCE DATA

The following performance data were provided in support of the substantial equivalence determination.

Biocompatibility testing

The biocompatibility evaluation for the Bindex BI-100 device was conducted in accordance with the FDA Blue Book Memorandum #G95-1 "Use of International Standard ISO-10993,'Biological Evaluation of Medical Devices Part 1: Evaluation and Testing,'"May 1, 1995, and International Standard ISO 10993-1 "Biological Evaluation of Medical Devices –Part 1: Evaluation and Testing Within a Risk Management Process," as recognized by FDA. The battery of testing along 10993-1 would recommend the following tests:

- Cytotoxicity
- Sensitization
- Irritation

The Bindex transducer is in skin contact for duration of less than 24 hours. Other parts of the device will not be in contact with the patient. Since the use of Bindex involves very short skin contact (typically less than 10 minutes) on a healthy skin and therefore poses a very low risk. Safety of the manufacturing and used materials has been further discussed in Biocompatibility report (Section 13).

Electrical safety and electromagnetic compatibility (EMC)

Electrical safety and EMC testing were conducted on the measurement system, consisting of the Bindex BI-100 and a laptop computer (on battery use or connected to power supply with isolation transformer). The system complies with the IEC 60601-1, and IEC 60601-2-37 standards for safety and the IEC 60601-1-2 standard for EMC.

Software Verification and Validation Testing

Software verification and validation testing were conducted and documentation was provided as recommended by FDA's Guidance for Industry and FDA Staff, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices."

The software for this device was considered as a "medium" level of concern, since a failure or latent flaw in the software could indirectly result in serious injury to the patient or operator.

Mechanical and acoustic testing

The acoustic output and mechanical properties have been tested along the principles presented in harmonized standards IEC 62359 and IEC 60601-1:

- Acoustic Testing (documents (Section 16, 004 - 006)

- Drop test (hand piece dropped from 1m on hard surface)
- Ball pressure test (pressed with steel ball 5mm in diameter with force of 20N one hour at a temperature of 75±2˚C)
- Moulding stress relief (device placed in circulating air oven at 70 ˚C for 7 hours and let cool down)

In vitro and In vivo proof of concept

The principle of ultrasonic assessment of cortical bone thickness has been examined with bovine cortical bone samples (*n=6*) and human volunteers (*n=20*) and published by Karjalainen et al. 2008, IEEE Trans Ultrason Ferroelectr Freq control, 55(10).

The values of cortical thickness showed high linear correlations ($r \geq 0.95$) with the thickness values obtained from in vitro measurements with a caliper or in vivo measurements by peripheral quantitative computed tomography (pQCT). No systematic errors that could be related to the cortical thickness were found. The in vivo accuracy of the measurements was 6.6% for the envelope method. Further, the in vivo precision for the envelope method was 0.26 mm.

The safety, effectiveness and feasibility of the methodology applied in Bindex device was evaluated by assessing the accuracy of cortical thickness measurement in comparison to reference methods such as caliper measurement of bone samples and pQCT measurement of volunteer subjects. No adverse effects were reported during the study. This study demonstrates that ultrasound measurement based on similar technology than applied in Bindex can be accurately used for determination of cortical thickness at distal and proximal tibia as well as in distal radius.

Clinical Studies

First, initial clinical testing of the Bindex device included an initial study of 30 patients, a study where association with ultrasound measurement of cortical thickness and subject weight, age and height and gold standard (for osteoporosis diagnostics) dual energy X-ray absorptiometry (DXA) was examined. The density index (DI) was introduced, which is an estimate of proximal femur total bone mineral density (BMD) as measured by DXA. (Karjalainen et al. Osteoporos Int 2012 ;23(4)

Second, clinical testing was continued in Finland (Karjalainen J. et al. Osteoporos Int 2016), involving 572 subjects. The study with Finnish population involved assessment of diagnostic thresholds for discrimination of osteoporotic patients from non-osteoporotic along the current guideline of International Society of Clinical Densitometry (ISCD) (Krieg et al., J Clin Densitom 2008; 11(1) and Hans et al., J Clin Densitom 2008; 11(1)). The effectiveness was evaluated as predictive ability and feasibility of the Bindex to identify Osteoporosis.

Third, in the study conducted (*n* = 560) in the United States (Schousboe et al. 2016), the thresholds developed in Karjalainen et al 2015 were validated. Further, fracture discrimination with Bindex was evaluated and compared to DXA.

Primary effectiveness endpoint:

The use of DI in conjunction with diagnostics with DXA to patients indicated by Bindex (yellow area) will identify 90% of osteoporotic and non-osteoporotic subjects correctly. As predicted by Blake et al. 2005, if thresholds are determined in a population that consists at least 70 osteoporotic and non-osteoporotic patients the true sensitivity and specificity will be above 80% with 95% confidence. This was realized in Karjalainen et al. 2016 and verified in U.S study, Schousboe et al. 2016. Further, it has been verified in both studies that approximately 30% of the patients would need a DXA examination. The similar odd ratios (OD) for clinical fractures with DXA (OD = 1.47) and Bindex DI (OD = 1.37), Ct.Th. (OD = 1.56) suggest similar fracture prediction capability of the technique than DXA. For each standard deviation decrease in DI there is a significant increase in odds for hip osteoporosis (OR=3.03).

Primary safety endpoint:

The primary safety endpoint consisted of adverse events during the ultrasound measurement including:

- Skin effects, inflammation
- Skin or tissue heating
- Other skin or tissue effects
- Adverse effect on operator
- Electrical malfunction
- Hazardous situations
- Other safety related issues reported by person responsible for measurements.

The safety and effectiveness of Bindex device has been discussed in clinical evaluation document (Section 16 – 007) in which no adverse events were reported with patient or operator.

Summary

The predicate device reports T-Scores (parameter value normalized by young adult mean) whereas subject device reports Density Index. The Class II Special Controls Guidance Document: Bone Sonometers suggests determination of device specific thresholds for osteoporosis. Since T-Score limit for osteoporosis (-2.5) cannot be applied with any other device than axial DXA, linear transformation of parameters measured by other devices to T-Scores is unnecessary. As the use of the thresholds is recommended, they have been determined for DI without normalization with healthy young individual average parameter value. This will not affect the classification performance for osteoporosis of the technique. Based on the clinical performance as documented in the clinical studies, the Bindex system was found to have a safety and effectiveness profile that is similar to the predicate device.

VIII. CONCLUSIONS

The non-clinical data support the safety of the device and the hardware and software verification and validation demonstrate that the Bindex device will perform as intended in the specified use conditions. The clinical data demonstrate that the Bindex device performs comparably to the predicate device that is currently marketed for the same intended use. Based on the performance testing the subject device is substantially equivalent to the predicate device.

Date: _____

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Janne Karjalainen, CTO
Bone Index Finland Ltd.