AI4MedImaging Medical Solutions S.A.
℅ Carla Almeida
Regulatory Affairs and Quality Manager
Rua do Parque Poente, Lote 35
Braga, Minho 4705-002
PORTUGAL

July 22, 2022

Re: K220624
Trade/Device Name: AI4CMR v1.0
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical image management and processing system
Regulatory Class: Class II
Product Code: QIH
Dated: June 17, 2022
Received: June 23, 2022

Dear Carla Almeida:

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 and Part 809); 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,

Jessica Lamb, Ph.D.
Assistant Director
Imaging Software Team
DHT8B: Division of Radiological Imaging Devices and Electronic Products
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)*
K220624

Device Name
AI4CMR v1.0

Indications for Use *(Describe)*
AI4CMR software is designed to report cardiac function measurements (ventricle volumes, ejection fraction, indices etc.) from 1.5T and 3T magnetic resonance (MR) scanners. AI4CMR uses artificial intelligence to automatically segment and quantify the different cardiac measurements. Its results are not intended to be used on a stand-alone basis for clinical decision-making.

The user incorporating AI4CMR into their DICOM application of choice is responsible for implementing a user interface.

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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Section 5. 510(k) Summary

1. General Information

510(k) Sponsor	AI4MedImaging Medical Solutions S.A.
Address	Rua do Parque Poente, lt 32 4705-002 Sequeira, Braga Portugal
Correspondence Person	Rory A. Carrillo Quality and Regulatory Consultant Cosm
Contact Information	Email: rory@cosmhq.com Phone: 562-533-7010
Date Prepared	June 17, 2022

2. Subject Device

Proprietary Name	AI4CMR v1.0
Common Name	AI4CMR
Classification Name	System, Image Processing, Radiological
Regulation Number	21 CFR 892.2050
Regulation Name	Medical Image Management and Processing System
Product Code	QIH
Regulatory Class	II

3. Predicate Device

Proprietary Name	Imbio RV/LV Software
Premarket Notification	K203256
Classification Name	System, Image Processing, Radiological
Regulation Number	21 CFR 892.2050
Regulation Name	Medical Image Management and Processing System
Product Code	QIH
Regulatory Class	II

4. Device Description

AI4CMR v1.0 is a cloud-hosted service used with any third-party DICOM viewer application where the DICOM viewer serves as the user interface and the interface to a PACS or scanner for AI4CMR. AI4CMR is implemented as a plug-in to the DICOM viewer by the user and automatically processes and analyses cardiac MR images received by the DICOM viewer to quantify relevant cardiac function metrics and makes the information available to the user at the user's discretion.

The following are the cardiac function metrics quantified and reported by the software:

Quantitative Analysis
The subject device performs the following anatomical measurements:

- Anatomy and tissue segmentation
- LV/RV stroke volume
- LV/RV cardiac output
- LV/RV ejection fraction
- LV/RV end-diastolic volume
- LV/RV end-systolic volume

Reporting
The subject device enables the following metrics to be reported as desired by the user:

Metric	Unit	Accuracy
LV/RV stroke volume	ml	n/a[1]
LV/RV cardiac output	L/min	n/a[1]
LV/RV ejection fraction (EF)	%	LV bias (std): 3.87 (5.74) LV ICC: 0.96 RV bias (std): 7.80 (7.32) RV ICC: 0.81
LV/RV end-diastolic volume (EDV)	ml	LV bias (std): 8.66 (17.28) LV ICC: 0.99 RV bias (std): 8.36 (15.59) RV ICC: 0.96
LV/RV end-systolic volume (ESV)	ml	LV bias (std): -2.90 (17.52) LV ICC: 0.99 RV bias (std): -9.08 (13.83) RV ICC: 0.95
LV myocardial mass	g	bias (std): 2.45 (18.04) ICC: 0.96
LV/RV end-systolic volume index[2]	ml/m^2	n/a[1]
LV/RV end-diastolic volume index[2]	ml/m^2	n/a[1]
LV/RV stroke volume index[2]	ml/m^2	n/a[1]
Myocardium mass index[2]	g/m^2	n/a[1]

Metric	Unit	Accuracy
Cardiac index[2]	L/(min m^2)	n/a[1]

Notes:
[1] These values are derived by performing simple mathematical operations and are derived from EDV, ESV, EF, and Mass metrics.
[2] These values are only provided if the patient's height and weight are included in the DICOM data.

Training Dataset

The AI4CMR training was performed on a dataset of 824 anonymized cases collected retrospectively from Hospital de Braga, Portugal. Acquisition occurred between 2015 to January 2019 and consisted of male (63%) and female (37%) patients ranging in age from 13 to 89 (mean of 58) years old from Siemens acquisition system. This dataset is independent from the clinical validation set. This dataset was split into the 3 sets (training, validation, test). The splitting ratio is 70% for the "training set", 15% for the "validation set" and 15% for the "test set", resulting in 577, 121 and 126 cases each, respectively.

5. Indications for Use

AI4CMR software is designed to report cardiac function measurements (ventricle volumes, ejection fraction, indices etc.) from 1.5T and 3T magnetic resonance (MR) scanners. AI4CMR uses artificial intelligence to automatically segment and quantify the different cardiac measurements. Its results are not intended to be used on a stand-alone basis for clinical decision-making.

The user incorporating AI4CMR into their DICOM application of choice is responsible for implementing a user interface.

6. Substantial Equivalence & Technical Characteristics

	Subject Device *AI4CMR v1.0*	**Predicate Device:** Imbio RV/LV (K203256)
Intended Use	AI4CMR software is designed to report cardiac function measurements (ventricle volumes, ejection fraction, indices etc.) from 1.5T and 3T magnetic resonance (MR) scanners. AI4CMR uses artificial intelligence to automatically segment and quantify the different cardiac measurements. Its results are not intended to be used on a	The Imbio RV/LV Software device is designed to measure the maximal diameters of the right and left ventricles of the heart from a volumetric CTPA acquisition and report the ratio of those measurements. RV/LV analyzes cases using an artificial intelligence algorithm to identify the location and measurements of the ventricles. The RV/LV software

	Subject Device *AI4CMR v1.0*	**Predicate Device:** Imbio RV/LV (K203256)
	stand-alone basis for clinical decision-making. The user incorporating AI4CMR into their DICOM application of choice is responsible for implementing a user interface.	provides the user with annotated images showing ventricular measurements. Its results are not intended to be used on a stand-alone basis for clinical decision-making or otherwise preclude clinical assessment of CTPA cases.

Feature/ Function	**Subject Device:** AI4CMR v1.0	**Predicate Device:** Imbio RV/LV (K203256)	**Substantially Equivalent?**
Indication for Use	See table above	See table above	Yes
Input Data Requirements	Cardiovascular images: multi-phase, multi-slice acquired from MRI scanners	Non-gated, CT Pulmonary Angiography images	Yes[1]
DICOM Compliant	Yes	Yes	Yes
LV Segmentation	Yes	Yes	Yes
RV Segmentation	Yes	Yes	Yes
Diameter Measurements	Yes	Yes	Yes
Fully Automated Segmentation	Yes	Yes	Yes
Interface	3rd party Viewer as a plug-in	Command line	Yes
Outputs	Report only	Report, DICOM Secondary Capture Series	Yes

[1]See discussion below

The subject device and predicate device have similar indications for use and technological characteristics. Differences with the input data requirement do not raise questions of safety or effectiveness as the underlying technology is similar with similar risks that are mitigated by the same general and special controls.

7. Performance Data

Safety and performance of the AI4CMR v1.0 has been evaluated and verified in accordance with software specifications and applicable performance standards through software verification and validation testing. Additionally, the software validation activities were performed in accordance

with *ANSI AAMI IEC 62304:2006/A1:2016 - Medical device software – Software life cycle processes,* in addition to the FDA Guidance documents, *"Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices"* and *"Content of Premarket Submission for Management of Cybersecurity in Medical Devices."*

7.1 Bench Testing

AI4MED performed a standalone performance test on the Society of Cardiac Magnetic Resonance (SCMR) Consensus Contour Data[1] which consists of a total of 15 CMR cases annotated by seven (7) independent expert readers from various core laboratories. The dataset consisted of male and female patients with an age range of 42 to 77 (average of 61) years old across various 1.5T and 3T scanners (Siemens, GE, Phillips). Readers performed myocardial segmentation and quantified End-diastolic volume (EDV), End-systolic volume (ESV), LV mass (LVM), and Ejection Fraction (EF). Agreement was evaluated and achieved between AI4CMR and the SCMR Consensus data. For myocardium segmentation, an average dice similarity coefficient (DSC) of 0.72 per image was achieved. For LVM, EDV, ESV, and EF the intraclass correlation coefficient (ICC) was evaluated and the following performance was obtained:

LV parameter	LOA (± 2 SD)	Bias ± SD	r^2	ICC
EDV	[-58.5912, 45.9097] ml	-6.3407 ± 26.1252 ml	0.85	0.95
ESV	[-30.2173, 22.4768] ml	-3.8703 ± 13.1735 ml	0.97	0.99
EF	[-7.2668, 6.9567] %	-0.155 ± 3.5559 %	0.95	0.99
LVM	[-57.2331, 11.7108] g	-22.7611 ± 17.236 g	0.72	0.78

7.2 Clinical Performance Assessment

AI4MED performed a multi-reader multi-center (MRMC) retrospective study consisting of 146 CMR cases with patients ranging from 17 to 85 years old (average of 51) that were predominantly male (77%) - consistent with cardiovascular disease incidence[2]. Patient data consisted of diseased (~60%) and non-diseased (~40%) where the diseased was spread across the prevalent cardiovascular diseases worldwide[3]. CMR cases was acquired and balanced across Siemens, GE, and Philips 1.5T scanners with slice thickness of 8mm and slice diameter ranging from 8 to 10.5mm.

The primary objective was to evaluate agreement between the AI4MED device and 2 expert readers who achieved excellent interrater variability (ICC > 0.75). Readers manually segmented the myocardium for each CMR case per standard of care and manually determined volumes, LV mass, and Ejection Fraction. The dataset was independent of the data used for model training and development.

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[1] SCMR. Cardiac Atlas Project - SCMR Consensus Contour Data [Internet]. Available from: https://www.cardiacatlas.org/studies/scmr-consensus-data/

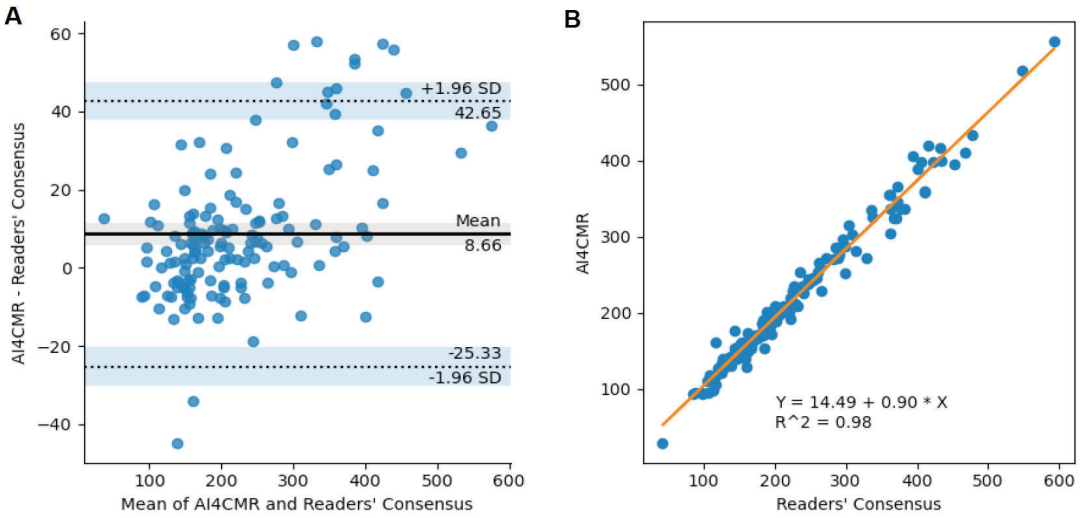
[2] Walli-Attaei, Marjan, et al. "Variations between women and men in risk factors, treatments, cardiovascular disease incidence, and death in 27 high-income, middle-income, and low-income countries (PURE): a prospective cohort study." The Lancet 396.10244 (2020): 97-109

[3] Ischemic heart disease, cardiomyopathies, myocarditis, pericardial abnormality, valve disease, cardiac mass tumor and others

A summary of the agreement for Left and Right Ventricular EDV, Left and Right Ventricular ESV, Left and Right Ventricular Ejection Fraction, LV Myocardial Mass is provided below:

Left Ventricular EDV

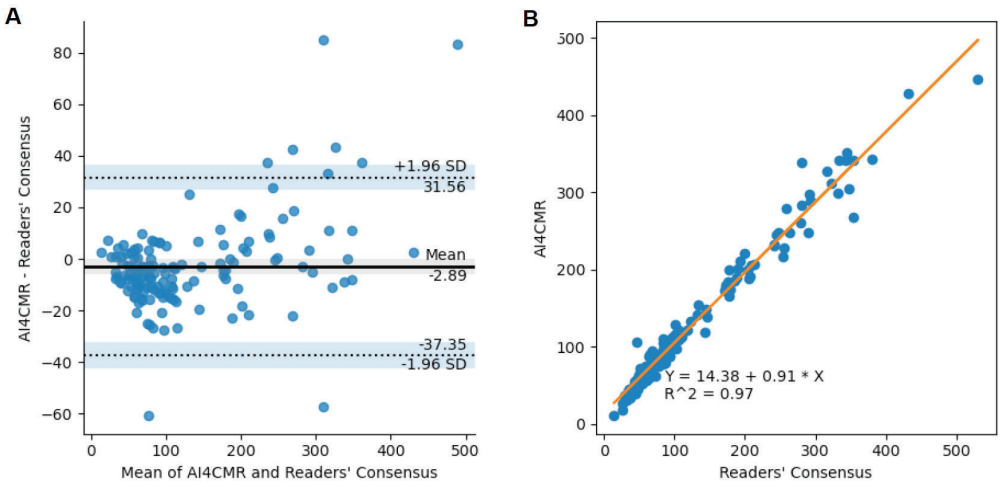
	Cronbach's Alpha	*Correlation Coef. (ρ)*	*Bias*	*ICC*	*95% Confidence Interval*	
					Lower Bound	**Upper Bound**
AI4CMR vs consensus	0,992	0,980	8,663	**0,990**	**0,98**	**0,99**



[see next page]

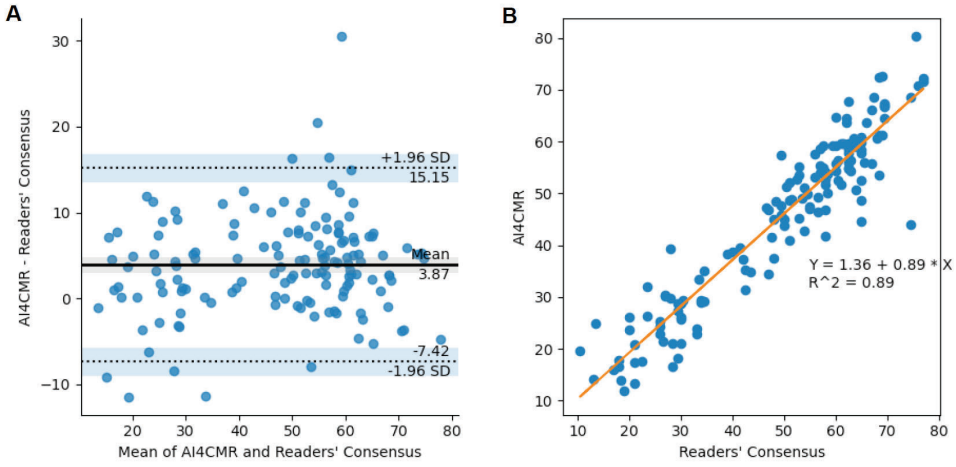
Left Ventricular ESV

	Cronbach's Alpha	Correlation Coef. (ρ)	Bias	ICC	95% Confidence Interval	
					Lower Bound	Upper Bound
AI4CMR vs consensus	0,992	0,975	-2.893	**0,991**	**0,99**	**0,99**



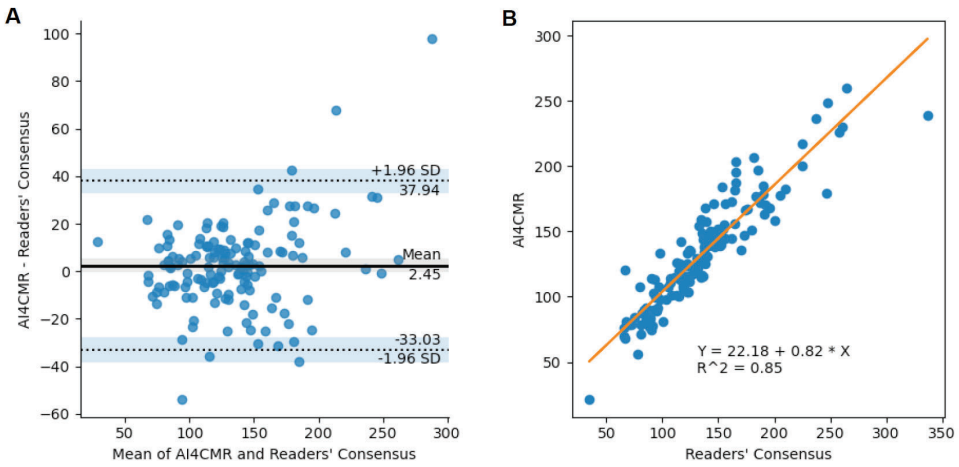
Left Ventricular Ejection Fraction

	Cronbach's Alpha	Correlation Coef. (ρ)	Bias	ICC	95% Confidence Interval	
					Lower Bound	Upper Bound
AI4CMR vs consensus	0,969	0,909	3,867	**0,956**	**0,87**	**0,98**



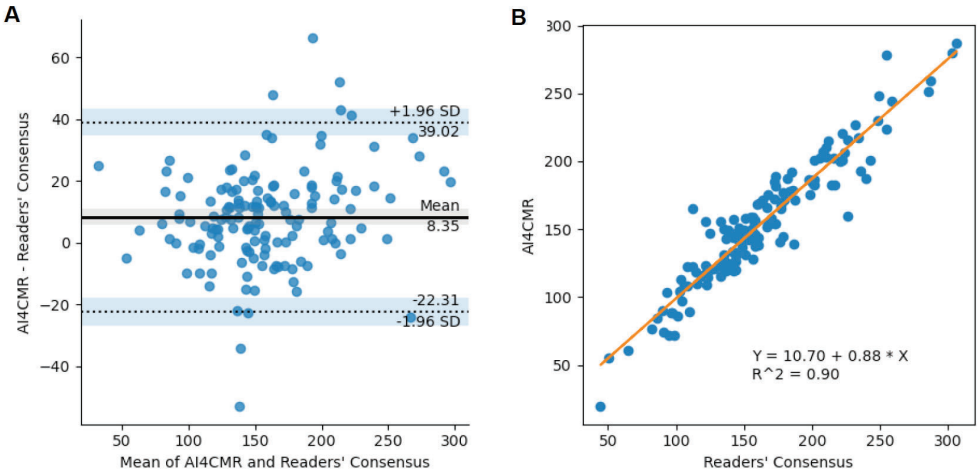
Left Ventricular Myocardial Mass

	Cronbach's Alpha	Correlation Coef. (ρ)	Bias	ICC	95% Confidence Interval	
					Lower Bound	Upper Bound
AI4CMR vs consensus	0,956	0,936	2,452	**0,955**	**0,94**	**0,97**



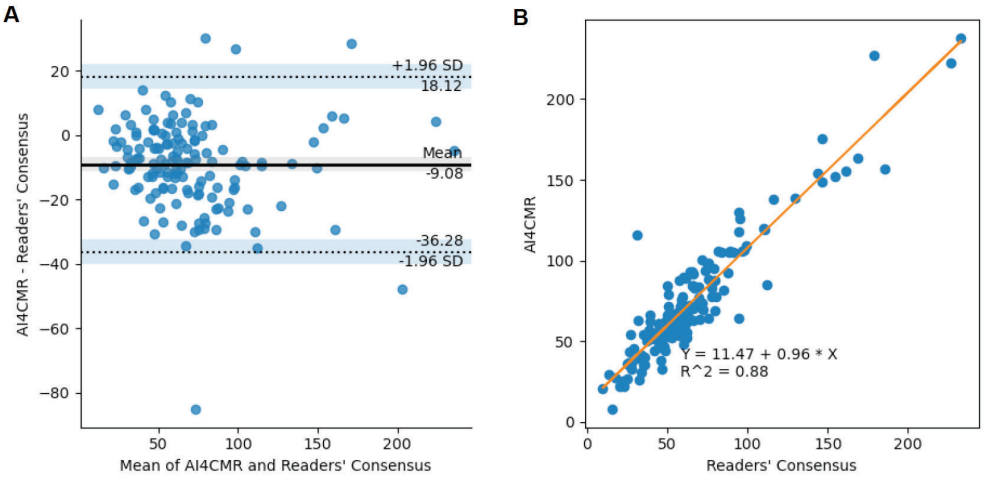
Right Ventricular EDV

	Cronbach's Alpha	Correlation Coef. (ρ)	Bias	ICC	95% Confidence Interval	
					Lower Bound	Upper Bound
AI4CMR vs consensus	0,972	0,924	8,355	**0,964**	**0,92**	**0,98**



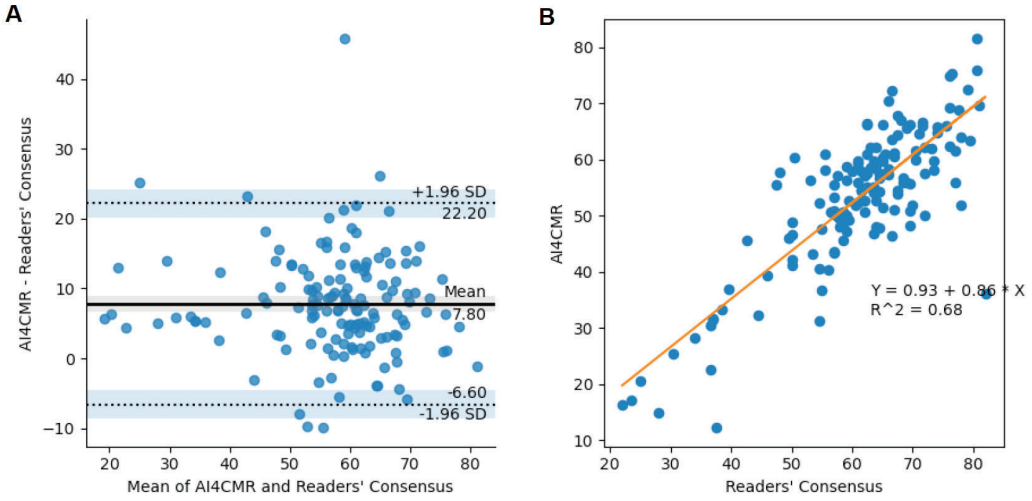
Right Ventricular ESV

	Cronbach's Alpha	Correlation Coef. (ρ)	Bias	ICC	95% Confidence Interval	
					Lower Bound	Upper Bound
AI4CMR vs consensus	0,967	0,888	-9,083	**0,953**	**0,87**	**0,98**



Right Ventricular Ejection Fraction

	Cronbach's Alpha	Correlation Coef. (ρ)	Bias	ICC	95% Confidence Interval	
					Lower Bound	Upper Bound
AI4CMR vs consensus	0,902	0,712	7,802	**0,814**	**0,15**	**0,93**



8. Conclusion

Based on the information submitted in this premarket notification, and based on the indications for use, technological characteristics and performance testing, the AI4CMR v1.0 raises no new questions of safety and effectiveness and is substantially equivalent to the predicate device in terms of safety and effectiveness.