July 25, 2023

Magentiq Eye LTD
% John Smith
Partner
Hogan Lovells US LLP
Columbia Square, 555 Thirteenth Street, NW
Washington, District of Columbia 20004

Re: K223473
Trade/Device Name: ME-APDS™; MAGENTIQ-COLO™
Regulation Number: 21 CFR 876.1520
Regulation Name: Gastrointestinal Lesion Software Detection System
Regulatory Class: Class II
Product Code: QNP
Dated: June 22, 2023
Received: June 22, 2023

Dear John Smith:

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,

Shanil P. Haugen -S

Shanil P. Haugen, Ph.D.
Assistant Director
DHT3A: Division of Renal, Gastrointestinal, Obesity and Transplant Devices
OHT3: Office of GastroRenal, ObGyn, General Hospital and Urology Devices
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)*

K223473

Device Name

ME-APDS™; MAGENTIQ-COLO™

Indications for Use *(Describe)*

The ME-APDS (Magentiq Eye's Automatic Polyp Detection System) is intended to be used by endoscopists as an adjunct to the common video colonoscopy procedure (screening and surveillance), aiming to assist the endoscopist in identifying lesions during colonoscopy procedure by highlighting regions with visual characteristics consistent with different types of mucosal abnormalities that appear in the colonoscopy video during the procedure. Highlighted regions can be independently assessed by the endoscopist and appropriate action taken according to standard clinical practice.

The ME-APDS is trained to process video images which may contain regions consistent with polyps.

The ME-APDS is limited for use with standard white-light endoscopy imaging only.

The ME-APDS is intended to be used as an adjunct to endoscopy procedures and is not intended to replace histopathological sampling as means of diagnosis.

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

510(k) SUMMARY

Magentiq Eye's ME-APDS

Submitter:

Magentiq Eye Ltd.
6 Ben-Gurion Blvd.,
Haifa, 3541416,
Israel

Phone: +972 (77) 2018838

Contact Person: Dr. Dror Zur

Date Prepared: July 23, 2023

Name of Device: Magentiq Eye's Automatic Polyp Detection System (ME-APDS™)

Common or Usual Name: Computer aided detection software for colorectal polyps

Classification Name: Gastrointestinal Lesion Software Detection System

Regulatory Class: II

Product Code: QNP

Predicate Device: Cosmo Artificial Intelligence - AI, LTD's GI Genius (K211951)

Device Description:

The ME-APDS (Magentiq Eye's Automatic Polyp Detection System) is intended to be used as an adjunct to the common video colonoscopy procedure. The system application aims to assist the endoscopist in identifying lesions, such as polyps, during the colonoscopy procedures in real time. The device is not intended to be used for diagnosis or characterization of lesions, and does not replace clinical decision making.

The system acquires the digital video output signal from the local endoscopy camera and processes the video frames. It runs deep machine learning and additional supporting algorithms in real time on the video frames in order to detect and identify regions having characteristics consistent with different types of mucosal abnormalities such as polyps. The output video with the detected lesions is presented on a separate touchscreen, supplied as part of the ME-APDS, highlighting the suspicious areas on the original video. The output of the system can also be presented on additional monitors in the procedure room using the 1x4 HDMI Splitter supplied with the system. The user can also take snapshots of the videos, with and without the highlighting of the suspicious areas, record videos and view in full screen mode.

Intended Use / Indications for Use:

The ME-APDS (Magentiq Eye's Automatic Polyp Detection System) is intended to be used by endoscopists as an adjunct to the common video colonoscopy procedure (screening and surveillance), aiming to assist the endoscopist in identifying lesions during colonoscopy procedure by highlighting regions with visual characteristics consistent with different types of mucosal abnormalities that appear

in the colonoscopy video during the procedure. Highlighted regions can be independently assessed by the endoscopist and appropriate action taken according to standard clinical practice.

The ME-APDS is trained to process video images which may contain regions consistent with polyps.

The ME-APDS is limited for use with standard white-light endoscopy imaging only.

The ME-APDS is intended to be used as an adjunct to endoscopy procedures and is not intended to replace histopathological sampling as means of diagnosis.

Summary of Technological Characteristics:

Computer-Aided Polyp Detection (CADe) engine is the technological principle for both the subject and predicate devices. The major roles of CADe engine during colonoscopy is to process a video frame and to indicate the presence and location of detected lesions (such as polyps) in real time during colonoscopy procedure in order to improve mucosal lesion detection rates, thus improving the performance of the endoscopist.

At a high level, the subject and predicate devices are based on the following same technological elements:

- Both systems have similar intended use, intended user and patient population.
- Both systems' computing devices retrieve the video stream from the Endoscope and run a deep machine learning algorithms from the type of Deep Neural Networks (DNN) technology in real time. It then feeds a video output with the detected lesions (such as polyps) in an overlay highlighting the suspicious areas on the original video.
- Both systems do not make any elaboration or alteration of the colonoscopy video streaming.
- Both systems are suitable for use in white-light endoscopic mode of operations.

The following technological differences exist between the subject and predicate device:

- The ME-APDS is comprises a cart, monitor, a computing device, transformer and 1x4 HDMI Splitter. The ME-APDS shall be positioned adjacent to the colonoscopy cart, connected to the electricity and to the video output of coloscopy device.
  The GI Genius is comprised from a computing module only that is positioned on the coloscopy cart and connected to the video output of coloscopy device and to the coloscopy device display monitor.
- The ME-APDS uses dual monitor display setup and is supplied together with a 1x4 HDMI Splitter to allow connecting the system's output to additional monitors in the procedure room. The predicate device uses a single monitor display setup and is connected directly to the coloscopy device display monitor.
- The ME-APDS user interface is a touchscreen monitor allowing touch control of the system. The GI Genius uses the existing colonoscopy system display monitor and control.

As validated in the clinical study, none of the identified technological differences introduce new aspects of safety or effectiveness. Both systems clinical efficacy and safety performances are very similar.

Performance Data:

Non-Clinical Testing:

The non-clinical performance studies of the subject device included:

- Pixel-level comparison of degradation of image quality
- Software validation
- EMC testing in accordance with the requirements of IEC 60601-1-2:2014
- Electrical safety testing in accordance with IEC 60601-1:2005.

In all instances, the ME-APDS functioned as intended and all tests' results observed were as expected.

Assessment of marker annotation delay

Marker annotation delay was assessed for all polyps all in the standalone performance testing. The marker annotation latency's median, calculated over all the polyps, is 0.166 sec (5 frames) and its average is 0.85 sec.

Standalone Performance Testing:

The algorithm was tested offline on 172 unique full colonoscopy videos, containing 449 polyps. 16 videos contained no polyps. Of the 449 polyps, 330 were small ($s \leq 5mm$), 76 have medium size ($5mm < s < 10mm$), and 43 were large ($s \geq 10mm$). 263 polyps had histology findings where 210 were found to be adenoma polyps. Polyps evaluated varied by subject sex (270 Male, 170 Female, 6 Unknown), age (27 under 50 years, 67 50-60 years, 169 older than 60 years), race (343 Caucasian, 6 African American, 100 Unknown).

ME-APDS recall and false positive performance was evaluated. Recall was measured both frame-wise and polyp-wise and classified according to polyp size and type. In addition, the number of False Positives Per Full Video (procedure) rate was assessed. A verification of the robustness scoring of the Polyp-Wise and Frame-Wise calculations was performed by varying the Intersection over Union (IoU) threshold from 0.01 to 0.1 and 0.2.

Polyp-wise Recall was defined as the number of polyps detected, each for a set number consecutive frames, out of the total number of polyps in the testing dataset, Polyp-wise Recall was evaluated a 1, 3, 5 and 7 consecutive frames as Precall1, Precall3, Precall5, and Precall7, respectively.

The system detects 100% to 99.6% (PRecall1 to PRecall7) of polyps verified by histology and 98.2% to 90% (PRecall1 to PRecall7) of the polyps when polyps without histology verification were included, showing the ability of the system to adequately aid in the detection of polyps when working with the ME-APDS. The median of the coverage of polyps with histology was high (82.0%). And the False Positives Per Video, when all the videos are normalized to a time length of 15 minutes is met the False Positives Per Frame (FPPF) threshold of 0.0328.

Results on polyps that were reported in the procedure report, classified according to polyps with histology and without

-	FRecall	CI	MPC	PRecall1	CI	PRecall3	CI	PRecall5	CI	PRecall7	CI
With Histology	**75.7%**	**[72.5%; 78.8%]**	**82.0%**	**100.0%**	**[100.0%; 100.0%]**	**99.6%**	**[98.8%; 100.0%]**	**99.6%**	**[98.8%; 100.0%]**	**99.6%**	**[98.8%; 100.0%]**
Without Histology	81.54%	[71.1%; 89.9%]	84.5%	100.0%	[100.0%; 100.0%]	100.0%	[100.0%; 100.0%]	100.0%	[100.0%; 100.0%]	100.0%	[100.0%; 100.0%]

Results on the Entire Testing Dataset

FRecall	CI	MPC	PRecall1	CI	PRecall3	CI	PRecall5	CI	PRecall7	CI
73.1%	[69.6%; 76.4%]	72.9%	98.2%	[96.1%; 100.0%]	94.2%	[92.0%; 96.1%]	91.5%	[88.7%; 94.0%]	90.0%	[87.0%; 92.7%]

Results on Polyps with Histology Classified by Polyp Size

-	FRecall	CI	MPC	PRecall1	CI	PRecall3	CI	PRecall5	CI	PRecall7	CI
Small (s≤5)	71.7%	[67.6%; 75.7%]	80.3%	100.0%	[100.0%; 100.0%]	99.5%	[98.5%; 100.0%]	99.5%	[98.5%; 100.0%]	99.5%	[98.5%; 100.0%]
Medium (5<s<10)	82.9%	[77.6%; 87.8%]	85.2%	100.0%	[100.0%; 100.0%]	100.0%	[100.0%; 100.0%]	100.0%	[100.0%; 100.0%]	100.0%	[100.0%; 100.0%]

Large (10≤s)	82.6%	[78.0%; 87.0%]	87.7%	100.0%	[100.0%; 100.0%]	100.0%	[100.0%; 100.0%]	100.0%	[100.0%; 100.0%]	100.0%	[100.0%; 100.0%]

Changing the IoU from 0.01 to 0.1 and 0.2, slightly influenced only the framewise recall, and did not influence the other results supporting the robustness of the system scoring. The testing demonstrates the system performs well on all polyps sizes (small, medium and large polyps), polyps with histology, and both adenomatous and non-adenomatous polyps.

Subgroup analysis by age group, device manufacturer, sex, race, BMI, US/OUS, and reason for colonoscopy demonstrated detection between 100% to 97.3% (PRecall1 to PRecall7) in all subgroups of polyps verified by histology.

Performance (IoU 0.01 and FPPF 0.328), over all the polyps verified by histology in the testing dataset, according to device manufacturer

-	FRecall	CI	MPC	PRecall1	CI	PRecall3	CI	PRecall5	CI	PRecall7	CI
Olympus	75.8%	[72.0%; 79.5%]	81.4%	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]
Pentax	75.5%	[69.8%; 80.8%]	82.1%	100%	[100.0%; 100.0%]	98.7%	[97.2%; 100.0%]	98.7%	[97.2%; 100.0%]	98.7%	[97.2%; 100.0%]

Performance (IoU 0.01 and FPPF 0.328), over all the polyps verified by histology in the testing dataset, according to age group

-	FRecall	CI	MPC	PRecall1	CI	PRecall3	CI	PRecall5	CI	PRecall7	CI
<50	83.6%	[75.2%; 90.9%]	87.4%	100%	[100.0%;	100%	[100.0%;	100%	[100.0%;	100%	[100.0%;

					100.0 %]		100.0 %]		100.0 %]		100.0 %]
50 to <60	76.6%	[69.8% ; 82.6%]	84.2%	100%	[100.0 %; 100.0 %]	100%	[100.0 %; 100.0 %]	100%	[100.0 %; 100.0 %]	100%	[100.0 %; 100.0 %]
60≤	74.2%	[70.2% ; 78.1%]	80.1%	100%	[100.0 %; 100.0 %]	99.4%	[98.2% ; 100.0 %]	99.4%	[98.2% ; 100.0 %]	99.4%	[98.2% ; 100.0 %]

Performance (IoU 0.01 and FPPF 0.328), over all the polyps verified by histology in the testing dataset, according to patient sex group

-	FRecall	CI	MPC	PRecall1	CI	PRecall3	CI	PRecall5	CI	PRecall7	CI
Male	76.7%	[72.5% ; 80.7%]	82.5%	100%	[100.0 %; 100.0 %]	100%	[100.0 %; 100.0 %]	100%	[100.0 %; 100.0 %]	100%	[100.0 %; 100.0 %]
Female	74.5%	[69.7% ; 79.2%]	82.6%	100%	[100.0 %; 100.0 %]	99.0%	[97.2% ; 100.0 %]	99.0%	[97.2% ; 100.0 %]	99.0%	[97.2% ; 100.0 %]
Unknown	70.4%	[70.4% ; 70.4%]	63.7%	100%	[100.0 %; 100.0 %]	100%	[100.0 %; 100.0 %]	100%	[100.0 %; 100.0 %]	100%	[100.0 %; 100.0 %]

Performance (IoU 0.01 and FPPF 0.328), over all the polyps verified by histology in the testing dataset, according to reason for colonoscopy

-	FRecall	CI	MPC	PRecall1	CI	PRecall3	CI	PRecall5	CI	PRecall7	CI
Screening	76.2%	[70.2%; 81.7%]	83.0%	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]
Surveillance	73.1%	[67.6%; 78.4%]	81.7%	100%	[100.0%; 100.0%]	99.1%	[97.5%; 100.0%]	99.1%	[97.5%; 100.0%]	99.1%	[97.5%; 100.0%]
Unknown	80.6%	[76.4%; 84.5%]	82.2%	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]

Performance (IoU 0.01 and FPPF 0.328), over all the polyps verified by histology in the testing dataset, according to race

-	FRecall	CI	MPC	PRecall1	CI	PRecall3	CI	PRecall5	CI	PRecall7	CI
Caucasian	75.0%	[71.3%; 78.6%]	81.5%	100%	[100.0%; 100.0%]	99.5%	[98.6%; 100.0%]	99.5%	[98.6%; 100.0%]	99.5%	[98.6%; 100.0%]
Afro-American	90.6%	[90.6%; 90.6%]	88.3%	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]
Unknown	79.4%	[74.8%; 84.0%]	82.6%	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]

Performance (IoU 0.01 and FPPF 0.328), over all the polyps verified by histology in the testing dataset, according to BMI group

-	FRecall	CI	MPC	PRecall1	CI	PRecall3	CI	PRecall5	CI	PRecall7	CI
<18.5	49.9%	[49.9%; 49.9%]	47.6%	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]
18.5 to <25	78.7%	[71.5%; 85.4%]	83.3%	100%	[100.0%; 100.0%]	97.3%	[90.2%; 100.0%]	97.3%	[90.2%; 100.0%]	97.3%	[90.2%; 100.0%]
25 to <30	74.8%	[65.2%; 83.6%]	83.1%	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]
30≤	72.1%	[59.4%; 81.5%]	78.2%	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]
Unknown	76.6%	[72.6%; 80.3%]	81.0%	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]	100%	[100.0%; 100.0%]

Performance (IoU 0.01 and FPPF 0.328), over all the polyps verified by histology in the testing dataset, according to US vs. OUS

-	FRecall	CI	MPC	PRecall1	CI	PRecall3	CI	PRecall5	CI	PRecall7	CI
US	80.4%	[75.9%;	83.5%	100%	[100.0%;	100%	[100.0%;	100%	[100.0%;	100%	[100.0%;

		84.8%]			100.0 %]		100.0 %]		100.0 %]		100.0 %]
OUS	74.9%	[71.2% ; 78.5%]	81.5%	100%	[100.0 %; 100.0 %]	99.5%	[98.4% ; 100.0 %]	99.5%	[98.4% ; 100.0 %]	99.5%	[98.4% ; 100.0 %]

The testing results were observed to be as expected and support that the device has similar performance to the predicate device.

Clinical Testing:

A randomized, two-arm, multi-center, controlled study to evaluate the safety and efficacy of the use of Magentiq Eye's Automatic Polyp Detection System (ME-APDS) during colonoscopy was conducted at 10 medical centers in Europe, the United States and Israel with 950 patients enrolled.

Patients due to undergo screening or surveillance colonoscopy of ≥3 years since last colonoscopy procedure, were randomized to undergo conventional colonoscopy, CC, (Cohort A1), or ME-APDS-assisted colonoscopy, MEAC, (Cohort B1). In each arm, a subset of patients was further randomized to undergo both colonoscopies in tandem (either CC followed by MEAC (Cohort A2) or MEAC followed by CC (Cohort B2). The final ratios between treatment arms were 6:6:1:1.An outline of the baseline demographics is provided below:

Population	**Treatment Group**				**Total, n (%) (N=916)**
	CC (N=398)	**CC-MEAC (N=69)**	**MEAC (N=385)**	**MEAC-CC (N=64)**	
Age (years)					
Mean (SD)	60.4 (9.2)	60.1 (10.1)	60.4 (8.8)	59.3 (9.0)	60.3 (9.1)
Median	60.0	61.0	60.0	59.5	60.0
Minimum, Maximum	27, 86	32, 86	31, 84	35, 79	27, 86
Age Group, n (%)					
< 50	33 (8.3)	6 (8.7)	27 (7.0)	7 (11.0)	73 (8.0)
50-60	160 (40.2)	25 (36.3)	155 (40.3)	25 (39.1)	365
> 60	205 (51.5)	38 (55.1)	203 (52.7)	32 (50.0)	478
Sex, n (%)					
Male	219 (55.0)	38 (55.1)	202 (52.5)	34 (53.1)	493(53.8)
Female	179 (45.0)	31 (44.9)	183 (47.5)	30 (46.9)	423
BMI (kg/m^2)					
Mean (SD)	27.5 (5.1)	25.9 (4.8)	27.0 (4.8)	27.2 (4.8)	27.2 (4.9)
Median	26.7	26.1	26.2	25.8	26.2

Minimum, Maximum	15.8, 57.4	15.5, 39.3	17.1, 52.6	19.4, 39.0	15.5,
Race, n (%)*					
Caucasian	374 (94.2)	67 (97.1)	370 (96.1)	63 (98.4)	874
African-American	18 (4.5)	2 (2.9)	12 (3.1)	1 (1.6)	33 (3.6)
Asian	1 (0.3)	-	1 (0.3)	-	2 (0.2)
Other	4 (1.0)	-	2 (0.5)	-	6 (0.7)
Reason for Colonoscopy, n					
Screening	222 (55.8)	37 (53.6)	219 (56.9)	36 (56.3)	514
Surveillance	176 (44.2)	32 (46.4)	166 (43.1)	28 (43.8)	402

*For one patient in the CC treatment group the race information was not reported

Primary endpoints:

- APC: total number of adenomas detected and removed per examination
- APE: the percentage of adenomas detected and removed divided by the total number of extractions (polypectomies or biopsies) during index colonoscopies

Success criteria:
More adenomas will be detected with MEAC compared to CC. This will result in higher APC with MEAC compared to CC. APE of MEAC is expected to be non-inferior to APE of CC.

- APC: Difference between the event rates of MEAC vs. CC were compared using a t test, with a two-sided alpha of 5%. The two-sided lower limit of a 95% confidence interval (CI) of the MEAC/CC ratio of events was expected to be >1.05.
- APE: A two-sided Wilcoxon test with a non-inferiority margin of 20% was performed with a two-sided alpha of 5%. The two-sided lower limit of the 95% CI of the difference between the APE of each colonoscopy technique was expected be above -0.20. In addition, 95% CIs of the APE proportions of MEAC and CC were calculated using normal approximation.

APC & APE Results
The primary analysis assessed APC and APE: the percentage of adenomas detected and removed divided by the total number of extractions (polypectomies or biopsies) during index colonoscopies

Adenoma per Colonoscopy (APC) and Adenoma per Extraction (APE) (ITT Population)

	Treatment	
	CC (N=467)	**MEAC (N=449)**
Total Adenomas	238	314
Total Colonoscopies	467	449
Adenomas Per Colonoscopy (APC)		
Mean (SD)	0.51 (1.03)	0.70 (1.30)
SE	0.05	0.06

95% CI	0.42, 0.60	0.58, 0.82
Total Adenomas	238	314
Total Extractions	360	536
Adenomas Per Extraction (APE)		
Mean (SD)	0.27 (0.43)	0.31 (0.43)
SE	0.02	0.20
95% CI	0.23, 0.31	0.27, 0.35

Subgroup Performance

Adenoma per Colonoscopy (APC) and Adenoma per Extraction (APE) by Study Region (ITT Population)

	Treatment									
	CC (N=467)					MEAC (N=449)				
	Total Adenomas	Total Colonoscopies	APC	Total Extractions	APE	Total Adenomas	Total Colonoscopies	APC	Total Extractions	APE
USA	102	84	1.21	142	0.72	105	77	1.36	171	0.61
OUS	136	383	0.36	218	0.62	209	372	0.56	365	0.57

Adenoma per Colonoscopy (APC) and Adenoma per Extraction (APE) by Subgroup (ITT Population)

	Treatment									
	CC (N=467)					MEAC (N=449)				
Subgroup	Total Adenomas	Total Colonoscopies	APC	Total Extractions	APE	Total Adenomas	Total Colonoscopies	APC	Total Extractions	APE
Reason for colonoscopy										
Screening	106	259	0.41	171	0.62	149	255	0.58	239	0.62
Surveillance	132	208	0.63	189	0.70	165	194	0.85	297	0.56
Sex										
Female	91	210	0.43	138	0.66	136	213	0.64	246	0.55
Male	147	257	0.57	222	0.66	178	236	0.75	290	0.61
Age Group										
<50 yrs	8	39	0.21	15	0.53	7	34	0.21	23	0.30
50-60 yrs	72	185	0.39	122	0.59	121	180	0.67	186	0.65
>60 yrs	158	243	0.65	223	0.71	186	235	0.79	327	0.57

The table below provides the two sided 95% CI's for APC and APE by subgroup. Calculations were made on patient level results assuming normal distribution.

Confidence Intervals for APC and APE by Subgroup

Endpoint	Subgroup	Treatment	Mean	Lower 95%	Upper 95%
APC	US	CC	1.214	0.872	1.556
		MEAC	1.364	0.976	1.751
	OUS	CC	0.355	0.277	0.434
		MEAC	0.562	0.444	0.679
	Screening	CC	0.409	0.305	0.514
		MEAC	0.584	0.455	0.714
	Surveillance	CC	0.635	0.471	0.798
		MEAC	0.851	0.630	1.071
	Female	CC	0.433	0.304	0.563
		MEAC	0.638	0.453	0.824
	Male	CC	0.572	0.439	0.705
		MEAC	0.754	0.596	0.912
	< 50	CC	0.205	0.020	0.390
		MEAC	0.206	0.039	0.373
	50- 60	CC	0.389	0.267	0.511
		MEAC	0.672	0.494	0.850
	> 60	CC	0.650	0.501	0.799
		MEAC	0.791	0.608	0.975
APE	US	CC	0.484	0.384	0.584
		MEAC	0.443	0.351	0.536
	OUS	CC	0.222	0.181	0.262
		MEAC	0.278	0.234	0.321
	Screening	CC	0.247	0.196	0.299
		MEAC	0.300	0.247	0.354
	Surveillance	CC	0.295	0.236	0.355
		MEAC	0.314	0.255	0.373
	Female	CC	0.240	0.183	0.297
		MEAC	0.269	0.214	0.325
	Male	CC	0.292	0.239	0.346
		MEAC	0.340	0.283	0.396
	< 50	CC	0.147	0.033	0.262
		MEAC	0.152	0.027	0.277
	50- 60	CC	0.205	0.149	0.261
		MEAC	0.312	0.249	0.376
	> 60	CC	0.337	0.279	0.395
		MEAC	0.324	0.269	0.379

The study results showed that the MEAC adenoma per colonoscopy (APC) was 37% higher (relative increase) than CC APC and was consistently higher across all patient subgroups. Inter-arm comparisons found consistently higher APC rates for MEAC as compared to CC procedures, regardless of colonoscopy indication, patient sex, or patient age, with a mean 0.20 increment between arms for each analyzed subgroup. In particular, MEAC proved more effective than CC in detecting ≤5mm polyps and in detecting >6-9 mm polyps, sessile and flat polyps and adenomas in the proximal colon. In addition, more sessile serrated adenomas (SSAs) were identified in MEACs as compared to CCs, which resulted in also a higher sessile serrated detection rate (SDR). Despite the increased detection rate, the MEAC adenomas per extraction (APE) proved non-inferior to that of CC, and did not involve clinically relevant longer withdrawal times or delayed bleeding. In line with these findings, AMR was significantly lower and ADR was significantly higher in the MEAC vs. CC arm. As expected, given the above findings, time to next scheduled colonoscopy was 4 months earlier in the MEAC as compared to the CC cohort.

These observations suggest a critical contribution of MEAC in minimizing the effects of confounding clinical and operator-related factors on colonoscopy outcomes. No intervention-related adverse events were reported during this study in either arm.

Based on the clinical performance as documented in the pivotal clinical study, the ME-APDS performs as intended under anticipated conditions of use and has a safety and effectiveness profile that is similar to the predicate device.

Conclusions:

The ME-APDS is as safe and effective as Cosmo Artificial Intelligence - AI, LTD's GI Genius. The ME-APDS has the same intended uses and similar indications, technological characteristics, and principles of operation as its predicate device. The minor differences in indications do not alter the intended use. In addition, the minor technological differences between the ME-APDS and its predicate devices raise no new issues of safety or effectiveness. Performance data demonstrate that the ME-APDS is as safe and effective as the GI Genius. Thus, the ME-APDS is substantially equivalent.