June 20, 2023

Resonance Health Analysis Services Pty Ltd
℅ Mitchell Wells
Managing Director
141 Burswood Road
Burswood, Western Australia 6100
Australia

Re: K231459
Trade/Device Name: HepaFatSmart (V2.0.0)
Regulation Number: 21 CFR 892.1000
Regulation Name: Magnetic resonance diagnostic device
Regulatory Class: Class II
Product Code: LNH
Dated: May 19, 2023
Received: May 19, 2023

Dear Mitchell Wells:

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
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.

Submission Number *(if known)*

K231459

Device Name

HepaFatSmart (V2.0.0)

Indications for Use *(Describe)*

Intended use:
HepaFatSmart is intended for the quantitative measurement of volumetric liver fat fraction (VLFF), proton density fat fraction (PDFF) and steatosis grading.
HepaFatSmart is an application that is used for the non-invasive evaluation of liver tissue by utilising magnetic resonance images to evaluate 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.

Indications for use:
Support clinical diagnoses in individuals with confirmed or suspected fatty liver disease;
Support the subsequent clinical decision making processes for patients under management for fatty liver related disease or metabolic syndromes;
Aid in the assessment and screening of living donors for liver transplant.
Results, when interpreted by a trained physician can be used to support clinical diagnoses about the status of liver fat content, the subsequent clinical decision making processes for the management of fatty liver related diseases, metabolic syndromes, liver donor screening and lifestyle change.
HepaFatSmart can be used to analyse the MRI images of patients of all populations independent of age and gender, with suspected clinical conditions related to the level of liver fat.

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.

510(K) SUMMARY

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

GENERAL INFORMATION

Date Prepared	07 June 2023
Submitted by	Resonance Health Analysis Service Pty Ltd 141 Burswood Rd Burswood 6100 AUSTRALIA
Main Contact	Mitchell Wells Managing Director, Resonance Health Analysis Services Pty Ltd mitchellw@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	HepaFatSmart
Trade/proprietary Name	HepaFatSmart (V2.0.0)
Classification	Class II
Product Code	LNH
CFR Section	892.1000 Magnetic Resonance Diagnostic Device
Panel	Radiology

Description of the Device

HepaFatSmart is an SaMD designed to automatically analyse magnetic resonance imaging (MRI) datasets for quantitative assessment of a patient's liver fat, in form of volumetric liver fat fraction (VLFF), proton density fat fraction (PDFF), and steatosis grade. It is an AI assisted, automated version of HepaFat-Scan (another SaMD of Resonance Health). To carry out an analysis, the user simply uploads DICOM images to FAST, Resonance Health's secured user portal and job management system. No other user input is required for the analysis thereby minimising the impact of human error on obtained results. HepaFatSmart requires DICOM images as input data that have been acquired according to the HepaFatSmart (same as HepaFat-Scan) protocol.

The key components for the HepaFatSmart are:

- MRI Protocol: A specific MRI protocol for acquisition of the raw image data. The MRI protocol is critical to ensure the quality of the end results. Its adherence is verified by the HepaFatSmart IQC module, an automated algorithm that checks the correctness of each parameter in the protocol.
- HepaFatSmart: An image analysis software predicting a suitable liver region of interest (ROI) utilizing AI-assisted SaMD technology then performing the Alpha measurement and anomaly (excessive iron) detection. It is composed of one (1) convolutional neural network (CNN) performing liver ROI detection with undesired components (artefacts and major blood vessels) considered/removed using a computer vision technique with machine learning technology. Background noise correction is not considered as there is no or very minimal impact on the analysis outcome. Following the training of the AI assisted device, the system is completely 'locked down' for final validation prior to release in commercial use to ensure reproducibility of the results. In principle, the HepaFatSmart v2.0.0 uses the same MRI data analysis approach as HepaFat-Scan.
- Volumetric Liver Fat Fraction Measurement (VLFF): A software module (algorithmic) that incorporates a conversion lookup table relating Alpha to VLFF is added to allow production of a VLFF report.
- Proton Density Fat Fraction Measurement (PDFF): A software module (algorithmic) that incorporates a conversion lookup table relating VLFF to PDFF is added to allow production of a PDFF report.
- Steatosis Grade Measurement: A software module (algorithmic) that incorporates a conversion lookup table relating VLFF to a steatosis grade.
- Excessive liver iron assessment: An additional software module (algorithmic) that estimates the impact of liver iron content as per the inclusion and exclusion criteria based on an algorithm to determine the analysis outcome (accept or reject).

The output of HepaFatSmart is the automatically generated reports in both PDF and DICOM (secondary captured) formats. Visually, the PDF and DICOM reports are identical except that the DICOM report also contains relevant header information. The HepaFatSmart report is populated with information stored in the DICOM header of the MRI images, the analysis result, where an Alpha value is converted into a VLFF value, a PDFF value, and a steatosis grade, and the associated confidence interval and normal range.

The HepaFatSmart report also contains pictures of two (2) echo times (TEs) (1st Out-of-Phase, 1st OP, and In-Phase, IP) of the analysed slice, a predicted liver ROI superimposed with one (IP) of the two TE images, and a fat distribution map. This is essential for the radiologist to check if the image

analysed is a liver image, the AI predicted ROI is placed correctly within the liver region, and the result provided is valid and consistent with other relevant clinical considerations.

HepaFatSmart SaMD can be accessed through a cloud-based or onsite platform. Resonance Health has developed its own cloud-based platform, called 'FAST'. Alternatively, HepaFatSmart can be offered on third parties' (channel partner) platforms.

It is important to note that HepaFatSmart as a medical device does not:

- come into direct contact with patients or end-users;
- control any other device used on the patient;
- deliver any treatment or energy to the patient; or
- provide diagnostic information upon which inappropriate (or lack of) treatment likely to result in serious adverse events is based; as clinical judgment would be used in the patient's clinical management, based upon a range of other factors relating to the patient.

INTENDED USE

The intended use of HepaFatSmart is:

HepaFatSmart is intended for the quantitative measurement of volumetric liver fat fraction (VLFF), proton density fat fraction (PDFF) and steatosis grading.

HepaFatSmart is an application that is used for the non-invasive evaluation of liver tissue by utilising magnetic resonance images to evaluate 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.

INDICATIONS FOR USE

- Support clinical diagnoses in individuals with confirmed or suspected fatty liver disease;
- Support the subsequent clinical decision-making processes for patients under management for fatty liver related disease or metabolic syndromes;
- Aid in the assessment and screening of living donors for liver transplant.
- Results, when interpreted by a trained physician can be used to support clinical diagnoses about the status of liver fat content, the subsequent clinical decision-making processes for the management of fatty liver related diseases, metabolic syndromes, liver donor screening and lifestyle change.

HepaFatSmart can be used to analyse the MRI images of patients of all population independent of age and gender, with suspected clinical conditions related to the level of liver fat.

PREDICATE INFORMATION

HepaFatSmart is substantially equivalent to the predicate device HepaFat-Scan (Resonance Health Analysis Services- K122035) and better than HepaFat-AI (Resonance Health Services – K201039).

SUBSTANTIAL EQUIVALENCE INFORMATION

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

	HepaFatSmart	HepaFat-AI	HepaFat-Scan
Regulatory Class	II	II	II
510(k) number	K231459	K201039	K122035
Classification Name	System, Nuclear Magnetic Resonance Imaging, System, Image Processing Radiological	System, Nuclear Magnetic Resonance Imaging, System, Image Processing Radiological	System, Nuclear Magnetic Resonance Imaging, System, Image Processing Radiological
CFR Section	892.1000	892.1000	892.1000
Product Code and Classification Panel	LNH	LNH	LNH
Device Name	HepaFatSmart	HepaFat-AI	HepaFat-Scan
Trade/Common Name	HepaFatSmart	HepaFat-AI	HepaFat-Scan
Description	Standalone software platform designed to automatically analyse within seconds magnetic resonance imaging (MRI) datasets using the method of HepaFat-Scan with the liver ROI predicted 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 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.

	HepaFatSmart	HepaFat-AI	HepaFat-Scan
Technology	Convolutional neural networks for the prediction of the liver region of interest (ROI). Algorithmic for the image quality checking and calculated Alpha conversion into VLFF, PDFF and Steatosis grade. Algorithms for the measurement and calculation of Alpha VLFF, PDFF and Steatosis grade.	Convolutional neural networks for the image analysis. Algorithmic for the image quality checking and Alpha conversion into VLFF.	Algorithmic, with human interaction for Region of Interest (ROI) selection.
Intended Use	HepaFatSmart is intended for the quantitative measurement of volumetric liver fat fraction (VLFF), proton density fat fraction (PDFF) and steatosis grading. HepaFatSmart is an application that is used for the non-invasive evaluation of liver tissue by utilising magnetic resonance images to evaluate 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 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	• Support clinical diagnoses in individuals with	HepaFat-AI is indicated to: • Assess the volumetric liver fat fraction,	HepaFat-Scan is a software device intended for quantitative measurement

	HepaFatSmart	HepaFat-AI	HepaFat-Scan
	confirmed or suspected fatty liver disease; • Support the subsequent clinical decision-making processes for patients under management for fatty liver related disease or metabolic syndromes; Aid in the assessment and screening of living donors for liver transplant. • Results, when interpreted by a trained physician can be used to support clinical diagnoses about the status of liver fat content, the subsequent clinical decision-making processes for the management of fatty liver related diseases, metabolic syndromes, liver donor screening and lifestyle change. HepaFatSmart can be used to analyse the MRI images of patients of all population independent of age and gender, with suspected clinical conditions related to the level of liver fat.	proton density fat fraction and steatosis grade in individuals with confirmed or suspected fatty liver disease; • Monitor liver fat content in patients undergoing weight loss management; Aid in the assessment and screening of living donors for liver transplant.	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.
User	Radiologist	Radiologist	Resonance Health's trained analyst
Hosting platform	Cloud-based or onsite platform	Cloud-based or onsite platform	Resonance Health's internal server
Image-type utilized	Magnetic Resonance	Magnetic Resonance	Magnetic Resonance
Image format	DICOM	DICOM	DICOM
Data Acquisition method	Gradient Recalled Echo (GRE)	Gradient Recalled Echo (GRE)	Gradient Recalled Echo (GRE)

	HepaFatSmart	HepaFat-AI	HepaFat-Scan
Anatomical Sites	Liver	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 2 TEs of the analysed slice and analysis liver ROI placed on 1 TE. 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 (%), 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	PDF (encrypted) and secondary capture (DICOM)	HTML and PDF	PDF

SUMMARY OF HEPAFATSMART PERFORMANCE – SUBSTANTIAL EQUIVALENCE

The device HepaFatSmart is in principle a new version of the predicate HepaFat-AI but with the name changed. As indicated in the Software Validation Report, three different technical analyses were performed to indicate the technical equivalency of HepaFatSmart compared with the reference standard HepaFat-Scan: Repeatability Study, Linear Regression Analysis and Bland Altman Analysis.

Repeatability Study (n = 42)

Repeatability study using a dataset with two different MRI scans for each subject to evaluate the device performance is a self-proven process as each paired data for a subject is supposed to produce the same analysis outcome. Briefly, the results are summarised as following:

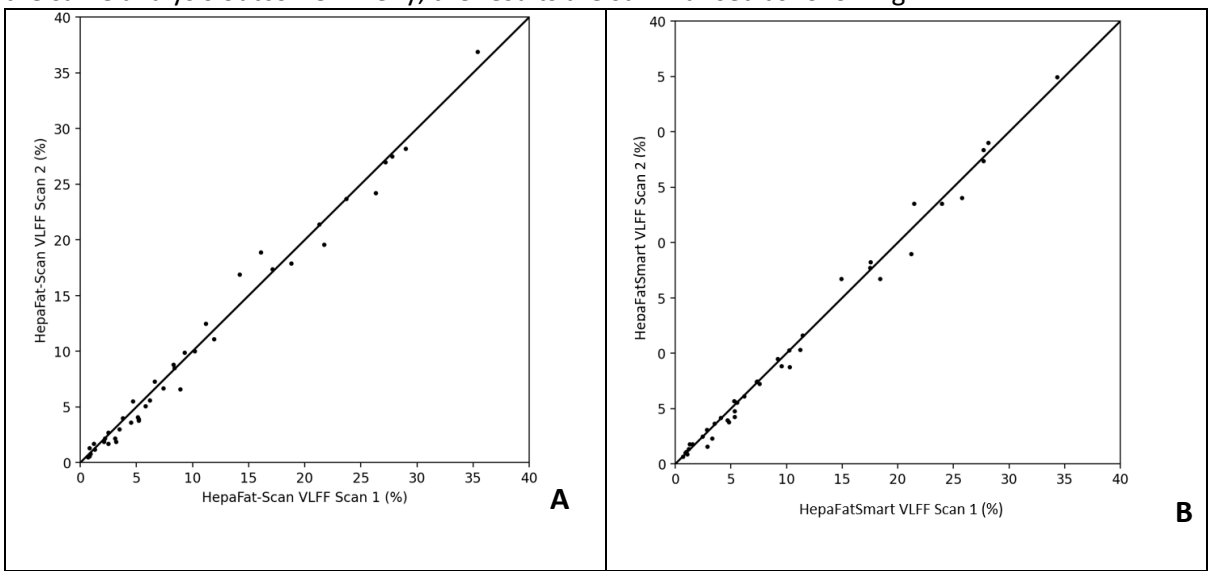

Figure 1. Plot **A** of HepaFat-Scan VLFF measured at scan 2 against HepaFat-Scan VLFF measured at scan 1 for the 42 subjects in the repeatability study. Plot **B** is for HepaFatSmart (41 subjects). The solid line is the line of equivalence. Note, 41 instead of 42 subjects were used in the HepaFatSmart related analysis as a single case was identified as a high iron case with the newly introduced excessive iron assessment algorithm. All the results are closely scattered around the equivalency line, indicating good performance and substantial equivalence for both the predicate HepaFat-Scan and the device HepaFatSmart,

From the linear regression analysis shown in Figure 1 for both the reference standard HepaFat-Scan (plot A) and HepaFatSmart (plot B), all the results are closely scattered around the equivalency line and difficult to tell visually which one is better.

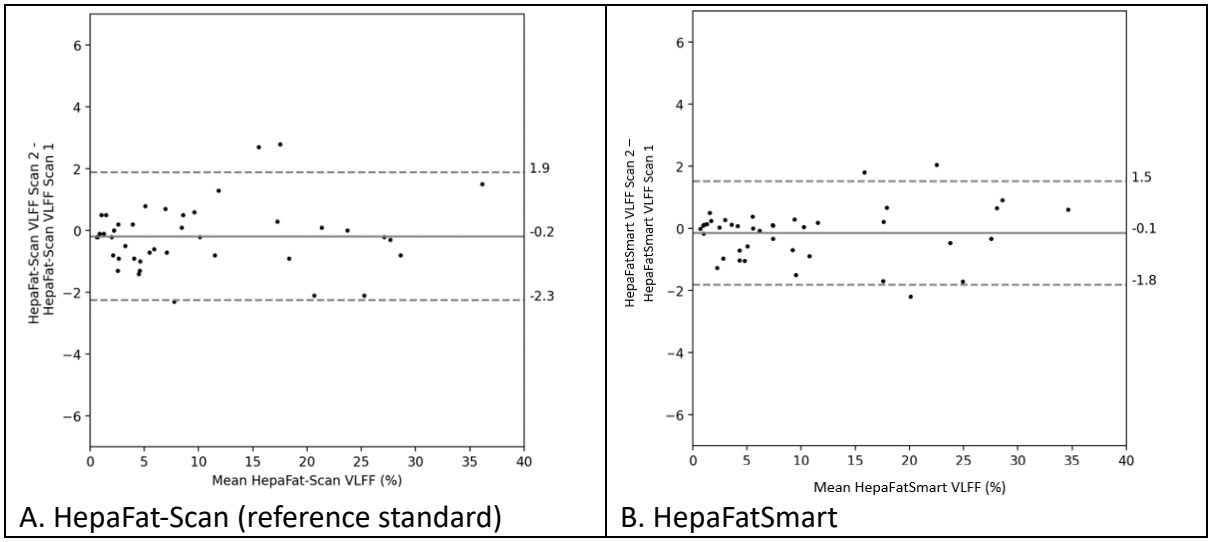

Figure 2. Bland Altman analysis of the repeatability study: plot **A** - HepaFat-Scan VLFF measured scan 1 and 2 for the 42 subjects; plot **B** is for HepaFatSmart (41 subjects). Bias and both repeatability coefficients are slightly better for HepaFatSmart compared with the reference standard HepaFat-Scan.

From the Bland Altman analysis shown in Figure 2 for both the reference standard HepaFat-Scan (plot A) and HepaFatSmart (plot B), bias and both repeatability coefficients for the HepaFatSmart are slightly better than those obtained from the repeated scans of HepaFat-Scan, indicating the performance of the HepaFatSmart is comparable (no worse) than human for the repeatability data analysed. This does not suggest yet that the HepaFatSmart is better than human analyst as the original human analysis (HepaFat-Scan) historically used two small liver ROIs rather than a single large liver ROI used in the HepaFatSmart with potentially slightly larger sampling error in the original HepaFat-Scan analysis. From the repeatability data, there was no statistically significant bias and tight repeatability coefficients for the HepaFatSmart, indicating the substantial equivalence to the predicate HepaFat-Scan and a possibility that the results from HepaFatSmart and HepaFat-Scan could be interchangeable.

In addition, HepaFatSmart demonstrated 100% repeatable (reproducible) in the repeatability study using the same datasets analysed twice with zero VLFF difference between the first and second analyses, which is better than human analysis with HepaFat-Scan.

Validation Study (n=300)

Validation study using a dataset with two different MRI scans for each subject to evaluate the device performance is a self-proven process as each paired data for a subject is supposed to produce the same analysis outcome. Briefly, the results are summarised as following (note the study population size is smaller than 300 as per the IQC module in place):

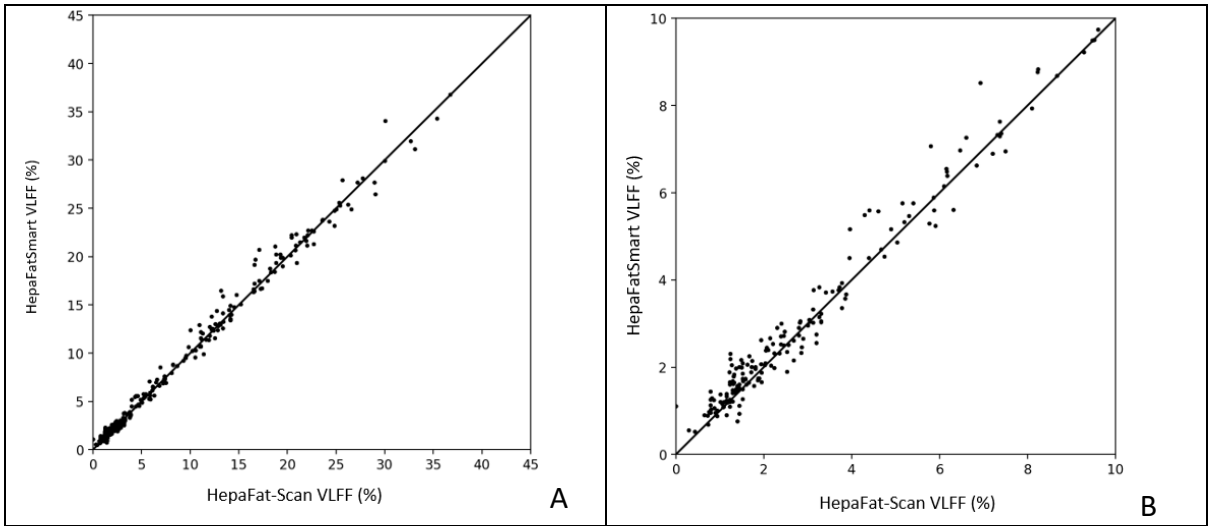

Figure 3. Linear regression analysis of the validation study (n = 281) by comparing HepaFatSmart with the reference standard HepaFat-Scan: plot **A** shows the full VLFF range and plot **B** shows the VLFF range between 0 – 10%. The solid line is the line of equivalence. 281 datasets out of 300 passed the IQC rules. All the results are closely scattered around the equivalency line, indicating good performance and substantial equivalence for both the predicate HepaFat-Scan and the device HepaFatSmart.

From the linear regression analysis shown in Figure 3 for both the reference standard HepaFat-Scan (plot A) and HepaFatSmart (plot B), all the results are closely scattered around the equivalency line and difficult to tell visually which one is better, indicating good performance and substantial equivalence for both the predicate HepaFat-Scan and the device HepaFatSmart.

From the Bland Altman analysis shown in Figure 4 for both the device HepaFatSmart (plot A) and another predicate HepaFat-AI (plot B) by comparing with the reference standard HepaFat-Scan, bias

and both 95% limits for the HepaFatSmart are significantly better than those obtained from the predicate HepaFat-AI, indicating the much improved and safer performance of the HepaFatSmart, which is as expected as the analysis outcomes are solely dependent on the liver ROI.. Despite the Bias of 0.2% is statistically significant (due to small variability), it is small and unlikely clinically significant. Both upper and lower 95% limits are small and close to the repeatability coefficients found in the repeatability study but significantly smaller than the predicate HepaFat-AI, indicating the new device HepaFatSmart is substantially equivalence to the predicate HepaFat-Scan and better than the predicate HepaFat-AI.

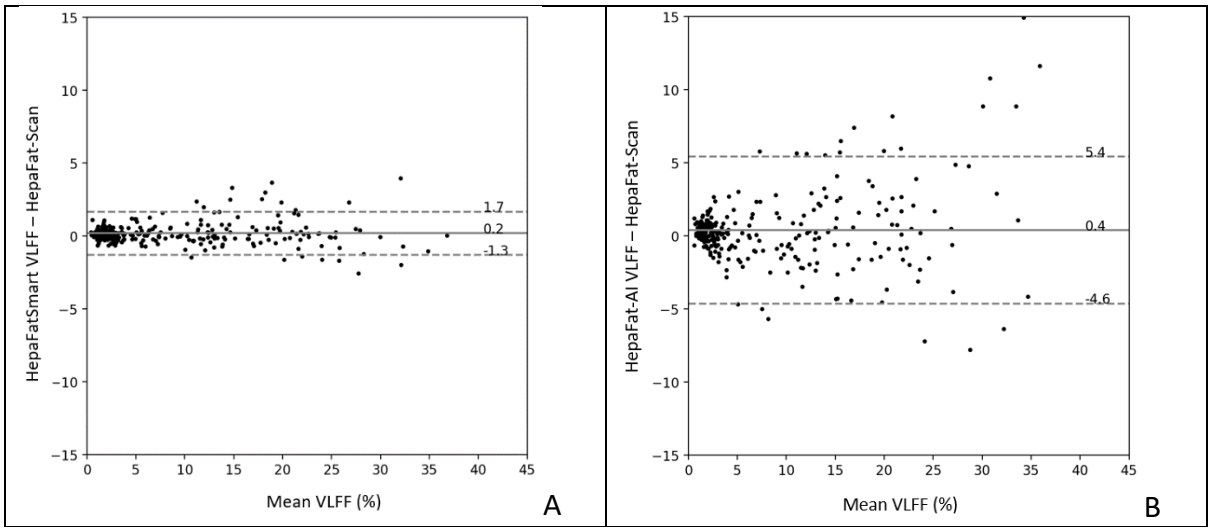

Figure 4. Bland Altman analysis of the validation study (n = 281) of the HepaFatSmart VLFF (plot A) and HepaFat-AI (plot B) by comparing with the reference standard HepaFat-Scan VLFF. For the HepaFatSmart, the Bias of 0.2% is statistically significant (due to small variability) but small and unlikely clinically significant. Both upper and lower 95% limits are small and close to the repeatability coefficients found in the repeatability study. Compared with the predicate HepaFat-AI, significant improvement is indicated by the small bias and 95% confident limits.

Table 1 summarises the Bland Altman analysis results performed in the repeatability study and validation study for the device HepaFatSmart and two predicates HepaFat-Scan and HepaFat-AI. In both studies, the performance of the device HepaFatSmart stands out and demonstrates the substantial equivalence to the predicate HepaFat-Scan and better outcomes than the predicate HepaFat-AI.

	Bias	**95% CI**	**Upper 95% LA/Repeatability**	**95% CI**	**Lower 95% LA/Repeatability**	**95% CI**
HepaFat-Scan Repeatability	-0.2 (-0.19)	-0.5 to 0.1	1.9	1.3 to 2.5	-2.3	-1.7 to -2.9
HepaFat-AI v1.2.17 Repeatability	-0.2 (-0.22)	-0.8 to 0.3	3.2	2.3 to 4.2	-3.6	-2.7 to -4.6
HepaFatSmart v2.0.0 Repeatability	**-0.1 (-0.14)**	**-0.4 to 0.1**	**1.5**	**1.1 to 2.0**	**-1.8**	**-1.4 to -2.4**
HepaFat-AI v1.2.17 Limits of Agreement (full quarantine dataset)	0.4 (0.41)	0.1 to 0.7	5.4	4.9 to 6.0	-4.6	- 4.1 to -5.2
HepaFatSmart v2.0.0 Limits of Agreement (full quarantine dataset)	**0.2 (0.19)**	**0.1 to 0.3**	**1.7**	**1.5 to 1.8**	**-1.3**	**-1.1 to -1.4**

Table 1. Upper and lower 95% limits of repeatability and upper and lower 95% limits of agreement between HepaFat-AI v1.2.17, HepaFatSmart and HepaFat-Scan VLFF measurements.

The fully quarantined 300 validation subjects with different clinical conditions across a broad age range and fat level scanned from different MRI centres with different MRI makes and models were used to validate the whole functionalities including IQC and to evaluate the technical and clinical performances. The sensitivities and specificities of HepaFatSmart for predicting HepaFat-Scan VLFF values in the fully quarantined dataset (n=281, successfully passed the IQC rules) above clinically relevant VLFF thresholds are given in Table 2 below, which demonstrate excellent performances and substantial equivalency of the new device HepaFatSmart compared with the reference standard and predicate HepaFat-Scan with both sensitivity and specificity well above 90% and close to 100%. A few very limited subjects with miscategorised outcomes were identified and discussed with minimal or non-clinical relevant impact. No adverse effects and complications have been identified for any of the miscategorised subjects.

VLFF threshold	Clinical relevance	Sensitivity (95% CI) (%)	Specificity (95% CI) (%)
4.1 %	• Boundary between grade 0 (<5%) and grade 1 (5 - 33%) steatosis by histological inspection. Used to define the absence (0) or presence (1) of NAFLD.	100.0 (97.3 – 100.0)	98.6 (94.9 – 99.6)
12.1 %	• Boundary between grade 1 (5-33%) and grade 2 (33-66%) steatosis by histological inspection.	98.8 (93.6 – 99.8)	98.0 (94.9 – 99.2)
16.2 %	• Boundary between grade 2 (33-66%) and grade 3 (> 66%) steatosis by histological inspection.	100.0 (93.8 – 100.0)	99.6 (97.5 – 99.9)

Table 2. Sensitivities and specificities of HepaFatSmart for predicting HepaFat-Scan VLFF values greater than three clinically relevant thresholds.

As shown in both technical and clinical tests from above, the new device HepaFatSmart produces almost the same analysis results as the reference standard and predicate HepaFat-Scan with the liver ROI approach, which is as expected because the analysis outcomes are purely governed by the liver ROI. In the meantime, both technical and clinical tests have demonstrated significant improvement compared with the predicate HepaFat-AI with safer and more effective outcomes.

CONCLUSION

The Special 510(k) submission for HepaFatSmart 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 evidence has been presented in this submission to conclude that HepaFatSmart is safe, effective and performs as well as the predicate HepaFat-Scan and safer, more effective, and better than the predicate HepaFat-AI.