Resonance Health Analysis Services Pty Ltd
Mitchell Wells
Official Correspondent
141 Burswood Road
Perth, Western Australia 6100
Australia

December 29, 2021

Re: K213776
Trade/Device Name: LiverSmart
Regulation Number: 21 CFR 892.1001
Regulation Name: Liver Iron Concentrattion Imaging Companion Diagnostic For Deferasirox
Regulatory Class: Class II
Product Code: PCS, LNH
Dated: November 24, 2021
Received: December 2, 2021

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,

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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K213776

Device Name
LiverSmart

Indications for Use *(Describe)*
LiverSmart is indicated to:

For Liver Iron Concentration
1. measure liver iron concentration in individuals with confirmed or suspected systemic iron overload;
2. monitor liver iron burden in transfusion dependent thalassemia patients and patients with sickle cell disease receiving blood transfusions;
3. aid in the identification and monitoring of non-transfusion-dependent thalassemia patients receiving therapy with Deferasirox.

For Liver Fat Assessment
1. 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:
2. monitor liver fat content in patients undergoing weight loss management;
3. 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.

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."

K213776

510(k) SUMMARY

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

GENERAL INFORMATION

Date Prepared	23 December 2021
Submitted by	Resonance Health Analysis Service Pty Ltd 141 Burswood Rd Burswood 6100 AUSTRALIA
Main Contact	Mr Mitchell Wells Managing Director 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	LiverSmart
Trade/proprietary Name	LiverSmart™
Classification	Class II
Product Code	90-PCS and LNH
CFR Section	892.1001 and 892.1000
Panel	Radiology

Description of the Device

LiverSmart is software that utilizes two existing FDA cleared devices, HepaFat-AI (K201039) and FerriSmart (K182218) and combines their respective results into a singular consolidated multi-parametric 'LiverSmart' report.

LiverSmart automatically sorts and sends magnetic resonance imaging (MRI) datasets to each of the existing HepaFat-AI and FerriSmart devices and then receives results from those devices to generate a summary report which combines the HepaFat-AI results (an estimate of the patient's volumetric liver fat fraction (VLFF), proton density fat fraction (PDFF), steatosis grade), and the FerriSmart result (an estimate of the patient's liver iron concentration (LIC)).

To conduct analysis, the user simply uploads a single zipped folder containing HepaFat-AI and FerriSmart DICOM images, acquired in accordance with their respective acquisition protocols, to the LiverSmart software. No user input is required for the analysis thereby minimising the impact of human error. The LiverSmart software requires image input data that has been acquired in accordance with the existing and now well established HepaFat-AI (K201039) and FerriSmart (K182218) imaging protocols.

LiverSmart has two new components that are in addition to the existing components of HepaFat-AI and FerriSmart, namely a:

(i) Data Preparation Module; and

(ii) Report Generation Module

The rest of the components for LiverSmart are the existing components of the FDA cleared HepaFat-AI and FerriSmart devices, as follows:

For HepaFat-AI:

(i) Magnetic Resonance Imaging Protocol

(ii) HepaFat-AI Analysis Software

(iii) Volumetric Liver Fat Fraction Measurement

(iv) Proton Density Fat Fraction Measurement

(v) Steatosis Grade Measurement

For FerriSmart:

(i) Magnetic Resonance Imaging Protocol

(ii) FerriSmart Analysis Software

(iii) Liver Iron Concentration Measurement

The above HepaFat-AI and FerriSmart components are the same as previously provided to the FDA as the time HepaFat-AI and FerriSmart regulatory clearances were sought (and subsequently obtained).

Intended Use

For Liver:

(i) For the measurement of R2 and iron concentration in the liver from MRI scans.
(ii) 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

LiverSmart is indicated to -

For Liver Iron Concentration:

(i) measure liver iron concentration in individuals with confirmed or suspected systemic iron overload;
(ii) monitor liver iron burden in transfusion dependent thalassemia patients and patients with sickle cell disease receiving blood transfusions; and
(iii) aid in the identification and monitoring of non-transfusion-dependent thalassemia patients receiving therapy with Deferasirox.

For Liver Fat Assessment:

(i) 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:

(ii) Monitor liver fat content in patients undergoing weight loss management; and
(iii) Aid in the assessment and screening of living donors for liver transplant

PREDICATE INFORMATION

LiverSmart is substantially equivalent to (and is a combination of) the following Resonance Health existing 510(k) cleared devices:

- FerriSmart - K182218
- HepaFat-AI - K201039

SUBSTANTIAL EQUIVALENCE INFORMATION

The table below summarizes the main similarities and differences between LiverSmart and the predicates.

	LiverSmart (Subject Device)	**FerriSmart (Predicate)**	**HepaFat-AI (Predicate)**
Regulatory Class	II	II	II
510(k) number	K213776	K182218	K201039
Classification Name	Liver Iron Concentration Imaging Companion Diagnostic for Deferasirox System, Nuclear Magnetic Resonance Imaging, System, Image Processing Radiological	Liver Iron Concentration Imaging Companion Diagnostic for Deferasirox	System, Nuclear Magnetic Resonance Imaging, System, Image Processing Radiological
CFR Section	892.1001 and 892.1000	892.1001	892.1000
Product Code and Classification Panel	90 PCS and 90 LNH	90 PCS	90 LNH
Description	Standalone software package that automatically analyses magnetic resonance imaging (MRI) datasets to generate an estimate of the patient's volumetric liver fat fraction (VLFF), proton density fat fraction (PDFF), steatosis grade, and liver iron concentration (LIC). LiverSmart evaluates images acquired using the FerriSmart and HepaFat-AI protocols and analyses the acquired data to produce a 'multi-parametric' reporting both fat metrics and LIC.	Standalone software package that automatically analyses multi-slice, spin-echo MRI data sets encompassing the abdomen to provide objective and reproducible determination of liver parameters to support clinicians in the assessment of liver iron status. The software tool determines the signal decay rate (R2) that is used to characterize iron loading in the liver, which is then transformed by a defined calibration curve to provide a quantitative measure of liver iron concentrations in vivo.	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.

	LiverSmart (Subject Device)	FerriSmart (Predicate)	HepaFat-AI (Predicate)
Technology	Convolutional neural networks for the image analysis. Algorithmic for the image's quality checks, R2 conversion into LIC, and Alpha conversion into VLFF.	Convolutional neural networks for the image analysis. Algorithmic for the image's quality checks and R2 conversion into LIC.	Convolutional neural networks for the image analysis. Algorithmic for the image's quality checking and Alpha conversion into VLFF.
Intended purpose(s)	1. Supporting clinical diagnoses about the status of LIC and 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 LIC and liver fat as a result of interventions.	1. Supporting clinical diagnoses about the status of LIC. 2. Supporting the subsequent clinical decision-making processes. 3. Supporting the use in clinical research trials, directed at studying changes in LIC 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.
Intended Use	1. For the measurement of R2 and iron concentration in the liver from MRI scans. 2. For quantitative measurement of the triglyceride fat fraction in magnetic resonance images of the liver, also known as volumetric liver fat fraction (VLFF).	1. Measurement of R2 and iron concentration in the liver from MRI scans	1. 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.

	LiverSmart (Subject Device)	FerriSmart (Predicate)	HepaFat-AI (Predicate)
Indications	LiverSmart is indicated to: <u>For Liver Iron Concentration</u> 1. measure liver iron concentration in individuals with confirmed or suspected systemic iron overload; 2. monitor liver iron burden in transfusion dependent thalassemia patients and patients with sickle cell disease receiving blood transfusions; 3. aid in the identification and monitoring of non-transfusion-dependent thalassemia patients receiving therapy with Deferasirox. <u>For Liver Fat Assessment</u> 1. 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: 2. monitor liver fat content in patients undergoing weight loss management; 3. aid in the assessment and screening of living donors for liver transplant.	FerriSmart is Indicated to: 1. measure liver iron concentration in individuals with confirmed or suspected systemic iron overload; 2. monitor liver iron burden in transfusion dependent thalassemia patients and patients with sickle cell disease receiving blood transfusions; 3. aid in the identification and monitoring of non-transfusion-dependent thalassemia patients receiving therapy with Deferasirox.	HepaFat-AI is indicated to: 1. 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: 2. monitor liver fat content in patients undergoing weight loss management; 3. aid in the assessment and screening of living donors for liver transplant.
User	Radiologist	Radiologist	Radiologist
Hosting platform	Cloud-based or on-site hosting	Cloud-based or on-site hosting	Cloud-based or onsite platform

	LiverSmart (Subject Device)	FerriSmart (Predicate)	HepaFat-AI (Predicate)
Image-type utilized	Magnetic Resonance	Magnetic Resonance	Magnetic Resonance
Image format	DICOM	DICOM	DICOM
Data Acquisition method	Single Spin Echo (SSE) Gradient Recalled Echo (GRE)	Single Spin Echo (SSE)	Gradient Recalled Echo (GRE)
Anatomical Sites	Liver	Liver	Liver
Analysis System Components	LiverSmart: (i) Data Preparation Module; and (ii) Report Generation Module FerriSmart: (i) Magnetic Resonance Imaging Protocol; (ii) FerriSmart Analysis Software; and (iii) Liver Iron Concentration Measurement. HepaFat-AI: (i) Magnetic Resonance Imaging Protocol; (ii) HepaFat-AI Analysis Software; (iii) Volumetric Liver Fat Fraction Measurement; (iv) Proton Density Fat Fraction Measurement; and	(i) Magnetic Resonance Imaging Protocol (ii) FerriSmart Analysis Software (iii) Liver Iron Concentration Measurement	(i) Magnetic Resonance Imaging Protocol (ii) HepaFat-AI Analysis Software (iii) Volumetric Liver Fat Fraction Measurement (iv) Proton Density Fat Fraction Measurement (v) Steatosis Grade Measurement

	LiverSmart (Subject Device)	FerriSmart (Predicate)	HepaFat-AI (Predicate)
	(v) Steatosis Grade Measurement		
Result report content	Page 1 (i) Report No., patient ID, patient name and date of birth for full identification of the patient. (ii) Scan date, and analysis date. (iii) Referrer and MRI centre. (iv) Results displayed: LIC (mg/g dry tissue), LIC (mmol/kg dry tissue), associated with confidence intervals and normal range. (v) Results displayed: VLFF (%), PDFF (%) and Steatosis grade, associated with confidence intervals and normal range. Page 2 As per FerriSmart report Page 3 As per HepaFat-AI report	(i) Patient ID, patient name and date of birth for full identification of the patient. (ii) Scan date, and analysis date. (iii) Referrer and MRI centre. (iv) Results displayed: LIC (mg/g dry tissue), LIC (mmol/kg dry tissue), associated with confidence intervals and normal range. (v) Pictures of the 5 TEs of the analysed slice. (vi) LIC thresholds table	(i) Patient ID, patient name and date of birth for full identification of the patient. (ii) Scan date, and analysis date. (iii) Referrer and MRI centre. (iv) Results displayed: VLFF (%), PDFF (%) and Steatosis grade, associated with confidence intervals and normal range. (v) NASH-CRN Steatosis Grading Guide (vi) Pictures of the 3 TEs of the analysed slice. (vii) Liver colour map (for illustration purpose only, not for diagnostic)
Result report format	HTML and PDF	HTML and PDF	HTML and PDF

SUMMARY OF CHANGE(S)

LiverSmart consists of two additional modules, over and above the FerriSmart and HepaFat-AI modules;

(i) the Data Preparation Module, and
(ii) the Report Generation Module.

PERFORMANCE PARAMETERS

No change from the predicates, FerriSmart (K182218) and HepaFat-AI (K201039).

SUMMARY OF DESIGN CONTROL ACTIVITIES

Hazard analysis has been performed and documented. Hazard analysis is included in this submission. The test methods used are the same as those documented in the previously cleared submissions of the predicate devices, FerriSmart (K182218) and HepaFat-AI (201039). A statement of conformity with design controls is included in this submission.

SAFETY

LiverSmart is designed and manufactured under the Quality System Regulations as outlined in 21 CFR § 820 and ISO 13485 Standards. LiverSmart is based upon the same technologies, operating principle, and software technology as the two predicate devices. Risk activities were conducted in concurrence with established medical device development standards and guidance.

TESTING

Risk analysis and verification testing conducted are documented and included in this submission, which demonstrate that the performance requirements have been met.

SUBSTANTIAL EQUIVALENCE

Verification testing confirms that the data preparation module of LiverSmart detects anomalies in the sequence acquisition and reports the accurate error message. If an error is detected LiverSmart prevents further analysis. Additionally, LiverSmart yields identical results for VLFF, PDFF, steatosis grade, and LIC, when the same image datasets are analysed by HepaFat-AI and FerriSmart devices independently.

CONCLUSION

The special 510(k) premarket notification for LiverSmart contains adequate information and data to enable the FDA-CDRH to determine substantial equivalence to the predicate devices. Resonance Health believes that enough evidence has been presented in this dossier to conclude that LiverSmart is safe, effective and performs as well as two the predicates.