February 22, 2023

Radiopharmaceutical Imaging and Dosimetry, LLC
℅ Nadine Bonds
Director of Quality Assurance
1800 Gough St.
BALTIMORE MD 21231

Re: K212587
Trade/Device Name: 3D-RD-S
Regulation Number: 21 CFR 892.1100
Regulation Name: Scintillation (gamma) Camera
Regulatory Class: Class I, reserved
Product Code: IYX
Dated: January 24, 2023
Received: January 24, 2023

Dear Nadine Bonds:

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,

Daniel M. Krainak, Ph.D.
Assistant Director
Magnetic Resonance and Nuclear Medicine Team
DHT8C: Division of Radiological Imaging
and Radiation Therapy Devices
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)*
K212587

Device Name
3D-RD-S

Indications for Use *(Describe)*
3D-RD-S is intended to estimate radiation absorbed dose (and related quantities) to tissues after administration of a radioactive product. For use with internally administrated radioactive products, 3D-RD-S should not be used to deviate from product dosing and administration instructions. Refer to the product's prescribing information for instructions.

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.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

K212587

510(k) Summary

I. SUBMITTER

Radiopharmaceutical Imaging & Dosimetry (Rapid®), LLC
1800 Gough Street
Baltimore, MD 21231

Phone: 443-524-7396
Email: nbonds@rapiddosimetry.com

Contact person: Nadine Bonds
Date Prepared: February 17, 2023

II. DEVICE

Name of Device: 3D-RD-S
Common or Usual Name: 3D-RD-S
Classification Name: Scintillation (gamma), Camera
Regulatory Class: Class I (21 CFR 892.1100)
Product Code: IYX

III. PREDICATE DEVICE

Primary: OLINDA/EXM v2.0, K163687

IV. DEVICE DESCRIPTION

3D-RD-S is a cloud-based software as a medical device (SaMD) that interacts with the user via web browsers (for example Google Chrome). Users are trained healthcare professionals with significant dosimetry knowledge and experience and also responsible for the input of the appropriate values and to make correct interpretation of the output data. 3D-RD-S takes numerical input data in the form of activity in source tissues as a function of time (TAC data) or the integral of the activity (TIA data) in source tissues over time. It then calculates the absorbed dose to a set of target tissues based on the organ sizes and anatomies of a set of standard phantoms. The software provides the user the ability to account for the differences in tissue masses between the phantoms and the subject and model uncertainties in the input data.

Calculation results can be viewed and updated by other users. The software provides the ability to calculate absorbed doses and related radiobiological quantities from input data. The calculations can be made for supported radionuclides based on data in the report 89 from the International Council on Radiation Protection (ICRP). Doses to

target tissues are a function of the activity integrated over time (time-integrated activity, TIA) in a set of specified source organs. The software provides two modules for the integration of input time vs. activity curve (TAC) data. First, the user can use curve fitting methods to estimate a curve that passes through the TAC data from a set of supported fitting functions. Visual and numerical indicators of how well the fitting function works with the data are provided. Notifications are given if fitting parameters are non-physical. The TAC data can then be integrated using the fitting function, or by approximating the activity between measured time points with line and assuming activity after the last time-point decays with the radionuclide's physical half-life. If desired, the user can use a combination of the curve fit, linear interpolation between the lines, and exponentially decaying extrapolation based on the physical half-life, to integrate the time-activity curves.

The calculated radiobiological quantities purport to relate physical dose to biological response and are dependent on the specification of radiobiological constants. The quantities supported include the whole-body effective dose and the relative biological effectiveness (RBE) weighted dose. The effective dose is calculated based on ICRP tissue weighting factors. The RBE weighted dose is calculated using user specified RBEs for the different radiation types (standard values are provided as defaults).

3D-RD-S provides total and individual dose estimates for the various particle types, i.e., alpha particles, beta (+ and -) particles, discrete electrons (e.g., Auger electrons), and photons (gamma and x-rays). The resulting doses are plotted in a bar graph and can, along with input data, be exported in a spreadsheet.

V. INDICATIONS FOR USE

3D-RD-S is intended to estimate radiation absorbed dose (and related quantities) to tissues after administration of a radioactive product. For use with internally administrated radioactive products, 3D-RD-S should not be used to deviate from product dosing and administration instructions. Refer to the product's prescribing information for instructions.

VI. COMPARISON OF TECHNOLOGICAL CHARACTERISTICS WITH PREDICATE

As summarized in the table below, the 3D-RD-S technological characteristics compare favorably with the predicate SaMD technological characteristics.

3D-RD-S can be used with any internal radioactivity supplied by any FDA approved radiopharmaceutical, radiopharmaceuticals under development (even before ever administered to humans based on extrapolations of activities in human tissues from, e.g., animal studies), or radionuclides present in the body due to environmental exposure.

Comparison Summary

Attributes	3D-RD-S	OLINDA/EXM, v2.0	Comments
Indications for Use	3D-RD-S is intended to estimate radiation absorbed dose (and related quantities) to tissues after administration of a radioactive product. For use with internally administrated radioactive products, 3D-RD-S should not be used to deviate from product dosing and administration instructions. Refer to the product's prescribing information for instructions.	The intended use of OLINDA/EXM is to provide estimates (deterministic) of absorbed radiation dose at the whole organ level as a result of administering any radionuclide and to calculate effective whole-body dose. This is dependent on input data regarding biodistribution being supplied to the application.	Indications for Use is Equivalent
Product Code Regulation	IYX / 21 CFR 892.1100	IYX / 21 CFR 892.1100	Product Code / Regulation is Equivalent
Target Population	Adults, Children	Adults, Children, Pregnant women	Target Population is Equivalent
Input	TIA, TIAC, or TAC	Fraction of injected activity in each organ or the TIAC	Input Data is Equivalent
Radionucleotides Supported	Supports 1,252 radionucleotides	Over 1000, including Alpha Emitters	Radionucleotides Supported is Equivalent
Dosimetry Calculation	Whole organ / tissue Dosimetry. Tissue S-Values	Whole organ / tissue Dosimetry. Tissue S-Values	Dosimetry Calculation is Equivalent
Output	Absorbed Dose tables	Absorbed Dose tables	Output Data is Equivalent
TAC Integration	Integration can be done based on user-selection of one of 4 fit functions, user specified washout half-life, physical decay, or a combination of the above and trapezoidal integration. The four fit functions constrain the shape of the fit and are selected by the user based on the data. The user can provide, or the software estimate initial values, of the fitting parameters. Uncertainty values provided with the data are used in the	Integration is performed based on fitting data with up to 3 exponentials. Fitting start and endpoints can be user specified. Allows specifying weights for data during fitting. The data and fit are plotted graphically.	TAC Integration is Equivalent

Attributes	3D-RD-S	OLINDA/EXM, v2.0	Comments
	fitting. Uncertainty values are used as weights in fitting. Integration is always from 0 to infinity. The fits and integration is displayed graphically.		
Anatomical Sites	Supports the 79 target and 43 target tissues from ICRP-133	Supports 26 source tissues and 30 target tissues	Anatomical Sites is Equivalent

VII. PERFORMANCE DATA

Software Verification and Validation Testing

Tests for verification and validation have been completed following Rapid's design control procedures. A risk analysis was completed, and risk controls have been implemented to mitigate identified hazards.

Benchmark Testing

Rapid performed the following benchmark tests:

(1) *Compared absorbed dose estimated from 3D-RD-S to those obtained using OLINDA/EXM v2.0 and inputs representative of the marketed use of 3D-RD-S including TIAC and TAC user input modes.*

The objective of the test was to demonstrate equivalence of absorbed dose calculations performed by 3D-RD-S against the predicate. Clinical data, obtained from Rapid's clinical trials dosimetry service business with clinically relevant administered activities, were used to compare absorbed doses calculated by 3D-RD-S to those calculated using the predicate device. This included the following radionuclides: photon emitters used for diagnostic agents (In-111, F-18, Ga-68), beta emitters used in therapy (I-131, Lu-177), and alpha emitters (Pb-212 (beta-emitting parent of the alpha-emitters, Bi-212 and Po-212), Ra-223 and Ac-225) used in therapy.

Absorbed doses to source tissues were considered acceptable if the absolute percent difference (defined as the difference divided by the mean multiplied by 100) between the dose calculated by the predicate and the dose from 3D-RD-S was less than 10%.

For almost all cases, the difference in source tissues absorbed doses calculated using 3D-RD-S and the predicate was below the 10% threshold. The reported differences in source and non-source tissues absorbed doses can be primarily attributed to the differences in the sources of data used to generate the S-values (the basis for MIRD dose calculations) used in 3D-RD-S and the predicate for the dose calculations.

(2) Compared the absorbed dose values obtained using 3D-RD-S to those reported in published literature.

Rapid surveyed several published studies that investigated a variety of radionuclides. Direct comparisons in calculated absorbed dose were made to literature results that meet the following criteria: 1) provided time-integrated activity coefficients (residence times) in specified source organs, 2) used the ICRP 110 phantoms and ICRP 133 SAF values for dose calculations, and 3) used nuclear decay data from ICRP 107. This enabled the ability to do direct comparisons between the absorbed doses for the same set of target tissues. The time integrated activity coefficients were used as direct inputs into 3D-RD-S. Radionuclides were chosen to represent gamma, beta, and alpha emitters such as F-18, Zr-89, Y-90, I-131, Lu-177 and At-211.

The differences in the absorbed doses calculated using 3D-RD-S and those published in literature were below 5% for each target organ included in the published study and available in 3D-RD-S.

(3) Compared 3D-RD-S dose outputs by having two (2) analysts independently process images from SNMMII Dosimetry Challenge data for patients A and B through the dosimetry workflow pipeline.

The objective of this test was to report the variability in the dose outputs as a result of having multiple operators processing the data. The test included SPECT/CT images from two patients (A and B) which were part of the SNMMI Lu-177 Dosimetry Challenge (Uribe et al. J Nuc Med. 2021). Images were acquired at four time points following Lu-177-DOTATATE administration. Source organs included the kidneys, liver, spleen (absent in Patient B), and abdominal tumors (two in Patient A; four in Patient B).

Tests were performed by two analysts with a background in medical physics and extensive experience in radiopharmaceutical therapy dosimetry. The analysts compared 3D-RD-S dose outputs by independently processing images from the SNMMI Dosimetry Challenge data for patients A and B through the dosimetry workflow pipeline (i.e., draw VOIs, extract TAC, … etc.). 3D-RD-S does not provide tools for image analysis, and this was done using an external image analysis package that is not part of this submission. Despite the subjectivity in manually drawn VOIs, the final absorbed dose values were found to agree within 10% for all target normal organs.

VIII. CONCLUSION

In summary, 3D-RD-S has the same intended use and similar technological characteristics that do not raise different questions of safety or effectiveness compared to the predicate device. Therefore, 3D-RD-S is demonstrated to be substantially equivalent to OLINDA/EXM v2.0 and supports its safety and intended use.