May 19, 2023

O.N. Diagnostics
℅ David Kopperdahl
Director, Research and Development
1936 University Ave., Suite 280
BERKELEY, CA 94704

Re: K220402
Trade/Device Name: VirtuOst
Regulation Number: 21 CFR 892.1170
Regulation Name: Bone Densitometer
Regulatory Class: Class II
Product Code: KGI
Dated: April 19, 2023
Received: April 19, 2023

Dear David Kopperdahl:

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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) for

devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Lu Jiang

Lu Jiang, Ph.D.
Assistant Director
Diagnostic X-ray Systems Team
DHT8B: Division of Radiological Imaging
Devices and Electronic Products
OHT8: Office of Radiological Health
Office of Product Evaluation and Quality
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Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*

K220402

Device Name

VirtuOst

Indications for Use *(Describe)*

VirtuOst uses data from computed tomography scans to estimate bone mineral density, bone strength, and a load-to-strength ratio. This information can be used by a physician to assess fracture risk, identify osteoporosis, and monitor therapy. For pediatric patients, VirtuOst provides these estimates without any classifications and should be used only when the benefit of obtaining these estimates outweighs the risk of radiation.

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

Date: May 18, 2023
510(k) Number: K220402

1) Applicant Information

510(k) Owner: O.N. Diagnostics, LLC
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Berkeley, CA 94704

Contact Person: David L. Kopperdahl, PhD
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Establishment Reg. No.: 3010687441

2) Device Identification

Trade Name: VirtuOst
Common Name: QCT Bone Densitometer
Regulation Number: 21 CFR 892.1170
Regulation Name: Bone Densitometer
Regulatory Class: II
Product Code: KGI

3) Predicate Device

Trade Name: VirtuOst – K113725
Common Name: QCT Bone Densitometer
Regulation Number: 21 CFR 892.1170
Regulation Name: Bone Densitometer
Regulatory Class: II
Product Code: KGI

4) Device Description

VirtuOst is a software-only medical device that analyzes data in computed tomography (CT) scans to measure bone mineral density (BMD), bone strength, and a load-to-strength ratio at the proximal femur and vertebral body. BMD is measured from both a 2D projection (in g/cm^2) and a volumetric scan reconstruction (in mg/cm^3) of the CT scan. *VirtuOst* measurements can be

used by a physician to identify osteoporosis, assess fracture risk, and monitor therapy.

The *VirtuOst* analysis is performed on previously physician-acquired image data and is unrelated to acquisition equipment and clinical workstations.

5) Intended Use

VirtuOst uses data from computed tomography scans to estimate bone mineral density, bone strength, and a load-to-strength ratio. This information can be used by a physician to assess fracture risk, identify osteoporosis, and monitor therapy.

6) Indications for Use

VirtuOst uses data from computed tomography scans to estimate bone mineral density, bone strength, and a load-to-strength ratio. This information can be used by a physician to assess fracture risk, identify osteoporosis, and monitor therapy. For pediatric patients, *VirtuOst* provides these estimates without any classifications and should be used only when the benefit of obtaining these estimates outweighs the risk of radiation.

7) Substantial Equivalence

This 510(k) premarket notification is an application to the FDA to modify *VirtuOst*, a class II software medical. The predicate device is the version of *VirtuOst* initially cleared in 2012 (K113725); the subject device is a modified version of *VirtuOst*. The subject and predicate devices both estimate bone mineral density, bone strength and a load-to-strength ratio using a computed tomography scan as input. Compared to the predicate device, the subject device includes several modifications, none of which affected the performance of the *VirtuOst* in terms of safety or effectiveness. A risk analysis was performed evaluating the effects of the device modifications on patient safety, and no new hazards were introduced. Functional black box tests and a regression test were used to verify that the functionality of and outputs from *VirtuOst* have remained consistent across software releases. Performance data are presented demonstrating no substantial changes in technical characteristics for the safety or effectiveness of *VirtuOst*.

Summary of Technology Characteristics and Comparison with Predicate Device

Device Characteristic	Predicate Device (K113725)	Subject Device (K220402)
Trade Name	*VirtuOst*	No change.
Version	1.2.1	2.5.0b

Device Characteristic	Predicate Device (K113725)	Subject Device (K220402)
Product Code	KGI	KGI
Device Classification	Class II	No change.
Construction	Software application coded primarily in Python, C and C++.	No change.
Intended Use	*VirtuOst* uses data from computed tomography scans to estimate bone mineral density, bone strength, and a load-to-strength ratio. This information can be used by a physician to assess fracture risk, identify osteoporosis, and monitor therapy.	No change.
Indications for Use	*VirtuOst* uses data from computed tomography scans to estimate bone mineral density, bone strength, and a load-to-strength ratio. This information can be used by a physician to assess fracture risk, identify osteoporosis, and monitor therapy. For pediatric patients, *VirtuOst* provides these estimates without any classifications and should be used only when the benefit of obtaining these estimates outweighs the risk of radiation.	No change.
Worklist	None.	A worklist organizes and tracks the status of *VirtuOst* jobs and can be populated from a PACS-driven modality worklist.

Device Characteristic	Predicate Device (K113725)	Subject Device (K220402)
Required Input	A. Computed tomography scan with adequate coverage of the hip (at least one proximal femur) or the spine (at least one complete vertebra from T1–L5). B. The CT scan must be an uncompressed transverse reconstruction.	A. Computed tomography scan with adequate coverage of the hip (at least one proximal femur) or the spine (at least one complete vertebra from T1–L5). B. The CT scan can be uncompressed or compressed, and the slice orientation can be transverse, sagittal, or coronal.
Bone segmentation	*Vertebra:* 3D active contour segmentation. *Femur:* Slice-by-slice manual 2D active contour segmentation.	*Vertebra:* 3D active contour segmentation. *Femur:* Slice-by-slice semi-automated 2D active contour segmentation with 3D segmentation of the femoral head.
Phantom calibration	Uses an external calibration phantom	No change
Phantomless calibration	Utilizes blood and air from the patient's CT scan.	Utilizes blood and air, or fat and air, from the patient's CT scan.
Slice spacing adjustment for femurs	No adjustment.	An adjustment is applied to BMD and strength measurements for CT scans having a slice spacing greater than 3mm.
Reported measurements and classifications from a hip analysis	• Femoral strength • Femoral neck areal BMD • Total hip areal BMD • BMD T- and Z-scores • Strength classification • BMD classification • Load-to-strength ratio	No change.

Device Characteristic	Predicate Device (K113725)	Subject Device (K220402)

Reported measurements and classifications from a spine analysis	• Vertebral strength
	• Vertebral trabecular BMD
	• BMD Z-score
	• Load-to-strength ratio
	• For levels T12–L3:
	  ○ Strength classification
	  ○ BMD classification
		No change.

Hip areal BMD (in g/cm^2)	Reported *VirtuOst* values are converted to be equivalent to Hologic DXA values.	Reported *VirtuOst* values are not converted and may differ from Hologic DXA values.
CT-to-DXA areal BMD conversion for the hip (used when calculating T- and Z-scores)	One equation for women and men.	Separate equations for women and men.
Hip areal BMD T-and Z-scores for diagnostic purposes using W.H.O. criteria	DXA-equivalent and NHANES compatible.	No change.
Overall fracture risk classification	Based on the worst (highest risk) classification for strength or BMD at the hip or spine.	No change.
Bone images on the results report	Greyscale projections showing BMD distribution and regions of interest for measuring BMD. Images are labeled "not for diagnostic use."	Greyscale projections showing BMD distribution and regions of interest for measuring BMD. Images are labeled "not for diagnostic use." Color images of the finite element model under virtual loading.
Strength vs. age plots on the results report	Plots are shown for bone mineral density versus age.	Plots are shown for bone mineral density versus age. Plots are shown for strength versus age.

Device Characteristic	Predicate Device (K113725)	Subject Device (K220402)
Automated range check	None.	Range checks are automatically calculated for multiple parameters and outlier values are identified. When a parameter is flagged, the technologist is prompted to review the CT scan for artifacts and the analysis procedure for errors.
Output file format for results	pdf	pdf DICOM encapsulated pdf DICOM structured report DICOM secondary capture image

For any technological characteristics that have been modified, none of the modifications substantially affect the safety or effectiveness of the medical device, as discussed below.

Worklist: A worklist organizes and tracks the status of *VirtuOst* jobs and can be populated from a PACS-driven modality worklist. This functionality improves workflow efficiency, reduces user input errors, and enables integration with other Radiology systems. This modification does not substantially affect the safety or effectiveness of the medical device.

Required input: *VirtuOst* can now open compressed CT scans, and the slice orientation can be transverse, sagittal, or coronal instead of just transverse. This change increases throughput by allowing *VirtuOst* to run on more types of CT images without the need to create an additional reconstruction if the image is not an uncompressed transverse reconstruction. This modification does not substantially affect the safety or effectiveness of the medical device.

Bone segmentation: A refinement of the femur segmentation increases throughput compared to the predicate. A technician still reviews all segmentations and adjusts if necessary. This modification does not substantially affect the safety or effectiveness of the device.

Phantomless Calibration: Adipose tissue is added as an option for phantomless calibration. For phantomless calibration, the predicate device measures the attenuation of aortic blood and air outside of the patient. However, CT scans taken with intravenous contrast agents are not suitable for this type of phantomless calibration because the contrast agent can appreciably alter the attenuation of the blood. Further, the measurement of blood might sometimes be unreliable due to a small volume of interest or local image artifacts from an aortic stent or calcification. The modified device enables adipose tissue instead of blood to be used for the phantomless calibration. Performance data shows fat-air calibration, like the predicate device blood-air calibration, is equivalent to using phantom-based calibration (which uses an external calibration phantom). Thus, this modification does not substantially affect the safety or effectiveness of the device.

Slice spacing adjustment for femurs: Measurements of strength and areal BMD at the hip can be slightly lower when measured from CT images reconstructed with large (> 3 mm) slice spacing compared to thinner slice spacing. To account for this, for CT scans having a slice spacing of greater than 3 mm, *VirtuOst* now applies an adjustment to the strength and areal BMD measurement values at the hip. This adjustment provides measurements that are equivalent to those from 1.25 mm scans. Performance data confirmed that this modification produced measurements with better agreement between thin- and thick-slice images. This modification does not substantially affect the safety or effectiveness of the device.

Hip areal BMD (in g/cm^2): Due to its 2D nature, DXA technology makes limiting assumptions about the patient's soft tissue surrounding the bone in order to measure BMD. As a result, two patients with the same true bone density but different body compositions can have different areal BMD measurements from DXA. This limitation is absent from CT-measured areal BMD by *VirtuOst*, which virtually removes all soft tissue in 3D before projecting the bone image. The predicate device reported hip BMD values after their conversion to a DXA-equivalent value. The modified device instead reports the CT-measured areal BMD before this conversion. However, when calculating BMD T- and Z-scores, a CT-to-DXA conversion is still applied in *VirtuOst* before using any DXA-based reference data (such as NHANES) so that the resulting T- and Z-scores from *VirtuOst* remain DXA-equivalent. Because the T- and Z-scores (and not the values of BMD) are used to identify osteoporosis and assess fracture risk, this modification does not substantially affect the safety or effectiveness of the device.

CT-to-DXA areal BMD conversion for the hip (used when calculating T- and Z-scores): The CT-to-DXA conversion equations for hip areal BMD measurements were refined to make them sex-specific, due in part to the limitations noted above for DXA because body composition typically differs between the sexes. As with the predicate device, the CT-to-DXA conversion equations are used in the subject device to make the hip areal BMD T- and Z-scores from *VirtuOst* be equivalent to those from DXA. Because the T- and Z-scores are used to identify osteoporosis and assess fracture risk, this modification does not substantially affect the safety or effectiveness of the device.

Bone images on the results report: Images of the finite element models showing the virtual loading in the stress analysis are now shown on the results report. As with the images showing bone density, all images are labeled "not for diagnostic use." These images help the physician and patient better understand the strength results. This modification does not substantially affect the safety or effectiveness of the device.

Strength vs. age plots on the results report: Images showing femoral strength and vertebral strength vs. age are shown on the results reports. Unlike BMD, Z-scores are not reported for strength measurements, thus the data in these plots are not used in the calculation of an outcome parameter. The plots provide information on how strength changes with age, which can aid interpretation of the strength measurements. This modification does not substantially affect the safety or effectiveness of the device.

Automated range check: During a *VirtuOst* analysis, range checks are automatically calculated for multiple parameters and outlier values are identified. When a parameter is flagged, the technologist is prompted to review the CT scan for artifacts and the analysis procedure for errors. The technologist must respond to the prompt in order to proceed with the analysis. This

modification helps to reduce user errors and improves throughput by detecting potential problems earlier in the analysis. This modification does not substantially affect the safety or effectiveness of the device.

Output file format for results: The results report can be provided in several DICOM formats to improve workflow efficiency and facilitate *VirtuOst* results being received and read by other Radiology applications such as PACS. This modification does not substantially affect the safety or effectiveness of the device.

Summary of Clinical and Non-Clinical Performance Data

Hip areal BMD (in g/cm^2): Areal BMD measurements for the hip for the modified device were compared to those for multiple types of FDA-cleared DXA devices in use in clinical practice, which together served as a reference standard. Paired CT and DXA images were obtained from 324 women and men age 48–85. BMD was measured at the femoral neck and total hip using the subject device and DXA. For the subject device, these measurements were then converted into DXA-equivalent values. Variance between femoral neck areal BMD measurements was acceptable (standard error of the regression of 0.048 g/cm^2 was below the highest pre-specified acceptable value of ≤ 0.051 g/cm^2). Stratified results for the women (0.044 g/cm^2, N=244) and men (0.051 g/cm^2, N=80) were also acceptable. These data demonstrate substantial equivalence of the hip areal BMD measurements for the modified device compared to DXA, a clinical reference standard.

Phantomless Calibration: Phantomless calibration using visceral fat is described. Utilizing visceral fat allows phantomless calibration when aortic blood is not available (such as with scans enhanced with intra-venous contrast). The reference data for visceral fat attenuation was derived from 268 patients scanned on 31 different CT scanners, plus scans of a custom torso phantom consisting of various tissue-equivalent chambers and scanned on 35 different CT scanners. Scanners were from the four major CT manufacturers (GE Healthcare, Siemens Medical Solutions, Philips Healthcare and Toshiba International) at various settings (80–140 kVp). For 40 independent patient CT scans, femoral strength and BMD were then compared for fat/air phantomless calibration versus phantom calibration (external calibration phantom, a reference standard). Mean values of measurements using the two calibration methods were not significantly different ($p>0.05$) and showed a high degree of agreement ($R^2 = 0.98–0.99$) with no fixed or proportional bias. These results indicate that phantomless calibration using visceral fat is substantially equivalent to calibration using an external calibration phantom and therefore does not substantially affect the safety or effectiveness of *VirtuOst*.

CT-to-DXA areal BMD conversion for the hip (used when calculating T- and Z-scores): VirtuOst applies a CT-to-DXA conversion to hip areal BMD measurements to enable the use of the NHANES normative reference data for the calculation of T- and Z-scores. In the modified device, the equations were updated and made sex-specific using data from 200 subjects scanned on both CT and DXA. The conversion equations were formulated from regression analysis of the paired CT and DXA areal BMD measurements, separately by sex and for the femoral neck, total hip, and trochanter. Following the acceptance criterion used for the predicate device, the

acceptance criterion was a standard error of the regression of less than 0.051 g/cm^2. The standard errors for the new equations ranged from 0.025–0.047 g/cm^2 and were thus considered acceptable.

Slice spacing adjustment for femurs: Using pairs of CT images, slice spacing adjustments were developed for femoral strength and areal BMD from the femoral neck, trochanteric, and total hip regions. Each image pair contained one thin and thick reconstruction. Measurements from images with thin and thick slice spacing were highly correlated ($R^2 \geq 0.98$). Linear regression analysis was used to develop adjustments so that measurements from images with a slice spacing greater than 3 mm are equivalent to measurements from images with a slice spacing of 1.25 mm. The modified device was since used in an observational study of hip fractures in which hip fracture prediction was compared between *VirtuOst* and DXA for 2,783 women and men (1,306 with hip fracture; case-cohort study design). Hazard ratios for hip fracture using femoral strength or hip areal BMD from *VirtuOst* were at least as good as hip areal BMD from DXA. Moreover, there was no evidence of a slice spacing effect on these results. Thus, we conclude that the slice spacing adjustment did not substantially affect the safety or effectiveness of *VirtuOst*.

Non-clinical tests: Verification and validation testing was also performed for all non-clinical modifications to the device. These tests, following best practices for software development, included automated unit and regression testing as well as manual component testing (i.e. black box testing). These tests ensure that software requirements are met, and that the device performs as intended. Each test includes preconditions for testing, test steps, an expected result, an observed result and a pass/fail determination. Tests included exercising each functionality of the worklist module such as loading jobs from the list and pulling CT scans from PACS; verifying that new inputs such as coronal and compressed images can be loaded, reconstructed and analyzed to obtain correct results; verifying that the modified femoral head segmentation completes and produces an appropriate segmentation mask; verifying that the fat/air calibration produces the expected calibration coefficients; verifying that slice spacing adjustments are applied correctly to scans of various spacing; verifying that the range checks correctly identify outliers as expected; verifying that all elements of the results report are present and display correctly such as the images of the finite element models and strength vs. age plots; and verifying that the DICOM results objects are correctly formatted and can be read and displayed by a DICOM compliant application entity. These non-clinical tests verified that the subject device met expected performance standards.

8) Conclusion

The subject device *VirtuOst* is a modified version of the predicate device, *VirtuOst* (K113725). The modifications to *VirtuOst* do not involve any change in the intended use or indications for use. Risk analysis and performance data together indicate that the modifications to *VirtuOst* have not substantially altered safety or effectiveness. O.N. Diagnostics believes, therefore, that subject device *VirtuOst* remains substantially equivalent to the predicate device.