



October 17, 2019

Hermes Medical Solutions AB  
% Joakim Arwidson  
VP Quality and Regulatory Affairs  
Strandbergsgatan 16  
112 51 Stockholm  
SWEDEN

Re: K191216

Trade/Device Name: Voxel Dosimetry™ v1.0  
Regulation Number: 21 CFR 892.2050  
Regulation Name: Picture archiving and communications system  
Regulatory Class: Class II  
Product Code: LLZ  
Dated: September 4, 2019  
Received: September 18, 2019

Dear Joakim Arwidson:

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](mailto: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)  
K191216

Device Name  
Voxel Dosimetry v1.0

### Indications for Use (Describe)

The intended use of Voxel Dosimetry™ is to provide estimates (deterministic) of absorbed radiation dose at voxel level as a result of administering one of the supported radionuclides and to provide a dose map. This is dependent on input data regarding bio distribution being supplied to the application.

Voxel Dosimetry™ only allows voxel-based dose calculations for patients who have been administered with radioisotopes.

Warning! The Voxel Dosimetry™ is only intended for calculating dose for FDA approved radiopharmaceuticals for any clinical purpose, and calculation of unapproved drugs can only be used for research purpose.

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

### A. Submitted by:

- **Submitters name and address:**  
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Joakim Arwidson  
VP Quality & Regulatory  
Hermes Medical Solutions AB  
Strandbergsgatan 16  
112 51 Stockholm  
Sweden
- **Registration number**  
9710645

### B. Preparation date:

2019-03-12

### C. Proprietary/Trade name, Common name, Classification name:

- **Proprietary/Trade name**  
Voxel Dosimetry™ v1.0
- **Common name**  
System, Image Processing, Radiological
- **Classification name**  
Picture archiving and communications system, Class II, 21CFR892.2050.

### D. Legally marketed device (predicate device):

Following legally marketed device has been used for comparison.

- MIM-MRT Dosimetry (K182624)
- OLINDA/EXM® v2.0 (K163687)

### E. Description of the device that is subject of this premarket notification:

Voxel Dosimetry™ is a tool for voxel level absorbed dose calculation resulting from radiotracer injection. Voxel Dosimetry™ workflow consists of the following steps:

- SPECT/CT or PET/CT DICOM data loading from the data manager GOLD or PACS
- Registration of different time-points to a common reference study
- Generation and integration of voxel-level time-activity curves

- Voxel-level absorbed dose calculation using a Monte Carlo-method
- Saving of the absorbed dose-map back to GOLD or PACS in DICOM format

**F. Intended use:**

The intended use of Voxel Dosimetry™ is to provide estimates (deterministic) of absorbed radiation dose at voxel level as a result of administering one of the supported radionuclides and to provide a dose map. This is dependent on input data regarding bio distribution being supplied to the application.

Voxel Dosimetry™ only allows voxel-based dose calculations for patients who have been administered with radioisotopes.

Warning! The Voxel Dosimetry™ is only intended for calculating dose for FDA approved radiopharmaceuticals for any clinical purpose, and calculation of unapproved drugs can only be used for research purpose.

**G. Technological characteristics:**

MIM – MRT Dosimetry is based on voxel S-values (VSV), which is a voxel-based schema published in MIRD Pamphlet No. 17 (MIRD pamphlet No. 17: The dosimetry of nonuniform activity distributions--radionuclide S values at the voxel level. MIRD, J Nucl Med. 1999 Jan;40(1):11S-36S), in which sources and targets are defined at the voxel level and voxel S-values calculated in a 3D matrix. The VSV approach is limited to lesions located in a homogeneous medium. As mentioned below, the Semi-Monte Carlo (SMC) method used in Voxel Dosimetry™ operates on a voxel level and performs dose calculation for photons and electrons based on patient specific CT scans. Voxel Dosimetry refers to the same patient population as MIM – MRT Dosimetry, support of the same isotopes (Lu-177, I-131) and has equivalent intended use.

The output from Voxel Dosimetry and MIM – MRT Dosimetry are dose maps containing voxel level doses to be used for dose volume histograms and curve analysis.

OLINDA/EXM® v2.0 is based on the use of S-factors, which are calculated on patient-like phantoms using a Monte Carlo method. The S-factors are equal to the average absorbed dose to a target organ generated by a unit of activity in a source organ. OLINDA/EXM® v2.0 dose calculations can thus be performed by multiplying the source organ time-activity curve integral by the S-factor. The SMC method used in Voxel Dosimetry™, on the other hand, operates on a voxel level and performs dose calculations for photons and electrons based on patient specific CT scans. Therefore, Voxel Dosimetry™ is patient-specific and produces voxel-level dose-maps instead of average organ-level dose estimates as OLINDA/EXM® v2.0 provides. Voxel Dosimetry™ can also perform accurate lesion dosimetry because doses are calculated on a voxel-level and the same method can be used for lesions as for organs. This is not possible with OLINDA/EXM® v2.0, with which only a rough estimate of lesion doses is possible.

The output from Voxel Dosimetry v1.0 is a dose map containing voxel level doses in comparison to the predicate device OLINDA/EXM® v2.0, where the output is a CSV file including estimated dose for the organs.

**H. Testing:**

The tests for verification and validation followed Hermes Medical Solutions AB design-controlled procedures. The Risk analysis was completed, and risk control implemented to mitigate identified hazards.

Voxel Dosimetry and OLINDA/EXM® v2.0 Lu177-DOTATATE kidney doses were compared, because this is one of the most common situations in internal radionuclide dosimetry today. The average of the relative differences between SMC and OLINDA/EXM® v2.0 was found to be 2% (Hippeläinen ET, Tenhunen MJ, Mäenpää HO, Heikkonen JJ, Sohlberg AO. Dosimetry software Hermes Internal Radiation Dosimetry: from quantitative image reconstruction to voxel-level absorbed dose distribution. Nuclear Medicine Communications 2017;38:5:357-365.), which is less than the uncertainty in Lu177 kidney dosimetry (Gustafsson J, Brolin G, Cox M, Ljungberg M, Johansson L, Gleisner KS. Uncertainty propagation for SPECT/CT-based renal dosimetry in Lu-177 peptide receptor radionuclide therapy. Phys Med Biol. 2015;60(21):8329–8346.) and thus the difference will not affect safety or effectiveness.

The validation (see TAB 5 - CL92.01\_P55V1.0 Clinical Validation in the original 510k application), was performed by generating an XCAT phantom for each isotope, with four time points dependent on the isotope. The XCAT phantom code also generated cumulated activities for each voxel using a mono-exponential model with the effective half-lives of the isotopes. The phantom data was processed in Voxel Dosimetry™ which generated cumulated activities for each voxel based on the trapezoidal integration. The Voxel Dosimetry cumulated activities were compared to the true cumulated activities calculated with the mono-exponential model and the mentioned effective half-lives. The true cumulated activity was obtained by analytically integrating the mono-exponential model. The true cumulated activity phantom data was also used to compare the Voxel Dosimetry™ dose calculations to the dose calculations made with the Monte Carlo code PENELOPE.

*Difference ( $100\% \times (\text{Voxel Dosimetry} - \text{true})/\text{true}$ ) between Voxel Dosimetry™ cumulated activity and the true cumulated activity.*

| Isotope | Difference [%] |       |        |
|---------|----------------|-------|--------|
|         | Kidney         | Tumor | Spleen |
| Ga68    | 6              | 6     | 7      |
| I123    | 3              | 1     | 2      |
| I131    | 7              | 2     | 3      |
| In111   | 11             | 7     | 7      |
| Lu177   | 7              | 3     | 3      |
| Tc99m   | 8              | 7     | 6      |
| Y90     | 12             | 8     | 8      |

*Difference ( $100\% \times (\text{Voxel Dosimetry} - \text{PENELOPE})/\text{PENELOPE}$ ) between Voxel Dosimetry™ dose and PENELOPE dose*

| Isotope | Difference [%] |       |        |
|---------|----------------|-------|--------|
|         | Kidney         | Tumor | Spleen |
| Ga68    | 12             | 12    | 12     |
| I123    | 2              | 3     | 3      |
| I131    | 3              | 3     | 3      |
| In111   | 2              | 2     | 3      |
| Lu177   | 1              | 1     | 1      |
| Tc99m   | 2              | 3     | 3      |
| Y90     | 5              | 6     | 4      |

The cumulated activities and doses obtained with Voxel Dosimetry™ match the reference values well. The differences in cumulated activities are due to differences in time-activity curve shapes. The piecewise linear model used in Voxel Dosimetry™ did not always perfectly match the simulated mono-exponential kinetics. Differences in doses were small. The only larger difference is seen with the Ga68 isotope, which has high positron energy.

In addition to phantom testing, Voxel Dosimetry™ was also validated against the predicate device OLINDA/EXM® v2.0. Twelve treatment cycles of six patients who underwent Lu177-DOTATATE treatments were compared. The patients were scanned with a Siemens Symbia T2 SPECT/CT-scanner 1, 24, 72 and 168 hours after the treatment. The SPECT/CT scans were reconstructed and left and right kidney doses obtained with Voxel Dosimetry™ and OLINDA/EXM® were compared. Voxel Dosimetry and OLINDA/EXM® v2.0 left and right kidney doses were found to be highly correlated (Pearson's  $r_{\text{left}}=0.97$  and  $r_{\text{right}}=0.98$ ). The average of the relative difference was -2% when compared to OLINDA/EXM® v2.0. These results are presented in more detail in the publication (Hippeläinen E, Tenhunen M, Mäenpää H, Heikkonen J, Sohlberg A. Dosimetry software Hermes Internal Radiation Dosimetry: from quantitative image reconstruction to voxel-level absorbed dose distribution. Nucl Med Commun 2017; 38:357-365).

The testing results support that all the software specifications have met the acceptance criteria.

#### **I. Substantially Equivalent/Conclusions:**

MIM – MRT Dosimetry is based on voxel S-values (VSV), which is a voxel-based schema published in MIRD Pamphlet No. 17 (MIRD pamphlet No. 17: The dosimetry of nonuniform activity distributions--radionuclide S values at the voxel level. MIRD, J Nucl Med. 1999 Jan;40(1):11S-36S), in which sources and targets are defined at the voxel level and voxel S-values calculated in a 3D matrix. The VSV approach is limited to lesions located in a homogeneous medium. As mentioned below, the Semi-Monte Carlo (SMC) method used in Voxel Dosimetry™ operates on a voxel level and performs dose calculation for photons and electrons based on patient specific CT scans. Voxel Dosimetry refers to the same patient population as MIM – MRT Dosimetry, support of the same isotopes (Lu-177, I-131) and has equivalent intended use.

OLINDA/EXM® v2.0 is based on the use of S-factors, which are calculated on patient-like phantoms using a Monte Carlo method. The S-factors are equal to the average absorbed dose to a target organ generated by a unit of activity in a source organ. OLINDA/EXM® v2.0 dose calculations can thus be performed by multiplying the source organ time-activity curve integral by the S-factor. The SMC method used in Voxel Dosimetry™, on the other hand, operates on a voxel level and performs dose calculations for photons and electrons based on patient specific CT scans. Therefore, Voxel Dosimetry™ is patient-specific and produces voxel-level dose-maps instead of average organ-level dose estimates as OLINDA/EXM® v2.0 provides. Voxel Dosimetry™ can also perform accurate lesion dosimetry because doses are calculated on a voxel-level and the same method can be used for lesions as for organs. This is not possible with OLINDA/EXM® v2.0, with which only a rough estimate of lesion doses is possible.

In summary, the Voxel Dosimetry™ v1.0, described in this submission has equivalent intended use and is, in our opinion, substantially equivalent to a combination of the predicate devices MIM-MRT Dosimetry (K182624) and OLINDA/EXM® v2.0 (K163687) and supports its clinical effectiveness, safety and intended use.