Alpha Intelligence Manifolds, Inc.
℅ Qingzong Tseng
Director
2F, No. 170, Zhonghe Rd., Zhonghe District
New Taipei City, 235068
TAIWAN

September 8, 2023

Re: K223621
Trade/Device Name: DeepXray
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical image management and processing system
Regulatory Class: Class II
Product Code: QIH
Dated: August 14, 2023
Received: August 14, 2023

Dear Qingzong Tseng:

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,

Jessica Lamb, PhD
Assistant Director
Imaging Software Team
DHT8B: Division of Radiological Imaging
Devices and Electronic Products
OHT8: Office of Radiological Health
Office of Product Evaluation and Quality
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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K223621

Device Name
DeepXray

Indications for Use *(Describe)*
DeepXray is a radiological fully automated image processing software device of either computed (CR) or directly digital (DX) images intended to aid medical professionals in the measurement of minimum joint space width; the assessment of the presence or absence of sclerosis, joint space narrowing, and osteophytes based on OARSI criteria for these parameters; and, the presence or absence of radiographic knee OA based on Kellgren & Lawrence Grading of standing, fixed-flexion radiographs of the knee.

It should not be used in-lieu of full patient evaluation or solely relied upon to make or confirm a diagnosis.

The system is to be used by trained professionals including, but not limited to, radiologists, orthopedists, physicians and medical technicians.

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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AIM
Alpha Intelligence Manifolds

K223621 510(k) SUMMARY

DeepXray
Alpha Intelligence Manifolds, Inc.

Applicant: Alpha Intelligence Manifolds, Inc.
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Date Prepared: Aug 14, 2023

Device Name: DeepXray

Regulation Number: 892.2050

Regulation Name: Medical Image Management and Processing System

Product Code: QIH

Classification Name: Automated Radiological Image Processing Software

Device Class: Class II

Review Panel: Radiology

Predicate Devices: IB Lab GmbH's KOALA (K192109)
Radiobotics ApS's RBknee (K203696)

Device Description

DeepXray is a standalone software device that utilizes artificial intelligence (AI) and computer vision algorithms to assist clinical professionals in analyzing and measuring radiographic abnormalities of knee osteoarthritis (OA) during review of posterior-anterior or anterior-posterior knee radiographs. DeepXray provides automated metric measurements of the joint space width and angular measurements of the femoral-tibial angle. DeepXray also performs assessments of knee osteoarthritis based on the Kellgren-Lawrence Grade (KL Grade), as well as individual radiographic features of osteoarthritis, including joint space narrowing, osteophyte and sclerosis based on the OARSI (Osteoarthritis Research Society International) grading criteria.

The output of DeepXray is rendered as a summary report and can be viewed on a web browser. Using this web interface, the user can verify the AI report side-by-side with the original radiograph

using standard DICOM image tools and review each AI analysis result with the help of markup images overlaid with highlighted disease location or reference lines used for automated measurements. The web report also notifies the user for potential data quality issues. The clinical professionals can make modifications to the AI analysis results based on their professional judgement before saving and outputting the report.

Intended Use / Indications for Use

DeepXray is a radiological fully automated image processing software device of either computed (CR) or directly digital (DX) images intended to aid medical professionals in the measurement of minimum joint space width; the assessment of the presence or absence of sclerosis, joint space narrowing, and osteophytes based on OARSI criteria for these parameters; and, the presence or absence of radiographic knee OA based on Kellgren & Lawrence Grading of standing, fixed-flexion radiographs of the knee.
It should not be used in-lieu of full patient evaluation or solely relied upon to make or confirm a diagnosis.

The system is to be used by trained professionals including, but not limited to, radiologists, orthopedists, physicians and medical technicians.

Comparison of Technological Characteristics

DeepXray has the same technological characteristics as the predicate devices: KOALA (K192109) and RBknee (K203696). DeepXray and predicate devices all utilize computer vision (CV) as well as artificial intelligence (AI) algorithms trained on medical images to perform automated image processing tasks such as knee detection, landmark detection, and joint space detection. DeepXray and predicate devices all operate within Docker containers on a Linux server.

The only differences with predicate devices are that, instead of outputting the knee osteoarthritis analysis report as DICOM images, DeepXray output a web report providing quality warnings, markup images as well as an editing interface for the clinical professionals to modify any automated analysis results they considered inappropriate. In addition to the disease status (KL Grade, JSN, osteophyte, sclerosis) and minimum joint space width value (mJSW) reported by the predicate devices, DeepXray also reports the quantitative measurement of the Femoral-Tibial Angle.

In general, the technological characteristics of the DeepXray is directly comparable to the predicate devices, KOALA and RBknee. A table comparing the key features of the subject and predicate devices is provided below:

Feature	DeepXray (Subject Device)	KOALA (K192109, Predicate Device)	RBknee (K203696, Predicate Device)
Classification Name and Product Code	**Automated Radiological Image Processing Software (QIH)**	System, Image Processing, Radiological (LLZ)	System, Image Processing, Radiological (LLZ)
Anatomical Area	Joint (knee)	Joint (knee)	Joint (knee)
Image Input	DICOM compliant images in either digitally computed (CR) or directly digital (DX) formats	DICOM compliant images in either digitally computed (CR) or directly digital (DX) formats	DICOM compliant images in either digitally computed (CR) or directly digital (DX) formats
Image Processing	Knee detection; Landmark detection; Joint space detection	Knee detection; Landmark detection; Joint space detection	Knee detection; Landmark detection; Joint space detection
Human Intervention for interpretation	Required	Required	Required
Intended User	Trained professionals	Trained professionals	Trained professionals
Output Format	**Web report with quality warning, markup images and editing interface**	A single DICOM Image	Markup images and textual report as static DICOM images
Output Information	- Knee OA status: KL grade ≥2 or ≤1 - JSN status: Absent/Present - Osteophyte status: Absent/Present - Sclerosis status: Absent/Present - Minimum Joint Space Width - **Femoral-Tibial Angle**	- Knee OA status: KL grade ≥2 or ≤1 - JSN status: Absent/Present - Osteophyte status: Absent/Present - Sclerosis status: Absent/Present - Minimum Joint Space Width	- Knee OA status: KL grade ≥2 or <2 - JSN status: Not present/Present - Osteophyte status: Not present/Present - Sclerosis status: Not present/Present - Minimum Joint Space Width
Runs on Server	Yes	Yes	Yes
Operating Environment	Linux/Docker	Linux/Docker	Linux/Docker

Performance Data

DeepXray's clinical performance validation was performed on an independent test dataset using data from one of the five clinical sites of the Osteoarthritis Initiative (OAI), a multicenter longitudinal study. This test dataset comprised of 6,125 knee radiographs, representing 1,121 individuals, for which the ground truth labeling of Kellgren-Lawrence grades as well as osteophyte, sclerosis, and joint space narrowing grades according to the OARSI criteria, and measurements of the minimum joint space width and femoral-tibial angle were established in the OAI study by multiple physicians following adjudication procedures for discrepancies.

The statistics of patient demography, image specifications as well as subgroups of radiographic findings are shown below:

Items	Testing Dataset	Training Dataset
#Patients	1121	3387
Male	499 (44.5%)	1390 (41%)
Female	622 (55.5%)	1997 (59%)
Age > 60	601 (53.6%)	1642 (48.5%)
Ethnicity		
White	937 (83.6%)	2675 (79.0%)
Black or African American	159 (14.2%)	626 (18.5%)
Asian	13 (1.2%)	25 (0.8%)
Unknown or not reported	12 (1.1%)	61 (1.9%)
#DICOM	6125	18406
CR	5783 (94.4%)	11213 (60.9%)
DX	342 (5.6%)	3438 (18.7%)
RG	0 (0%)	3755 (20.4%)
Visiting Timepoint:		
Baseline	1121 (18.3%)	3385 (18.4%)
12 month	1058 (17.3%)	3158 (17.2%)
24 month	978 (16%)	2999 (16.3%)
36 month	939 (15.3%)	2877 (15.6%)
48 month	897 (14.6%)	2757 (15.0%)
72 month	558 (9.1%)	1602 (8.7%)
96 month	574 (9.4%)	1628 (8.8%)
X-ray Manufacturer:		
Agfa	4671 (76.3%)	3914 (21.3%)
Fujifilm	1144 (18.7%)	3030 (16.5%)
GE	310 (5.1%)	3450 (18.7%)
Konica-Minolta	0 (0%)	2055 (11.2%)
Philips	0 (0%)	66 (0.4%)
Siemens	0 (0%)	318 (1.7%)
Swissray	0 (0%)	3873 (21.0%)
Others (Not reported)	0 (0%)	1700 (9.2%)
#Knees:	11816	35217
KL ≤ 1	6850 (58%)	20536 (58.3%)
KL ≥ 2	4966 (42%)	14681 (41.7%)
JSN Absent	6862 (58.1%)	21089 (59.9%)
JSN Present	4954 (41.9%)	14128 (40.1%)
Osteophyte Absent	8018 (69.4%)	18997 (55.0%)
Osteophyte Present	3538 (30.6%)	15533 (45.0%)
Sclerosis Absent	8520 (74.8%)	25813 (75.6%)
Sclerosis Present	2865 (25.2%)	8336 (24.4%)

DeepXray's automatic quality control mechanism blocked 0.3% of test samples and did not give analysis results on those samples. Of the remaining test samples, the performance for the status indicators (expressed in Sensitivity/Specificity) of the radiographic findings are shown in the table below:

DeepXray Output	Sample Number	Performance Metric	Result (95% C.I.)
Kellgren-Lawrence Grade	11775 knees/ 6114 DICOM/ 1121 subjects	Sensitivity (KL Grade ≥2)	0.87 (0.86/0.88)
		Specificity (KL Grade ≥2)	0.84 (0.83/0.85)
Joint Space Narrowing	11775 knees/ 6114 DICOM/ 1121 subjects	Sensitivity (OARSI Grade ≥1)	0.88 (0.87/0.89)
		Specificity (OARSI Grade ≥1)	0.82 (0.81/0.83)
Osteophyte	11518 knees/ 5993 DICOM/ 1121 subjects	Sensitivity (OARSI Grade ≥1)	0.86 (0.85/0.87)
		Specificity (OARSI Grade ≥1)	0.80 (0.79/0.81)
Sclerosis	11348 knees/ 5904 DICOM/ 1119 subjects	Sensitivity (Presence/Absence)	0.84 (0.83/0.85)
		Specificity (Presence/Absence)	0.88 (0.87/0.89)

The performance of the measurements for the Joint Space Width (JSW) and the Femoral-Tibial Angle (FTA) by the DeepXray were quantified by orthogonal linear regression against reference measurements from the OAI study. The performance test results are summarized below:

DeepXray Output	Sample Number	Orthogonal linear regression	Result (95% C.I.)
Medial mJSW (mm)	7748 knees/ 4432 DICOM/ 862 subjects	Slope	1.02 (1.00, 1.03)
		Intercept	0.04 (-0.03, 0.11)
Lateral mJSW (mm)	7605 knees/ 4377 DICOM/ 861 subjects	Slope	0.98 (0.95, 1.01)
		Intercept	0.06 (-0.10, 0.26)
Femoral-Tibial Angle (degree°)	7546 knees/ 4310 DICOM/ 854 subjects	Slope	0.97 (0.96, 0.99)
		Intercept	-0.10 (-0.17, -0.04)

The performance data support that the knee OA assessments and measurements given by DeepXray are in good agreement with clinical professionals' labeling provided by the OAI study.

Substantial Equivalence

DeepXray has the same intended use, similar indications, technological characteristics, and principles of operation as its predicate devices. The differences between DeepXray and its predicate devices do not alter the intended use of the device and do not raise new or different questions regarding its safety and effectiveness when used as labeled. Performance data demonstrates that DeepXray performs as intended. Thus, DeepXray is substantially equivalent to its predicate devices.