July 24, 2024

Odin Medical Limited
Luke Sampson, COO
43-45 Foley Street
London, W1W 7TS
United Kingdom

Re: K240044
Trade/Device Name: CADDIE
Regulation Number: 21 CFR 876.1520
Regulation Name: Gastrointestinal Lesion Software Detection System
Regulatory Class: Class II
Product Code: QNP, SBX
Dated: June 24, 2024
Received: June 24, 2024

Dear Luke Sampson:

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 (the 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 available 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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,

Shanil P. Haugen -S

Shanil P. Haugen, Ph.D.
Assistant Director
DHT3A: Division of Renal, Gastrointestinal, Obesity and Transplant Devices
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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: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K240044

Device Name
CADDIE

Indications for Use *(Describe)*
The CADDIE computer-assisted detection device is intended to assist the gastroenterologist in detecting suspected colorectal polyps only. The gastroenterologist is responsible for reviewing CADDIE suspected polyp areas and confirming the presence or absence of a polyp based on their own medical judgment.

CADDIE is not intended to replace a full patient evaluation, nor is it intended to be relied upon to make a primary interpretation of endoscopic procedures, medical diagnosis, or recommendations of treatment/course of action for patients. The CADDIE computer-assisted detection device is limited for use with standard white-light endoscopy imaging only.

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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Date Prepared: 23-Jul-24

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Official Contact: Luke Sampson - COO

Submission Correspondent: Luke Sampson – COO

Proprietary or Trade Name: CADDIE

510(k) number: K240044

Common/Usual Name: Gastrointestinal Lesion Software Detection System

Classification CFR: 21 CFR 876.1520

Classification Code: QNP, SBX

Classification Name: Gastrointestinal Lesion Software Detection System

Class: Class II

Predicate Device: DEN200055 GI Genius - Cosmo Artificial Intelligence, AI LTD

Device Description:

CADDIE is cloud based artificial intelligence medical device software. CADDIE interfaces with the video feed generated by an endoscopic video processor during a colonoscopy procedure

The software is intended to be used by trained and qualified healthcare professionals as an accompaniment to video endoscopy for the purpose of drawing attention to regions with visual characteristics consistent with colonic mucosal lesions (such as polyps and adenomas).

CADDIE analyses the data from the endoscopic video processor in real-time and provides information to aid the endoscopist in detecting suspected colorectal polyps, if they are in the field of view of the endoscope.

The areas highlighted by CADDIE are not to be interpreted as definite polyps or adenomas. The responsibility to make a decision as to whether or not a highlighted region contains a polyp or is an adenoma lies with the user. The endoscopist is responsible for reviewing CADDIE suspected polyp areas and confirming the presence or absence of a polyp and its classification based on their own medical judgement.

Indications for Use:

The CADDIE computer-assisted detection device is intended to assist the gastroenterologist in detecting suspected colorectal polyps only. The gastroenterologist is responsible for reviewing CADDIE suspected polyp areas and confirming the presence or absence of a polyp based on their own medical judgment.

CADDIE is not intended to replace a full patient evaluation, nor is it intended to be relied upon to make a primary interpretation of endoscopic procedures, medical diagnosis, or recommendations of treatment/course of action for patients.

The CADDIE computer-assisted detection device is limited for use with standard white-light endoscopy imaging only.

Patient Population:

CADDIE is intended to be used on patients aged 45 and over referred for screening and surveillance endoscopic mucosal evaluations. This does not include pregnant women, for which no clinical evaluation has been carried out.

Environments of use:

Hospitals and clinics or in other secure endoscopy units where colonoscopies are performed.

Summary of Technological Characteristics:

At a high level we present the technological comparison of the subject device and the predicate in the **Table** below.

Summary of Technological Characteristics

Characteristics	**Subject Device: CADDIE**	**Predicate Device:** GI Genius **DEN200055**
Manufacturer	Odin Medical Ltd	Cosmo Artificial Intelligence – AI, Ltd
Regulation Number	21 CFR 876.1520	21 CFR 876.1520
Regulation Title	Gastrointestinal lesion software detection system	Gastrointestinal lesion software detection system
Classification	Class II	Class II
Classification Product Code	QNP, SBX	QNP
Intended Use - definition	A gastrointestinal lesion software detection system is a computer-assisted detection device used in conjunction with endoscopy for the detection of abnormal lesions in the gastrointestinal tract. This device with advanced software algorithms brings attention to images to aid in the detection of lesions. The device may contain hardware to support interfacing with an endoscope.	A gastrointestinal lesion software detection system is a computer-assisted detection device used in conjunction with endoscopy for the detection of abnormal lesions in the gastrointestinal tract. This device with advanced software algorithms brings attention to images to aid in the detection of lesions. The device may contain hardware to support interfacing with an endoscope.
Indications for Use	The CADDIE computer-assisted detection device is intended to assist the gastroenterologist in detecting suspected colorectal polyps only. The gastroenterologist is responsible for reviewing CADDIE suspected polyp areas and confirming the presence or absence of a polyp based on their own medical judgment. CADDIE is not intended to replace a full patient evaluation, nor is it intended to be relied upon to make a primary interpretation of endoscopic procedures, medical diagnosis, or recommendations of treatment/course of action for patients.	The GI Genius System is a computer-assisted reading tool designed to aid endoscopists in detecting colonic mucosal lesions (such as polyps and adenomas) in real time during standard white-light endoscopy examinations of patients undergoing screening and surveillance endoscopic mucosal evaluations. The GI Genius computer-assisted detection device is limited for use with standard white-light endoscopy imaging only. This device is not intended to replace clinical decision making.

Characteristics	**Subject Device: CADDIE**	**Predicate Device:** GI Genius **DEN200055**
	The CADDIE computer-assisted detection device is limited for use with standard white-light endoscopy imaging only.	
Patient Population	CADDIE is intended to be used on patients aged 45 and over referred for screening and surveillance endoscopic mucosal evaluations. This does not include pregnant women, for which no clinical evaluation has been carried out.	Adult patients undergoing screening and surveillance endoscopic mucosal evaluations.
Technological Characteristics	CADDIE is standalone software that is deployed on the cloud and accessed via a web browser. The device is designed to highlight portions of the colon where the device detects potential colorectal polyps. CADDIE requires a network connection.	The GI Genius system is composed of software and hardware designed to highlight portions of the colon where the device detects potential colorectal polyps.
Convenience Features	When the clinician confirms the cecum and photo documents the cecal landmarks in standard clinical workflow, Cecum AI is triggered, and the image is sent for analysis. If the cecal landmarks are confirmed in the image, by the AI, the user will be given a reminder to check the status of Polyp detection. If polyp detection is turned off, the cross icon will flash three times along with the cecum icon. If detection is on, the cecum icon will flash three times next to the tick icon. This is a convenience feature that provides a check to the user that the CADDIE polyp detection function is on and in use.	Not Available
Software Algorithm	CADDIE utilizes an artificial intelligence-based algorithm to perform the polyp detection function.	The GI Genius system utilizes an artificial intelligence-based algorithm to perform the polyp detection function.
Device Output	During a colonoscopy, CADDIE generates markers, which look like green squares and are accompanied by a short, low-volume sound, and superimposes them on the video from the endoscope camera when it identifies a potential	During a colonoscopy, the GI Genius system generates markers, which look like green squares and are accompanied by a short, low-volume sound, and superimposes them on the video from the endoscope camera when it identifies a potential

Characteristics	**Subject Device: CADDIE**	**Predicate Device:** GI Genius **DEN200055**
	lesion.	lesion.

Discussion of Differences

CADDIE and the predicate device have the same intended use and similar indications for use, patient populations, device outputs and software algorithms.

Both the subject device CADDIE and the predicate GI Genius are intended for use to aid physicians in detecting suspected lesions in the colorectal area. The devices are both intended to be used by trained healthcare providers (endoscopists and gastroenterologists) during standard white-light endoscopy. Neither device is intended to replace clinical decision making. The minor differences in the wording of the indications for use are not critical since these do not impact the purpose of the devices which for both devices is to assist in the detection of colorectal lesions in real time during standard white-light endoscopy examinations of adult patients undergoing screening and surveillance endoscopic mucosal evaluations. The devices have the same intended use.

Both devices take a colonoscopy video as an input from an endoscopy image processor and provide an output of a green bounding box that highlights the detected polyps. Both devices are used in real-time to aid the clinician in detecting abnormal lesions live during a colonoscopy.

The patient population is restricted for the subject device to patients aged 45 and over referred for screening and surveillance endoscopic mucosal evaluations. This aligns with the U.S. Multisociety Task Force (MSTF) on Colorectal Cancer, which represents the American College of Gastroenterology, the American Gastroenterological Association, and the American Society for Gastrointestinal Endoscopy recommendation that colonoscopy for colorectal cancer screening in average-risk patients starts at 45 and continuing through to age 75.

A technological difference between the predicate and the subject device (CADDIE) is that the subject device does not utilize bespoke hardware, as it is accessed using a networked connection on an off-the-shelf computer, operating system and browser. The submission is for network accessed cloud-based software. This difference, however, does not raise any additional questions of safety and effectiveness as demonstrated by the clinical and non-clinical performance testing based on the intended purpose of the device.

There is a minor difference between the two devices. Cecum AI, in the subject device, serves as a feature to remind the clinician to check the on/off status of the CADe polyp detection. It is the responsibility of the clinician to confirm that the cecum has been reached before photo documentation is taken that may trigger the reminder. It is the responsibility of the user to turn the CADe functionality on and off, this is identical to the predicate device. This difference does not raise different questions of safety and effectiveness. This function does not introduce any primary functionality that would be deemed inconsistent with regulatory standards, specifically those outlined in 21 CFR 876.1520.

The technological and other minor differences discussed above between the subject device and predicate device do not raise any new questions of safety and effectiveness as demonstrated by the non-clinical and clinical performance evaluation results.

Performance Testing

Special Control Technical Testing

Pixel-level comparison of degradation of image quality due to the device was below the predefined threshold in all test samples. The average per-pixel difference was found to be 0.94 and 0.87 with a CV-1500 and a CV-190 image processor respectively.

Note: The minor variation of the results between the systems is a statistical effect due to the variation of the images acquired in the tests.

Assessment of video delay due to marker annotation - The average video delay due to marker annotation was found to be 32.59ms and 33.61ms with a CV-1500 and a CV-190 image processor respectively.

Assessment of real-time endoscopic video delay due to the device - The average video delay was found to be 32.50ms and 32.50ms with a CV-1500 and a CV-190 image processor respectively.

Human Factors and Usability Testing

The CADDIE device has been found to be safe and effective for the intended users, uses and use environments based on the Human Factors Engineering/Usability Engineering activities performed and in accordance with the Human Factors Engineering and Usability Engineering Plan.

The usability assessment demonstrates that the intended users can safely and correctly use the device, in accordance with 21 CFR 876.1520 and special control 3.

CADDIE Data Description and Non-Clinical testing

Polyp Detection Development Datasets

The development data it is separate from the bench-testing data. It included a total of 1711 polyps, from 906 patients distributed across training, tuning and testing. In total 318,603 frames were used in the development datasets (162,207 polyp frames and 156,396 non-polyp frames). 1296 polyps from 714 patients had histology and additional meta data that may include size, location and morphology. The polyp histology was diverse, containing adenomas, hyperplastic polyps, and SSLs. Polyp sizes ranged from diminutive to large. Morphologically, the dataset included polypoid and non-polypoid

polyps. Polyp locations were well-distributed across proximal and distal regions. Polyp morphology and location was not always collected/made available by the hospitals due to limitations in local data acquisition/anonymization/sharing processes. The information was available for the majority of the polyps with histopathology. 415 polyps confirmed through resection or photo-documentation, but not histopathology, were included in the development data set. Furthermore, these polyps were optically confirmed by additional endoscopists in the truthing process.

The dataset included a variety of video processors, including the Evis Exera II (CV-180), Evis Exera III (CV-190), Evis Lucera Elite (CV-290), Evis X1 (CV-1500) and endoscopes including Olympus 180, 190, 260, 290. The dataset included a diverse patient population distribution acquired in five European countries, as shown in the table below. Data collected in those sites represented a balanced distribution of sex, wide age range, and indications for colonoscopy, including surveillance, screening, or diagnostic. Ethnic and racial diversity was well-represented across different sites and reflects the target population.

Demographics of Patients Undergoing Colonoscopies in Development Dataset Hospitals.

Data origin	United Kingdom (%)	48.33%
	Czech Republic (%)	44.77%
	Norway (%)	3.74%
	Spain (%)	1.99%
	Germany (%)	1.17%
Sex	Male (%)	54.96%
	Female (%)	45.04%
Age	Mean (years)	61.5
	Standard deviation (years)	14.1
Reason for colonoscopy	surveillance	50.25%
	diagnostic	35.82%
	therapeutic	2.71%
	symptomatic	1.17%
	screening	10.06%
Ethnicity	Other / Hispanic / Latino	8.80%
	Not Hispanic / Latino	91.20%
Race	American Indian or Alaska Native	0.01%
	Asian	6.76%
	Black or African American	3.15%
	Native Hawaiian or Other Pacific Islander	1.91%
	White	85.21%
	Other	2.96%

Data limitations: As described above, the development dataset contains instances where the accompanying lesion information was not available e.g. histology, location, etc. This was due to local hospital constraints in data acquisition/anonymization processes, or limitations in local ethics/data-sharing procedures.

Polyp Detection Standalone Bench-testing Dataset

Standalone performance testing was performed to assess the ability of CADDIE to discriminate between normal mucosa and polyp tissue on video frames from a standard colonoscopy procedure. A set of recorded colonoscopy videos was analyzed by CADDIE and the results were compared to the historical control (known polyp status per frame).

	Test Set (No. of subjects=389*)	
	Mean (years)	**SD (years)**
Age	58.83	8.67
Sex	**Count**	**%**
Male	193	49.61
Female	196	50.39
Indication for Colonoscopy		
Surveillance	109	28.02
Screening	280	71.98
Race/Ethnicity		
African American	110	28.28
American Indian	1	0.26
Asian	12	3.08
Caucasian	148	38.05
Hispanic	65	16.71
Other	2	0.51
Unknown	51	13.11

The following table presents the standalone bench-testing dataset for polyp detection patients' demographic distribution, including the reason for colonoscopy.

	Polyp count
Histopathology	
Adenoma	382
Non-Adenoma	368
Polyp Location	
Cecum	79
Ascending Colon	101
Hepatic Flexure	25
Transverse Colon	132
Splenic Flexure	5
Descending Colon	79
Sigmoid Colon	184
Rectum	145
Polyp Morphology	
Polypoid	503
Non-Polypoid	237
Unknown	10
Polyp Size	
Diminutive	567
Small	136
Large	47
Video Processor	
CV-180	48
CV-190	437
CV-1500	265
Endoscopic family	
CF-HQ190	184
CF-H190	52
CF-HQ1100	27
CF-HQ190 or PCF-H190	485

Annotation was performed on a per-frame basis, where a team of trained clinical annotators labelled polyp structures with a bounding box, followed by an additional layer of review by a separate team of experts (with over 2000 endoscopic procedures experience). Each polyp was histologically confirmed. These polyp annotations were used as ground truth reference standards. The table above shows the distribution of polyp characteristics.

Polyp Detection Summary of Endpoints, Success Criteria, and Results.

Name	**Description**	**Success criteria (if applicable)**	**Results [95% CI]**
Object-level true positive rate (TPR)*	The proportion of polyps (%) detected by the device (> 0.5 seconds & IoU > 20%) and confirmed to be polyps using pathology findings.	Object Level TPR > 80% (to show a lower miss rate than in clinical practice of 25%[1])	98.27% [97.33, 99.20]
Frame-Level FPR*	The proportion of frames (%) in which CADDIE detects a box (> 0.5 seconds) that is not a histopathologically confirmed polyp.	Frame Level FPR < 5 % (to provide a good user experience, avoid distractions, and reduce false predictions)	1.54 [1.31, 1.76]

Object-level false positive rate (FPR)**	The average of suspected regions per minute that CADDIE finds per procedure (> 0.5 seconds) that are not histopathology-confirmed polyps.	Not applicable	0.89 [0.79, 1.00]
Frame-Level TPR**	The proportion of frames (%) with confirmed polyps in which CADDIE detects the polyp (> 0.5 seconds & IoU > 20%).	Not applicable	54.92 [53.02, 56.81]

*primary endpoints; **secondary endpoints.

Polyp Detection Non-Clinical Performance Testing Results

Non-clinical performance testing was performed on the standalone bench-testing dataset, which is separate to the development datasets.

Persistence is defined as the detection's duration on the same target. The following table shows the variation of the endpoint metrics when only considering predictions with IoU overlap criteria applied with respect to certain persistence. The metrics in the following table correspond to the polyp detection endpoints and are summarized as follows:

- Frame-level TPR: proportion of frames with polyps detected by the device
- Object-level TPR: proportion of polyps detected by the device
- Frame-level FPR: proportion of non-polyp frames where the device detects a polyp
- Object-level FPR: number of false alarms per minute per patient.

Persistence	Frame-Level TPR	Object-Level TPR	Frame-Level FPR	Object-Level FPR
> 0	59.69%	99.60%	2.88%	4.21
> 100 ms	59.54%	99.33%	2.88%	4.20
> 200 ms	58.70%	98.93%	2.53%	2.94
> 300 ms	57.37%	98.53%	2.09%	1.77
> 400 ms	56.13%	98.53%	1.78%	1.22
> 500 ms	**54.92%**	**98.27%**	**1.54%**	**0.89**
> 1000 ms	49.09%	94.13%	0.84%	0.29
> 1500 ms	43.98%	88.80%	0.53%	0.14
> 2000 ms	39.77%	85.05%	0.35%	0.07

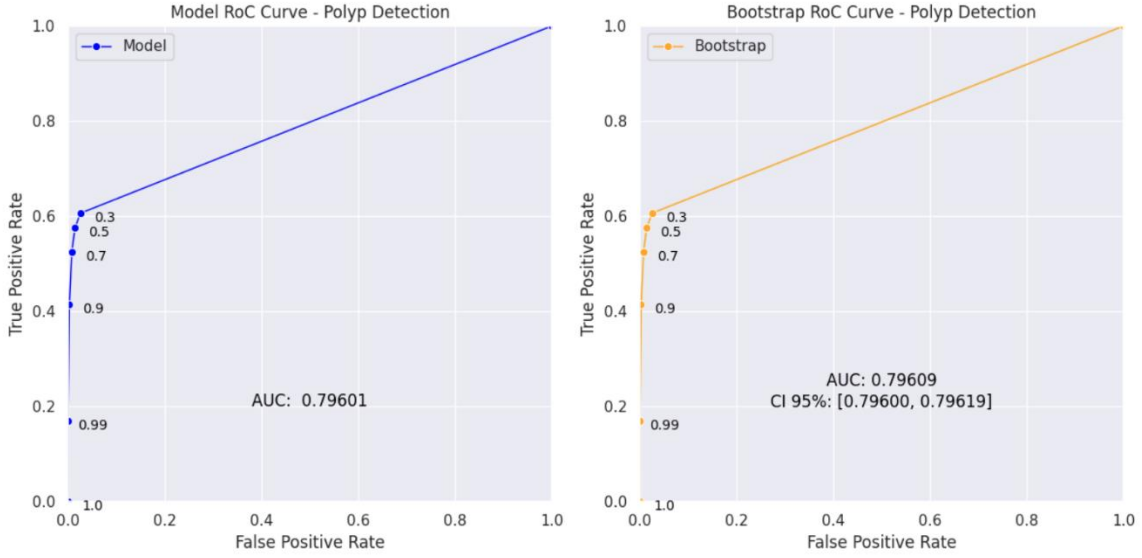
The table below shows a subgroup analysis. These results are computed at a persistence > 500 ms and IoU > 20% (when applicable). The metrics in the following table correspond to the polyp detection endpoints and are summarized as follows:

- Frame-level TPR: proportion of frames with polyps detected by the device
- Object-level TPR: proportion of polyps detected by the device
- Frame-level FPR: proportion of non-polyp frames where the device detects a polyp

	Frame-Level TPR [95% CI]	Object-level TPR [95% CI]	Detected polyps	Procedures
Overall	54.92% [53.02, 56.81]	98.27% [97.33, 99.20]	737/750	311
Histology				
Adenoma	59.96% [57.43, 62.49]	98.95% [97.93, 99.97]	378/382	199
Non-Adenoma	49.68% [46.94, 52.42]	97.55% [95.98, 99.13]	359/368	201

Lesion Size				
Diminutive (0-5mm)	52.77% [50.58, 54.97]	98.24% [97.15, 99.32]	557/567	275
Small (6-10mm)	60.85% [56.55, 65.15]	97.79% [95.33,100.0]	133/136	95
Large (> 10mm)	63.58% [56.80, 70.36]	100.0% [100.0, 100.0]	47/47	38
Video Processors				
CV-190	55.13% [52.62, 57.64]	99.08% [98.19, 99.98]	433/437	167
CV-1500	52.76% [49.60, 55.92]	96.98% [94.92, 99.04]	257/265	117
Endoscope Families				
CF-HQ190	52.85% [49.14, 56.56]	96.20% [93.43, 98.96]	177/184	85
CF-H190	51.88% [44.73, 59.03]	98.08% [94.34, 100.0]	51/52	21
CF-HQ1100D	54.09% [43.17, 65.00]	100.00% [100.0, 100.0]	27/27	9
CF-HQ-190 or PCF-H190	56.09% [53.73, 58.46]	98.97% [98.07, 99.87]	480/485	194
	Frame-Level FPR [95% CI]			**Procedures**
Overall	1.54% [1.31, 1.76]	-	-	85

The algorithm Receiver Operating Characteristic (ROC) curve and area Under the Curve (AUC) are shown in the figure below. The ROC curves illustrate the False Positive Rate versus the True Positive Rate at the frame level. The left subplot displays the non-parametric frame-level ROC curve and the corresponding estimated area under the ROC curve (AUC), derived from model performance. The right subplot presents the non-parametric frame-level ROC curve, including the estimated AUC and 95% confidence intervals, derived from patient-level bootstrapping.



Cecum AI Development Datasets

The dataset used to develop the Cecum AI algorithm consisted of a diverse sample of patients and images. It included data from 1467 patients and 17,844 images, spanning training, tuning, and testing phases. It was composed of informative static photo-

documentation images, as well as images extracted from videos of cecal landmarks including appendiceal orifice (AO), ileocecal valve (ICV).

Data limitations: demographic information was not available. The dataset contains instances where the video processor is unknown. Missing information is due to limitations in data acquisition/anonymization or local hospital collection/sharing protocols.

Cecum AI Summary of endpoints, success criteria, and results.

Name	**Description**	**Success criteria (if applicable)**	**Results [95% CI]**
Frame-Level true positive rate (TPR)	The proportion (%) of all the frames annotated with cecum which the Cecum AI identifies correctly.	Frame-level TPR > 80%	94.05% [91.58, 96.52]
Frame-level false positive rate (FPR)*	The proportion (%) of all the frames annotated without cecal landmarks which the Cecum AI incorrectly identifies the cecum.	Frame-level FPR < 20%	12.08% [10.14, 14.02]

Cecum AI Standalone Bench-testing Dataset

Standalone performance testing was performed to assess the ability of the Cecum AI to discriminate between normal mucosa and cecal landmarks, such as the appendiceal orifice or the ileocecal valve, on photo-documented frames from a standard colonoscopy procedure. A set of recorded colonoscopy frames were analyzed by the Cecum AI and the results were compared to the historical control (known cecal structure status per frame).

Annotation was performed on a per-frame basis, where a team of trained clinical annotators labelled cecal structures with a bounding box. These annotations were used as ground truth reference standards.

The table below shows the distribution of cecal structure characteristics.

	Positive Frames	Appendiceal Orifice (AO)	Ileocecal Valve (ICV)	Negative Frames	**Total Frames**
Static Dataset	397	193	228	1041	1438
Video Dataset	2436	1541	895	1218	3654
Total	2833	1734	1123	2259	5092

Cecum AI Non-Clinical Performance Testing Results

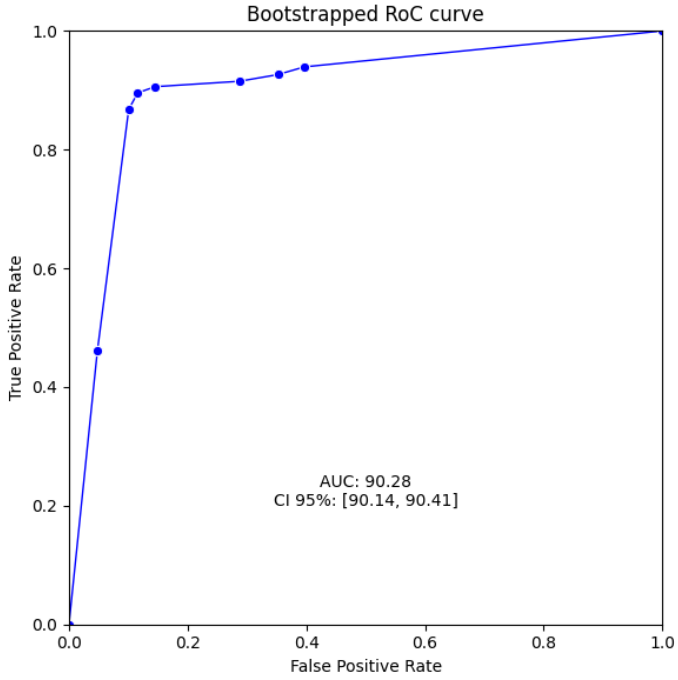
Non-clinical performance testing was performed on the standalone bench-testing dataset, which is separate to the development datasets. The metrics in the following table correspond to the Cecum AI endpoints and are grouped by type of data and cecal structure, summarized as follows:

- Frame-level accuracy: proportion of frames correctly classified by the device
- Frame-level TPR: proportion of frames with cecum detected by the device

- Frame-level FPR: proportion of non-cecum frames where the device detects a cecal landmark

	Frame-level accuracy	**Frame-level TPR**	**Frame-level FPR**	**Frames**
Overall	90.27% [88.73, 91.80]	94.05% [91.58, 96.52]	12.08% [10.14, 14.02]	5092
Structure				
Appendiceal Orifice (AO)	93.14% [91.81, 94.47]	92.68% [88.71, 96.65]	6.94% [5.53, 8.35]	5092
Ileocecal Valve (ICV)	95.21% [94.10, 96.32]	92.28% [88.67, 95.89]	4.71% [3.53, 5.89]	5092
Type of data				
Videos	88.34% [80.15, 96.53]	84.06% [65.73, 100]	10.49% [4.65, 16.33]	3654
Static Frames	90.28% [88.73, 91.82]	94.29% [91.80, 96.77]	12.09% [10.14, 14.04]	1438

The algorithm Receiver Operating Characteristic (ROC) curve and area Under the Curve (AUC) are shown in the figure below for the Cecum AI considering Appendiceal Orifice and Ileocecal Valve as the positive class. The ROC curves illustrate the False Positive Rate versus the True Positive Rate at the frame level. The plot presents the non-parametric frame-level ROC curve, along with the estimated AUC and 95% confidence intervals, derived from patient-level bootstrapping.



Summary of Clinical Performance

The efficacy and safety of CADDIE was assessed in a prospective, multi-center, MRMC, randomized controlled, parallel group trial, across 8 medical centers in Europe. Eligible patients were randomized (1:1) to either a colonoscopy with the aid of CADDIE (CADe) or a standard high-definition white light colonoscopy (SoC).

Inclusion and Exclusion Criteria:
Patients were enrolled who were at least 40 years of age and were scheduled to undergo a screening or surveillance colonoscopy where the last colonoscopy was performed ≥3 years prior. Patients were excluded if they were scheduled for an emergency, inpatient, therapeutic, or surveillance (if previous was <3 years prior) colonoscopy, or if they had inflammatory bowel disease (IBD), current or previous colorectal cancer (CRC), previous colonic resection, polyposis syndromes, contraindication for biopsy or polypectomy, or other high-risk indications.

Endoscopists:
The primary analysis included data from endoscopists who had performed ≥ 1000 colonoscopy procedures with an ADR of ≥ 25%.

A total of 841 patients were included in the modified Intention to Treat (mITT) population for primary analysis, including 417 who received a colonoscopy with the CADDIE and 424 who received a standard colonoscopy. The evaluation of our primary and secondary endpoints for the mITT population is summarized below.

Patient Demographics								
Variable	**Category**	**All Patients [N=841]**		**SoC [N=424]**		**CADe [N=417]**		**P**
		N	**Summary**	**N**	**Summary**	**N**	**Summary**	
Colonoscopy Indication	Screening Surveillance	841	653 (77.7%) 188 (22.3%)	424	329 (77.6%) 95 (22.4%)	417	324 (77.7%) 93 (22.3%)	0.97
Age	-	841	58.5 ± 9.3	424	58.2 ± 9.5	417	58.7 ± 9.0	0.43
Gender	Female Male Other	841	412 (49.0%) 428 (50.9%) 1 (0.1%)	424	218 (51.4%) 205 (48.4%) 1 (0.2%)	417	194 (46.5%) 223 (53.5%) 0 (0.0%)	0.21
Ethnicity	Not Latino/Hispanic Latino/Hispanic	827	686 (82.9%) 141 (17.1%)	415	349 (84.1%) 66 (15.9%)	412	337 (81.8%) 75 (18.2%)	0.38
Race	American Indian African American White Other	840	0 (0.0%) 1 (0.1%) 837 (99.6%) 2 (0.2%)	424	0 (0.0%) 1 (0.2%) 423 (99.8%) 0 (0.0%)	416	0 (0.0%) 0 (0.0%) 414 (99.5%) 2 (0.5%)	0.25

Summary statistics are mean ± standard deviation, or number (percentage)
Continuous variables were compared between groups using the unpaired t-test, if normally distributed, or the Mann-Whitney test otherwise. Ordinal outcomes were analysed using the Mann-Whitney test, and categorical variables using the Chi-square test.

Primary Endpoints:

The co-primary endpoints of the study included a performance endpoint (adenomas per colonoscopy, APC) and a safety endpoint (positive percent agreement, PPA).

- APC: The total number of histologically confirmed adenomas and adenocarcinomas divided by the total number of colonoscopies.
- PPA: Percentage of histologically confirmed adenomas, sessile serrated lesions, and large (> 10 mm) hyperplastic polyps of the proximal colon (caecum, ascending colon, hepatic flexure, and transverse colon) out of the total number of resections.

Primary Endpoints					
Endpoint	**Study Arm**	**N patients**	**Mean ± SD**	**Ratio (95% CI)**	**P-value**
APC	SoC CADe	424 417	0.62 ± 1.19 0.82 ± 1.40	1 1.33 (1.06, 1.67)	**0.01**
Endpoint	**Study Arm**	**N polyps**	**n positive (%)**	**% difference (1 sided 97.5% CI)**	**P-value**
PPA	SoC CADe	517 700	276 (53.4%) 377 (53.9%)	0 0.5% (-5.0%, ∞)	-

APC Stratified by Lesion Size – Exploratory Endpoints				
Lesion size	**Study Arm**	**Mean ± SD**	**Difference (95% CI)**	**P-value**
≤ 5 mm	SoC CADe	0.44 ± 0.83 0.57 ± 1.07	1 1.29 (1.01, 1.64)	**0.04**
6 – 9 mm	SoC CADe	0.13 ± 0.49 0.17 ± 0.48	1 1.28 (0.84, 1.94)	0.25
≥ 10 mm	SoC CADe	0.04 ± 0.23 0.09 ± 0.36	1 1.93 (1.03, 3.62)	**0.04**

Secondary Endpoints:

The secondary endpoints included the following:

- Adenoma Detection Rate (ADR). Proportion of examinations with at least one histologically confirmed adenoma detected.
- Sessile serrated adenomas per colonoscopy (SSAPC). Total number of histologically confirmed sessile serrated adenomas, traditional serrated adenomas, or serrated lesions with cytological dysplasia, excluding hyperplastic polyps.
- Sessile serrated adenomas per colonoscopy (SSAPC*). Total number of histologically confirmed sessile serrated adenomas or serrated lesions with cytological dysplasia.
- Neoplastic Polyps Per Colonoscopy (NPPC). Total number of histologically confirmed adenomas, adenocarcinomas, sessile serrated adenomas, and traditional serrated adenomas divided by the total number of colonoscopies.
- Polyps Per Colonoscopy (PPC). The total number of histologically confirmed polyps detected (adenomas, adenocarcinomas, sessile serrated, traditional serrated adenomas, and hyperplastic), divided by the total number of colonoscopies.
- Colonoscope withdrawal time of negative procedures only. The time it takes to withdraw the colonoscope from the furthest point (TI or caecum) for colonoscopies that did not require any biopsies.

- Colonoscope withdrawal time. The time it takes to withdraw the colonoscope from the furthest point (TI or caecum) including time for polypectomy or other interventions.
- Total procedure time. Entire duration of the procedure.

Secondary Endpoints					
Outcome	**Study Arm**	**N patients**	**Summary (*)**	**Difference (#) (95% CI)**	**P-value**
ADR	SoC CADe	424 417	152 (35.9%) 179 (42.9%)	0 7.1% (0.5%, 13.7%)	**0.04**
SSAPC	SoC CADe	424 417	0.04 ± 0.21 0.09 ± 0.46	1 2.15 (1.07, 4.32)	**0.03**
SSAPC*	SoC CADe	424 417	0.03 ± 0.16 0.08 ± 0.45	1 3.30 (1.41, 7.571	**0.006**
NPPC	SoC CADe	424 417	0.66 ± 1.20 0.91 ± 1.48	1 1.39 (1.12, 1.73)	**0.002**
PPC	SoC CADe	424 417	1.06 ± 1.53 1.41 ± 1.85	1 1.35 (1.13, 1.61)	**0.001**
Withdrawal time (Negative Procedures)	SoC CADe	178 138	8 [7, 10] 8 [7, 11]	1 1.02 (0.96, 1.09)	0.44
Withdrawal time (All procedures)	SoC CADe	424 417	10 [8, 13] 11 [8, 15]	1 1.10 (1.05, 1.15)	**<0.001**
Procedure time (All procedures)	SoC CADe	424 417	18 [15, 24] 19 [16, 26]	1 1.07 (1.02, 1.12)	**0.003**

(*) Summary statistics are mean ± standard deviation, median [inter-quartile range], or number (percentage)
(#) Group differences are ratio of values in CADe relative to SoC (continuous outcomes), or difference in percentages for adenoma detection rate.

All Polyps Stratified by Lesion Size and Histopathology (#) – Exploratory Endpoints					
Characteristic	**Category**	**Study Arm**	**Mean ± SD**	**Difference (95% CI)**	**P-value**
Lesion size (PPC)	≤ 5 mm	SoC CADe	0.76 ± 1.13 1.00 ± 1.46	1 1.33 (1.10, 1.61)	**0.003**
	6 – 9 mm	SoC CADe	0.25 ± 0.62 0.28 ± 0.71	1 1.16 (0.85, 1.60)	0.35
	≥ 10 mm	SoC CADe	0.05 ± 0.24 0.12 ± 0.44	1 2.36 (1.33, 4.17)	**0.003**
Histology (*)	Adenocarcinoma	SoC CADe	0.00 ± 0.00 0.007 ± 0.08	-	-
	Adenoma	SoC CADe	0.62 ± 1.19 0.82 ± 1.40	1 1.32 (1.05, 1.66)	**0.02**
	SSA	SoC CADe	0.03 ± 0.16 0.08 ± 0.45	1 3.30 (1.41, 7.57)	**0.006**
	TSA	SoC CADe	0.02 ± 0.14 0.01 ± 0.12	1 0.53 (0.11, 2.44)	0.41

	Hyperplastic	SoC CADe	0.40 ± 0.80 0.50 ± 1.01	1 1.24 (0.95, 1.63)	0.12
	Inflammatory	SoC CADe	0.005 ± 0.07 0.010 ± 0.10	-	-
	Colonic mucosa	SoC CADe	0.13 ± 0.45 0.19 ± 0.50	1 1.43 (0.96, 2.13)	0.08

(*) Histopathology subgroups do not include polyps which were lost/unrecovered, non-diagnostic material, or samples described as 'other'. There were too few adenocarcinomas and inflammatory polyps to perform a statistical analysis.
(#) Lesion size endpoints include all polyps as per the PPC definition, whereas histology endpoints also include inflammatory polyps and colonic mucosa.
Group differences are ratio of values in CADe relative to SoC. For all comparisons, there were 424 patients in the SoC arm and 417 in the CADe arm.

Efficacy
CADDIE had significant superiority over standard colonoscopy in the detection of adenomas, with a significant increase in APC of 33%. Moreover, the CADDIE device significantly increased the detection of both diminutive (≤5 mm) and large (≥10 mm) sized adenomas/adenocarcinomas, 29% and 93% more adenomas detected respectively.

Safety
The PPA for CADDIE was non-inferior to SoC, as the lower bound of the confidence interval for the difference between groups was above the prespecified -15% margin. This suggests that despite an increase in the number of polyps resected, there was no increase in unnecessary biopsies/extractions using CADDIE. In support of this, while CADDIE resulted in resection of more adenomas and sessile serrated adenomas (clinically relevant biopsies), there was no significant increase in resections of non-adenomatous polyps or colonic mucosa (unnecessary biopsies). There were also no adverse events during the study that related to the use of CADDIE.

Overall, the clinical study demonstrated that the performance of CADDIE achieved benchmark expectations and a safety and effectiveness profile comparable to the predicate device. The results of each trial demonstrated the superiority of the CADe systems in the detection of adenomas/adenocarcinomas and non-inferiority in the PPA.

Substantial Equivalence Conclusion

CADDIE has similar indications for use, technological characteristics, and principles of operation as the predicate GI Genius. There are minor technological differences that are addressed using performance testing, showing that there are no new issues with safety or effectiveness when used as labelled. Minor technological differences between the CADDIE system and the predicate device do not raise different issues of safety or effectiveness. The performance data demonstrates that CADDIE is as safe and effective as the predicate device. As a result, the CADDIE device can be considered substantially equivalent.