EXINI Diagnostics AB   July 27, 2021
℅ Donna-Bea Tillman, Ph.D.
Senior Consultant
Biologics Consulting Group
1555 King Street, Suite 300
ALEXANDRIA VA 22314

Re: K211655
    Trade/Device Name: aPROMISE
    Regulation Number: 21 CFR 892.2050
    Regulation Name: Medical image management and processing system
    Regulatory Class: Class II
    Product Code: LLZ
    Dated: May 27, 2021
    Received: May 28, 2021

Dear Dr. Tillman:

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,

For

Thalia T. Mills, Ph.D.
Director
Division of Radiological Health
OHT7: Office of In Vitro Diagnostics
    and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number *(if known)*
K211655

Device Name
aPROMISE

Indications for Use *(Describe)*

aPROMISE is intended to be used by healthcare professionals and researchers for acceptance, transfer, storage, image display, manipulation, quantification and reporting of digital medical images. The system is intended to be used with images acquired using nuclear medicine (NM) imaging using PSMA PET/CT. The device provides general Picture Archiving and Communications System (PACS) tools as well as a clinical application for oncology including marking of regions of interest and quantitative analysis.

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.

In accordance with 21 CFR 807.87(h) and 21 CFR 807.92 the 510(k) Summary for aPROMISE is provided below.

1.   SUBMITTER

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Date Prepared: May 28, 2021

2.   DEVICE

Device Trade Name: aPROMISE
Device Common Name: Picture Archiving and Communication System
Classification Name   21 CFR 892.2050 Medical Image Management and
                             Processing System
Regulatory Class: II
Product Code: LLZ

3.   PREDICATE DEVICE

Predicate Device: Exini aBSI (K191262)

Secondary Predicate Device: Keosys Medical Imaging Suite KSWVWR (K160334
                               Advanced Medical Imaging Software Suite)

4.   DEVICE DESCRIPTION

aPROMISE (automated PROstate specific Membrane Antigen Imaging SEgmentation) consists of a cloud-based software platform with a web interface where users can upload body scans of PSMA PET/CT image data in the form of DICOM files, review patient studies and share study assessments within a team. The software complies with the Digital Imaging and Communications in Medicine (DICOM) 3 standard.

Multiple scans can be uploaded for each patient and the system provides a separate review for each study. The review page display studies in a 4-panel view showing PET, CT, PET/CT fusion and maximum intensity projection (MIP) simultaneously and includes the option to display each view separately. The device is used to review entire patient studies, using image visualization and analysis tools for users to identify and mark regions of interest (ROIs). While reviewing image data, users can mark ROIs by selecting from pre-defined hotspots that are highlighted when hovering with the mouse pointer over the segmented region, or by manual drawing, i.e selecting individual voxels in the image slices to include as hotspots. Selected or drawn hotspots are subject to automatic quantitative analysis. The user can review the results of this quantitative analysis and determine which hotspots should be reported as suspicious lesions.

To create a report the signing user is required to confirm quality control, and electronically sign the report preview. Signed reports are saved in the device and can be exported as a JPG or DICOM file.

5.   INTENDED USE/INDICATIONS FOR USE

aPROMISE is intended to be used by healthcare professionals and researchers for acceptance, transfer, storage, image display, manipulation, quantification and reporting of digital medical images. The system is intended to be used with images acquired using nuclear medicine (NM) imaging, using PSMA PET/CT. The device provides general Picture Archiving and Communications System (PACS) tools as well as a clinical application for oncology including marking of regions of interest and quantitative analysis.

6.   SUBSTANTIAL EQUIVALENCE

Comparison of Indications

Both aPROMISE and the predicate aBSI are software-only devices that are used in the acceptance, transfer, storage, image display, manipulation, quantification and reporting of nuclear medicine images by healthcare providers. Both devices perform segmentation of the body in the radiological image and automatically segment hotspots, regions with high tracer uptake. Both devices rely on the user to make the final selection of regions of interest that are considered as lesions. Both devices provide a quantitative metric of radiotracer uptake that can be used to inform patient care decisions.

The subject aPROMISE device differs from the primary predicate device in that it is intended to be used with PSMA PET/CT images while the predicate device is intended to be used with bone scans.

These differences in the Indications for use do not affect the fundamental intended use of the devices, which is to provide a software tool to aid the user, a healthcare professional or researcher, to mark regions of interest as lesions and provide quantitative analysis. The intended use to aPROMISE in PET/CT is the same as that of aBSI in bone scan images – a PACS device with a clinical application of oncology to mark and quantify regions of interest, intended to be used by healthcare professionals and researchers. Therefore, aBSI can be used as a primary predicate for aPROMISE.

Technological Comparisons

The table below compares the key technological feature of the subject device aPROMISE to the predicate devices, Exini aBSI (K191262) and Keosys Medical Imaging Suite KSWVWR (K160334).

Table 1:   Technological Comparison

Specification/ Characteristic	*aPROMISE* (proposed device)	*aBSI* (predicate device)	*Comparison to predicate*
General			
Intended user	Health care professionals and researchers	Health care professionals and researchers	No difference
Intended use environment	Healthcare clinics	Healthcare clinics	No difference
Classification	21 CFR 892.2050 System, Image Processing, Radiological (LLZ) Class II	21 CFR 892.2050 System, Image Processing, Radiological (LLZ) Class II	No difference
Installation	Cloud-based service and access with personal log-in.	Cloud-based service and access with personal log-in.	No difference
Operating system	Windows or macOS with Chrome browser	Windows or macOS with Chrome browser	No difference
DICOM compatibility and Imaging Modalities	DICOM 3: Whole body ● PET ● CT	DICOM 3: Whole body ● Bone scans ● SPECT	The differences in DICOM 3 compatibility reflect the different image modalities which is supported by a secondary predicate, the Keosys Medical Imaging Suite KSWVWR (K160334), as discussed below. The difference

Specification/ Characteristic	*aPROMISE* (proposed device)	aBSI (predicate device)	*Comparison to predicate*
			does not affect the clinical use of the device and does not raise different questions of safety or effectiveness.
Image upload	Via file selector **or drag and drop** from local computer or network. **Upload can handle zip files.**	Via file selector on local computer or network	The difference involves an additional option for image upload. The difference does not affect the clinical use of the device and does not raise different questions of safety or effectiveness.
Support for multiple scans	Yes, multiple scans can be analyzed **one at a time**.	Yes, if multiple scans are provided, **the images are automatically aligned vertically**	The difference in support for multiple scans does not affect the clinical use of the device and does not raise different questions of safety or effectiveness.
Colormaps	A selection of commonly used colormaps supported: For PET image: Cool - Inverted grayscale **Grayscale with overflow** **Hot Iron** **Spectrum** **Warm** For CT image: - Grayscale	A selection of commonly used colormaps supported: - Cool **Electric** - Inverted grayscale **Inverted grayscale overflow** - Grayscale **Thermal**	Same feature, both devices offer a selection of commonly used colormaps. The differences in colormaps are dependent on the different image modalities. The difference does not affect the clinical use of the device and do not raise different questions of safety or effectiveness.
Zoom	Automatically adjusted image size. Manually adjustable zoom in planar views	Automatically adjusted image size. Manually adjustable zoom in planar views	No difference
Windowing	Manual adjustment of windowing. Slider for **PET. Click'n'drag and by a drop-down menu for CT.**	Manual adjustment of windowing. Slider for **bone scans.**	Same feature, the difference in windowing is an adjustment for the different image modalities. The difference does not affect the clinical use of the device and do not raise different

Specification/ Characteristic	*aPROMISE* (proposed device)	**aBSI** (predicate device)	*Comparison to predicate*
			questions of safety or effectiveness.
Image layouts	4 panel view showing PET, CT, PET/CT fusion and MIP simultaneously and option to display each view separately. Coronal, axial and sagittal views can be displayed	Anterior and posterior images shown side by side	The difference in image layout is dependent on the different image modalities. The difference does not affect the clinical use of the device and do not raise different questions of safety or effectiveness.
Intensity display	Local intensity displayed in left corner of the image when hovering over image	Local intensity displayed in left corner of the image when hovering over image	No difference
Hotspot display	Segmented hotspots can be displayed in planar views	Segmented hotspots can be displayed in planar views	No difference
Organ Segmentation	AI enabled automated segmentation of skeleton **and soft tissue organs**	AI enabled automated segmentation of skeleton	Same feature but adjusted for the different image modalities. The difference does not affect the clinical use of the device and do not raise different questions of safety or effectiveness.
Normalization	Images are normalized so that healthy bone tissue intensities are automatically set to a predefined level.	Images are normalized so that healthy bone tissue intensities are automatically set to a predefined level.	No difference
Hotspot detection	Algorithm to detect high intensity regions of interest **in the PET series** within the segmented structures (skeleton **and soft tissue**).	Algorithm to detect high intensity regions of interest within the segmented structures (skeleton).	Same feature but adjusted for the different image modalities. The difference does not affect the clinical use of the device and do not raise different questions of safety or effectiveness.
Hotspot pre-selection	All detected high intensity ROIs can be shown for review by the user **without** pre-selection.	Detected high intensity ROIs are sorted into two groups (high and low) using artificial neural network (ANN) classifiers. Hotspots,	The devices have a difference in hotspot preselection; showing all detected high intensity regions (no preselection as of the predicate), but both devices still

Specification/ Characteristic	*aPROMISE* (proposed device)	**aBSI** (predicate device)	*Comparison to predicate*
		classified as high, are preselected and displayed to the user for review.	require the user to select and make the final call of what regions to include as lesions. The difference does not affect the clinical use of the device and do not raise different questions of safety or effectiveness.
Hotspot verification	The user can select pre-defined segmentation of hotspots or segment each hotspot manually that are considered to be lesions by the user.	Preselected hotspots are shown to and reviewed by the user. The hotspot selection is editable by the user.	The difference in hotspot verification constitutes of the user to manually review and select predefined- or draw hotspots in the subject device, instead of being presented automatically preselected hotspots to be reviewed as of the predicate. The difference does not affect the clinical use of the device and do not raise different questions of safety or effectiveness.
Hotspot Quantification	-Bone Scan Index (BSI)	Standard Uptake Values (SUV): -SUV-max -SUV-mean -SUV-peak -Volume -Lesion Index (LI) -Intensity-weighted Tissue Lesion Volume (ITLV)	The differences in calculated values reflect the different imaging modalities. The use of the SUV calculation is supported by a secondary predicate, the Keosys Medical Imaging Suite KSWVWR (K160334), as discussed in section 12.3.2.
Quality Control	SW enforced requirement to verify the user review of - Image quality - PET/CT image alignment - Patient study data - **Reference values** - **Study is not a superscan**	SW enforced requirement to verify the user review of - Image quality - The skeletal outlining (Atlas) - The selected hotspots	Same feature with adjustment for the different image modalities. The difference does not affect the clinical use of the device and do not raise different questions of safety or effectiveness.

Specification/ Characteristic	*aPROMISE* (proposed device)	**aBSI** (predicate device)	*Comparison to predicate*
User confirmation for report generation	User confirmation that the requirements for **image** assessment have been followed is required for report creation	User confirmation that the requirements for **BSI** assessment have been followed is required for report creation	No difference
Report (Summary page export)	The user can export the results of a study to the hard drive as an image or as a DICOM Secondary Capture.	The user can export the results of a study to the hard drive as an image or as a DICOM Secondary Capture.	No difference
CSV export	Supports export of study and **lesion** values as a CSV file for all created reports	Supports export of study and **BSI** value as a CSV file for all created reports	No difference

7.   PERFORMANCE DATA

Sterilization and Shelf Life

aPROMISE consists entirely of software; accordingly, there are no sterilization concerns. As a software only device, shelf-life (including performance date) is also not applicable because of low likelihood of time-dependent product degradation.

Biocompatibility Testing

There are no direct or indirect patient-contacting components of the subject device. Therefore, patient contact information is not needed for this device.

Electrical safety and electromagnetic compatibility (EMC)

Not applicable. The subject device is a software-only device. It contains no electric components, generates no electrical emissions, and uses no electrical energy of any type.

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 **moderate** level of concern.

Bench Testing

Exini performed the following studies verify and validate the performance of aPROMISE.

- Digital Phantom Validation Study. This study assessed the accuracy, linearity, and limit of detection of aPromise against the known values of a digital reference object (NEMA phantom). All SUV and volume quantification tests of aPROMISE met their predetermined acceptance criteria.

- Comparison to Predicate. This study demonstrated the equivalent performance of APROMISE as compared to the predicate KSWVWR (K160334) for standard functions in marking and quantitative assessments of user defined region of interest in PSMA PET/CT.

- Analytical Performance in Clinical Study. This study compared the performance of aPROMISE to that of clinicians and demonstrated that aPROMISE enables the automated quantification of tracer uptake in reference organs that are more reproducible, and consistent than those obtained manually. The study also demonstrated that aPROMISE has high sensitivity in pre-selection of regions of interest that are determined to be suspicious for metastatic disease.

These results demonstrate that aPROMISE performs in accordance with specifications and meets user needs and intended uses.

Animal Testing

Not applicable. Animal studies are not necessary to establish the substantial equivalence of this device.

Clinical Data

Not applicable. Clinical studies are not necessary to establish the substantial equivalence of this device.

8.   CONCLUSION

Based on the detailed comparison, the differences between the subject and predicate devices do not raise new questions of safety and effectiveness. The software verification (Section 16.9) and the performance testing demonstrates that the device performs according to the device requirements. Therefore, the aPROMISE device can be found substantially equivalent to the predicate device.