Resonance Health Analysis Services Pty Ltd.
℅ Ms. Alison Laws
CEO
141 Burswood Road
Burswood, Western Australia 6100
AUSTRALIA

December 7, 2020

Re: K201039
Trade/Device Name: HepaFat-AI
Regulation Number: 21 CFR 892.1000
Regulation Name: Magnetic resonance diagnostic device
Regulatory Class: Class II
Product Code: LNH
Dated: October 15, 2020
Received: November 2, 2020

Dear Ms. Laws:

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

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*

K201039

Device Name
HepaFat-AI

Indications for Use *(Describe)*

HepaFat-AI is indicated to:

• Assess the volumetric liver fat fraction, proton density fat fraction and steatosis grade in individuals with confirmed or suspected fatty liver disease;

When interpreted by a trained physician, the results can be used to

• monitor liver fat content in patients undergoing weight loss management and can be used to

• aid in the assessment and screening of living donors for liver transplant.

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

This Summary has been prepared in accordance with 21 CFR 807.92.

GENERAL INFORMATION

Date Prepared	4th December 2020
Submitted by	Resonance Health Analysis Service Pty Ltd 141 Burswood Rd Burswood 6100 AUSTRALIA
Main Contact	Ms Alison Laws CEO alisonl@resonancehealth.com Tel: +61 8 9286 5300 Fax: +61 8 9286 5399
US Contact (US Agent)	Michael van der Woude Director & GM Emergo Global Representation LLC 2500 Bee Cave Road, Building 1, Suite 300 Austin, TX 78746 Phone: 512 3279997 Fax: 512 3279998 Email: USAgent@ul.com

DEVICE INFORMATION

Name of Device	HepaFat-AI
Trade/proprietary Name	HepaFat-AI
Classification	Class II
Product Code	90-LNH
CFR Section	892.1000 Magnetic Resonance Diagnostic Device
Panel	Radiology

Description of the Device

The HepaFat-AI Analysis System is a software platform designed to automatically analyse magnetic resonance imaging (MRI) datasets to generate an estimate of the patient's volumetric liver fat fraction (VLFF). To carry out an analysis, the user simply uploads raw DICOM images to the HepaFat-AI Analysis System. No user input is required for the analysis thus minimising the impact of human error on obtained results. The HepaFat-AI system requires image input data that have been acquired according to the HepaFat-Scan protocol.

The key components for the HepaFat-AI Analysis System for volumetric liver fat fraction measurement are:

- Magnetic Resonance Imaging Protocol: The use of a specific magnetic resonance imaging protocol for acquisition of the raw image data. The imaging protocol is critical to ensure the quality of the end results. Its adherence is verified by the IQC Module, an automated algorithm that checks the correctness of each parameter in the protocol.
- HepaFat-AI Analysis Software: Custom-designed image analysis software performing the Alpha measurement and anomaly detection based on Artificial Intelligence (AI) technology. It is composed of 2 convolutional neural networks. The primary network is for the prediction of Alpha and a secondary network is for anomaly detection. This element is considered the medical device for a regulatory perspective. Following the training of the AI tool, the system is 'locked-down' for final validation prior to release in commercial use to ensure reproducibility of the results.
- Volumetric Liver Fat Fraction Measurement: An additional software module (algorithmic) that incorporates a conversion lookup table relating Alpha to volumetric liver fat fraction (VLFF) is added to allow production of a volumetric liver fat fraction report.
- Proton Density Fat Fraction Measurement: An additional software module (algorithmic) that incorporates a conversion lookup table relating VLFF to proton density fat fraction (PDFF) is added to allow production of a proton density fat fraction report.
- Steatosis Grade Measurement: An additional software module (algorithmic) that incorporates a conversion lookup table relating VLFF to the steatosis grade.

The output of the HepaFat-AI Analysis System is an automated generated report. This report is populated with the information stored in the DICOM header of the MRI images, and the analysis result Alpha converted into a VLFF value, a PDFF value and a steatosis grade, associated confidence interval and normal range. The report also contains pictures of the 3 TEs of the analysed slice. This is essential for the radiologist to check if the image analysed is a liver image, and the result provided is consistent with other relevant clinical results.

Intended Use

The intended use of HepaFat-AI is:

> *HepaFat-AI is intended for quantitative measurement of the triglyceride fat fraction in magnetic resonance images of the liver, also known as volumetric liver fat fraction (VLFF).*

Indications for Use

HepaFat-AI is indicated to:

- Assess the volumetric liver fat fraction, proton density fat fraction and steatosis grade in individuals with confirmed or suspected fatty liver disease;

When interpreted by a trained physician, the results can be used to

- Monitor liver fat content in patients undergoing weight loss management and can be used to
- Aid in the assessment and screening of living donors for liver transplant

PREDICATE INFORMATION

HepaFat-AI is substantially equivalent to the predicate device HepaFat-Scan (Resonance Health Analysis Services) – K122035.

SUBSTANTIAL EQUIVALENCE INFORMATION

The table below summarizes the main similarities and differences between HepaFat-AI and the predicate.

	HepaFat-AI	**HepaFat-Scan**
Regulatory Class	II	II
510(k) number	K201039	K122035
Classification Name	System, Nuclear Magnetic Resonance Imaging, System, Image Processing Radiological	System, Nuclear Magnetic Resonance Imaging, System, Image Processing Radiological
CFR Section	892.1000	892.1000
Product Code and Classification Panel	90 LNH	90 LNH
Device Name	HepaFat-AI	HepaFat-Scan
Trade/Common Name	HepaFat-AI	HepaFat-Scan
Description	Standalone software platform designed to automatically analyse within seconds magnetic resonance imaging (MRI) datasets to generate an estimate of the patient's volumetric liver fat fraction (VLFF), converted into proton density fat fraction (PDFF) and steatosis grade. No user input is required for the analysis thus minimising the impact of human error on obtained results.	Standalone software application to facilitate the import and visualization of multi-slice, gradient-echo MRI data sets encompassing the abdomen, with functionality independent of the MRI equipment, to provide objective and reproducible determination of the triglyceride fat fraction in magnetic resonance images of the liver. It utilises magnetic resonance images that exploit the difference in resonance frequencies between hydrogen nuclei in water and triglyceride fat. The quantitative triglyceride fat fraction is based on the measurement of a magnetic resonance parameter that reflects the ratio of the proton density signal of triglyceride fat to the total proton density signal in the liver.

	HepaFat-AI	HepaFat-Scan
Technology	Convolutional neural networks for the image analysis. Algorithmic for the images quality checking and Alpha conversion into VLFF.	Algorithmic, with human interaction for Region of Interest (ROI) selection.
Intended purpose(s)	1. Supporting clinical diagnoses about the status of liver fat content. 2. Supporting the subsequent clinical decision-making processes. 3. Supporting the use in clinical research trials, directed at studying changes in liver fat as a result of interventions.	1. Supporting clinical diagnoses about the status of liver fat content. 2. Supporting the subsequent clinical decision-making processes. 3. Supporting the use in clinical research trials, directed at studying changes in liver fat as a result of interventions. 4. It contains an image viewer for importing DICOM images, browsing through patient datasets, viewing images and performing region of interest analysis.
Intended Use	HepaFat-AI is intended for quantitative measurement of the triglyceride fat fraction in magnetic resonance images of the liver, also known as volumetric liver fat fraction (VLFF). It utilises magnetic resonance images that exploit the difference in resonance frequencies between hydrogen nuclei in water and triglyceride fat. The quantitative triglyceride fat fraction is based on the measurement of a magnetic resonance parameter that reflects the ratio of the proton density signal of triglyceride fat to the total proton density signal in the liver. When interpreted by a trained physician, the results provide information that can aid in diagnosis.	HepaFat-Scan is a software device intended for quantitative measurement of the triglyceride fat fraction in magnetic resonance images of the liver. It utilises magnetic resonance images that exploit the difference in resonance frequencies between hydrogen nuclei in water and triglyceride fat. The quantitative triglyceride fat fraction is based on the measurement of a magnetic resonance parameter that reflects the ratio of the proton density signal of triglyceride fat to the total proton density signal in the liver. When interpreted by a trained physician, the results provide information that can aid in diagnosis.
Indications	HepaFat-AI is indicated to: Assess the volumetric liver fat fraction, proton density fat fraction and steatosis grade in individuals with confirmed or suspected fatty liver disease;	HepaFat-Scan is a software device intended for quantitative measurement of the triglyceride fat fraction in magnetic resonance images of the liver. It utilises magnetic resonance images that exploit the difference in resonance frequencies between hydrogen nuclei

	HepaFat-AI	HepaFat-Scan
	When interpreted by a trained physician, the results can be used to • Monitor liver fat content in patients undergoing weight loss management and can be used to • Aid in the assessment and screening of living donors for liver transplant	in water and triglyceride fat. The quantitative triglyceride fat fraction is based on the measurement of a magnetic resonance parameter that reflects the ratio of the proton density signal of triglyceride fat to the total proton density signal in the liver. When interpreted by a trained physician, the results provide information that can aid in diagnosis.
User	Radiologist	Resonance Health's trained analyst
Hosting platform	Cloud-based or onsite platform	Resonance Health's internal server
Image-type utilized	Magnetic Resonance	Magnetic Resonance
Image format	DICOM	DICOM
Data Acquisition method	Gradient Recalled Echo (GRE)	Gradient Recalled Echo (GRE)
Anatomical Sites	Liver	Liver
Result report content	• Unique Report ID • Patient ID, patient name and date of birth for full identification of the patient. • Scan date, and analysis date. • Referrer and MRI centre. • Results displayed: VLFF (%), PDFF (%) and Steatosis grade, associated with confidence intervals and normal range. • Pictures of the 3 TEs of the analysed slice. • Liver colour map (for illustration purpose only, not for diagnostic)	• Unique Report ID • Patient ID, patient name and date of birth for full identification of the patient. • Scan date, and analysis date. • Referrer and MRI centre. • Results displayed: VLFF (%) associated with confidence intervals and normal range. • Picture of the analysed slice.
Result report format	HTML and PDF	PDF

Furthermore the substantial equivalence has been demonstrated clinically by processing the same anonymized clinical MRI datasets by both techniques, which:

- assessed the limit of agreement between the two analysis techniques;
- determined the performance of HepaFat-AI (NPA and PPA); and
- assessed the repeatability of HepaFat-AI.

PERFORMANCE DATA

The following bench performance data were provided in order to support the substantial equivalence determination

Software Verification and Validation

Resonance Health has followed the principles developed by the IMDRF published by the FDA: Software as a Medical Device (SaMD): Clinical Evaluation. Final Guidance for Industry and FDA Staff. December 2017, to design the performance testing that support HepaFat-AI

HepaFat-AI Clinical Evaluation can be broken down as follows:

- Valid Clinical Association: using HepaFat-Scan as the reference standard.
- Analytical Validation: HepaFat-AI software has been developed, verified and validated following the Design Control principles and in accordance with the General Principles of Software Validation; Final Guidance for Industry and FDA Staff. U.S. Department Of Health and Human Services Food and Drug Administration. January 2002.
- Clinical Validation: the different studies conducted gather data to support the relevance of HepaFat-AI use as intended. This includes sensitivity, specificity, the negative percent agreement (NPA) and positive percent agreement (PPA) of HepaFat-AI, repeatability, and user testing results. Literature review and demographics of the validation datasets support the patient population as stated in the Indications for Use. Specifically, HepaFat-Scan data were acquired in two independent studies of 145 adult and paediatric NAFLD/NASH patients who also received a liver biopsy with histological scoring of steatosis. The diagnostic performance of HepaFat-Scan and HepaFat-AI at three previously determined VLFF thresholds (equivalent to three steatosis grade boundaries) were then determined and are shown in the table below. HepaFat-AI has a very similar diagnostic ability compared to HepaFat-Scan across all thresholds when both methods are tested directly against biopsy grades of steatosis. In particular, at the clinically important boundary separating no steatosis from any steatosis (Grade 0 vs Grades 1-3), the sensitivities and specificities of HepaFat-AI are no worse than HepaFat-Scan.

  Sensitivities and specificities of HepaFat-Scan and HepaFat-AI generated for the 145 cases with biopsy at the three previously determined VLFF thresholds.

Steatosis Boundary	**Grade 0 vs Grades 1-3**	**Grades 0 & 1 vs Grades 2 & 3**	**Grades 0-2 vs Grade 3**
VLFF Threshold (%)	4.1	12.1	16.2
HepaFat-Scan			
Sensitivity (%) (95% CI)	96.1 (91.2% to 98.3%)	88.6 (79.7% to 93.9%)	94.4 (74.2% to 99.0%)
Specificity (%) (95% CI)	88.2 (65.7% to 96.7%)	78.8 (67.5% to 86.9%)	74.8 (66.6% to 81.5%)
HepaFat-AI			
Sensitivity (%) (95% CI)	97.6 (93.3% to 99.2%)	86.1 (76.8% to 92.0%)	100.0 (81.6% to 100.0%)
Specificity (%) (95% CI)	88.2 (65.7% to 96.7%)	74.8 (66.6% to 81.5%)	71.4 (62.4% to 78.1%)

CONCLUSION

The 510(k) premarket notification for HepaFat-AI contains adequate information and data to enable the FDA-CDRH to determine substantial equivalence to the predicate devices. Resonance Health Analysis Services Pty Ltd believes that enough evidences have been presented in this Dossier to conclude that HepaFat-AI is safe, effective and performs as well as the predicate.