October 16, 2018

Inova Diagnostics, Inc.
Roger Albesa
Manager
9900 Old Grove Road
San Diego, California 92131-1638

Re: K180971
Trade/Device Name: Fecal Extraction Device
Regulation Number: 21 CFR 866.5180
Regulation Name: Fecal calprotectin immunological test system
Regulatory Class: Class II
Product Code: NXO
Dated: April 11, 2018
Received: April 13, 2018

Dear Roger Albesa:

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/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). 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 (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Leonthena R. Carrington -S

Lea Carrington
Director
Division of Immunology
and Hematology Devices
Office of In Vitro Diagnostics
and Radiological Health
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: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*

Device Name
Fecal Extraction Device

Indications for Use *(Describe)*
The Fecal Extraction Device is a single use tube containing extraction buffer intended for sampling and extracting human stool specimens and subsequent analysis with the QUANTA Flash Calprotectin assay.

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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Table of Contents

This summary of the 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

Administrative data

Submitter:
Inova Diagnostics, Inc
9900 Old Grove Road,
San Diego, CA, 92131

Purpose of submission:
The reason for submission is the addition of an optional new device to aid in the stool extraction process, the Fecal Extraction Device, to work with the QUANTA Flash Calprotectin assay.

Devices in the submission:
Fecal Extraction Device

Scientific contact:
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Quality Systems contact:
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Email: relliot@inovadx.com

Device name:

Proprietary name:	Fecal Extraction Device
Common name:	Chemiluminescence Fecal Calprotectin assay with Fecal Extraction Device
Classification name:	Calprotectin, Fecal

Regulation Description	Fecal Calprotectin Immunological Test System
Regulation Medical Specialty	Immunology
Review Panel	Immunology
Product Code	NXO
Regulation Number	866.5180
Device Class	2

Predicate device

QUANTA Flash Calprotectin (using manual extraction), 510(k) number: k170993. Date declared: December 22nd, 2017.

Device description

The Fecal Extraction Device acquires the amount of stool necessary to perform the QUANTA Flash Calprotectin assay directly from the primary specimen container instead of weighing the sample. The device consists of a tube, containing 2.8 mL of extraction buffer, and a stick shaped with seven grooves for collecting the sample. The upper end of the device is made up of two parts which can be removed with two separate rotations: the white screw cap (connected to the plastic stick with grooves) is removed by twisting counter-clockwise. The red lower part (for retaining the excess material) is removed by twisting clockwise. Once having completed the extraction procedure, remove both the white and red upper parts. The tube containing the extracted sample can be placed directly into the BIO-FLASH instrument sample rack.

The principle of the assay is chemiluminescent microparticle immunoassay, a variation of solid phase immunoassay. The QUANTA Flash® Calprotectin assay is designed to run on the BIO-FLASH® instrument. This platform is a fully automated closed system with continuous load and random access capabilities that automatically processes the samples, runs the assay and reports the results. It includes liquid handling hardware, luminometer and computer with software-user interface. The QUANTA Flash® Calprotectin assay utilizes a reagent cartridge format, which is compatible with the BIO-FLASH® instrument.

Calprotectin-specific capture antibodies are coated on to paramagnetic beads, which are stored in the reagent cartridge under conditions that preserve the antibody in its reactive state. Prior to use in the BIO-FLASH® system, the reagent pack containing all the necessary assay reagents is mixed thoroughly by being inverted several times. The sealed reagent tubes are pierced with the reagent cartridge lid, and the reagent cartridge is loaded onto the instrument. Reagents are calibrated when the lot is first used. A patient extracted stool sample is prediluted by the BIO-FLASH® with sample buffer in a disposable plastic cuvette. Small amounts of the diluted patient extracted stool, the beads, and the assay buffer are all combined into a second cuvette, and mixed. This cuvette is then incubated at 37°C. The beads are magnetized and washed several times. Isoluminol conjugated monoclonal anti-calprotectin antibodies are then added to the cuvette, and again incubated at 37°C. The beads are magnetized and washed repeatedly. The isoluminol conjugate is oxidized when Trigger 1 (Fe(III)coproporphyrin in sodium hydroxide solution) and Trigger 2 (urea-hydrogen peroxide in sodium chloride solution) are added to the cuvette, and the flash of light produced from this reaction is measured as Relative Light Units (RLU) by the BIO-FLASH® optical system. The measured RLU is proportional to the amount of bound isoluminol conjugate, which is in turn proportional to the amount of calprotectin antigen captured by the antibodies (anti-calprotectin polyclonal antibodies in this case) on the beads. For quantitation, the QUANTA Flash® Calprotectin will utilize a predefined lot specific Master Curve that is uploaded onto the instrument through the reagent cartridge barcode. The Master Curve is generated by Inova Diagnostics for each reagent pack lot with in-house Standards with assigned unit values (ng/mL). The RLU and assigned ng/mL values of the Standards are used to create a 4 parameter logistic curve. These four parameters are embedded in the reagent pack barcode. When the lot is used the first time, the Calibrators are run, and based on the results obtained on the Calibrators, an instrument specific Working Curve is created; The Working Curve is used to calculate units (ng/mL) based on RLU values

obtained on each sample. The obtained ng/mL values will be converted to mg/kg by a calculation that takes into account the dilution of the samples. This unit conversion is calculated automatically by the software.

The Fecal Extraction Device kit contains the following materials:

One hundred (100) Fecal Extraction Devices

The Fecal Extraction Device tube contains the following materials for a single stool extraction:

a. 2,8 mL of extraction buffer, colorless, ready to use.

Intended use(s)

The Fecal Extraction Device is a single use tube containing extraction buffer intended for sampling and extracting human stool specimens and subsequent analysis with the QUANTA Flash Calprotectin assay.

Indications for use

Same as Intended use.

Substantial equivalence

The QUANTA Flash Calprotectin assay system using the Fecal Extraction Device performs equivalently as the predicate device.

Comparison to predicate device

QUANTA Flash Calprotectin Reagents

Similarities		
Item	**QUANTA Flash Calprotectin with Fecal Extraction Device.**	**QUANTA Flash Calprotectin**
Intended use	QUANTA Flash Calprotectin is a chemiluminescent immunoassay for the quantitative determination of fecal calprotectin in extracted human stool samples. Elevated levels of fecal calprotectin, in conjunction with clinical findings and other laboratory tests, can aid in the diagnosis of inflammatory bowel disease (IBD) (ulcerative colitis and Crohn's disease), and in the differentiation of IBD from irritable bowel syndrome (IBS). The Fecal Extraction Device is a single use tube containing extraction buffer intended for sampling stool specimens and subsequent analysis with the QUANTA Flash Calprotectin assay.	QUANTA Flash Calprotectin is a chemiluminescent immunoassay for the quantitative determination of fecal calprotectin in extracted human stool samples. Elevated levels of fecal calprotectin, in conjunction with clinical findings and other laboratory tests, can aid in the diagnosis of inflammatory bowel disease (IBD) (ulcerative colitis and Crohn's disease), and in the differentiation of IBD from irritable bowel syndrome (IBS).
Assay methodology	Solid phase (heterogeneous) immunoassay	Same
Antigen	Rabbit polyclonal anti-calprotectin antibody	Same
Shelf life	One year	Same
Sample type	Extracted Human Stool	Same
Units	mg/kg (milligram of calprotectin per kilogram of stool)	Same
Detection/ Operating principle	Chemiluminescent immunoassay	Same
Solid phase	Paramagnetic microparticles (beads)	Same
Conjugate	Isoluminol conjugated monoclonal anti-calprotectin antibody	Same
Analytical Measuring Range	16.1 – 3,500.0 mg/kg	Same
Calibration	Lot specific Master Curve + three calibrators (sold separately)	Same

Analytical performance characteristics

Same as approved in 510k submission #k170993 plus the following additional data.

Stool Extraction method comparison: Fecal Extraction Device vs. Manual weighing method

Ninety seven human stool samples containing different levels of calprotectin were extracted in parallel using the manual weighting method and the Fecal Extraction Device. All resulting stool extracts were tested in singleton for calprotectin concentration levels using the QUANTA Flash Calprotectin assay. A scatter plot with a linear fit was created by plotting the mean values obtained with the manual weighting method against those obtained with the Fecal Extraction Device, using the Passing-Bablok fit function of Analyse-it for Excel software. This study has been conducted according to CLSI EP09-A3 Method Comparison and Bias Estimation Using Patient Samples: Approved Guideline.

Acceptance criteria:

- Intercept of regression line ± 15% of cut-off (18 mg/kg)
- Slope of regression line between 0.90 and 1.10
- Predicted Bias at cut-off ≤ 15%
- 95% CI of the bias: does not exceed medically significant difference, 20% of cut-off
- Correlation r > 0.95

Results are summarized in the Table below:

Passing-Bablok fit	Y-Intercept (95% CI)	Slope (95% CI)	Bias at 120mg/kg (95% CI)	Correlation r
Fecal Collection Device vs Manual Extraction comparison n=97	-1.2 (-9.7 to 6.4)	0.93 (0.82 to 1.06)	-7.8 % (-16.0% to 0.6%)	0.975

All acceptance criteria were met.

Additionally, a percent agreement analysis has been performed between the two methods of extraction using the data generated obtaining the following results:

		Manual Extraction			
		Positive	Indeterminate	Negative	Total
Fecal Extraction Device	Positive	43	3	0	46
	Indeterminate	3	20	3	26
	Negative	0	5	20	25
	Total	46	28	23	97
Indeterminate as positive					
Positive agreement (95%CI):		93.2% (85.1 – 97.1%)			
Negative agreement (95%CI):		87.0 % (67.9 - 95.5%)			
Total agreement (95%CI):		91.8% (84.6 - 95.8%)			
Indeterminate as negative					
Positive agreement (95%CI):		93.5% (82.5 - 97.8%)			
Negative agreement (95%CI):		94.1% (84.1 - 98.0%)			
Total agreement (95%CI):		93.8% (87.2 - 97.1%)			

Device Validation

To validate the amount of fecal material that is collected by the Fecal Extraction Device five different human stool samples, encompassing different stool consistencies, were collected using the Fecal Extraction Device in replicates of five by three independent operators. Data were analyzed with the Analyse-it for Excel method evaluation software to calculate weight distribution.

Acceptance criteria: weight collected by the FED is 56 mg ±10% (between 50 and 62 mg).

Results of the study are summarized in the Table below:

Sample collection performance of FED	
Mean Sample Weight (95% CI)	56 (55 - 57) mg
Median Sample Weight	56 mg
Range	50 – 62 mg
Standard Deviation	± 3.8 mg
% Coefficient of Variation	6.9%

All acceptance criteria were met.

Reproducibility Studies

Extraction Reproducibility

Eight samples were extracted and tested, according to CLSI EP05-A3 Evaluation of Precision of Quantitative Measurement Procedures, in replicates of 5, once a day, for 5 days, to generate 25 data points per sample per operator, for a total of 75 data points per sample. The extractions were performed daily by three independent operators using the Fecal Extraction Device. Data were analyzed with the Analyse-it for Excel method evaluation software to calculate between operator precision.

Acceptance criteria: Within Laboratory (Total Imprecision) %CV: ≤ 15% or SD: ≤ 7.5 mg/kg for negative samples.

Results are summarized in the Table below.

			Repeatability		**Between-Day**		**Within Operator**		**Between Operator**		**Within Laboratory**	
Sample ID	**N**	**Mean (mg/kg)**	**SD (mg/kg)**	**CV (%)**	**SD (mg/kg)**	**CV (%)**	**SD (mg/kg)**	**CV (%)**	**SD (mg/kg)**	**CV (%)**	**SD (mg/kg)**	**CV (%)**
Sample 1	75	29.5	2.2	7.3%	7.2	24.4%	7.5	25.4%	0.0	0.0%	7.5	25.4%
Sample 2	75	40.0	2.3	5.7%	6.0	15.0%	6.4	16.1%	2.2	5.5%	6.8	17.0%
Sample 3	75	53.2	2.1	3.9%	5.4	10.2%	5.8	10.9%	4.8	9.0%	7.5	14.1%
Sample 4	75	108.2	4.3	4.0%	8.0	7.4%	9.1	8.4%	7.3	6.8%	11.7	10.8%
Sample 5	75	222.9	7.3	3.3%	20.9	9.4%	22.1	9.9%	5.4	2.4%	22.8	10.2%
Sample 6	75	535.4	15.7	2.9%	41.2	7.7%	44.1	8.2%	21.9	4.1%	49.2	9.2%
Sample 7	75	1278.3	45.0	3.5%	114.6	9.0%	123.2	9.6%	8.9	0.7%	123.5	9.7%
Sample 8	75	1560.0	63.9	4.1%	197.1	12.6%	207.2	13.3%	0.0	0.0%	207.2	13.3%

All acceptance criteria were met.

Sample Stability and Handling

Seven human stool samples, encompassing indeterminate range (n=1), around the cut-off (n=2), and positive samples (n=4) were extracted using the Fecal Extraction Device and tested in duplicates using the QUANTA Flash Calprotectin assay for up to 21 days while stored at 2-8°C, up to 73 hours while stored at room temperature, and after repeated freeze/thaw cycles up to 5 cycles (thaw samples were homogenized and clarified before its testing by vortex the samples for 30 seconds and centrifugation for 10 min at 3,000 x g)

Results were compared to those obtained on control samples (time zero / zero cycles).

Acceptance criteria: 80-120% average recovery.

All samples fulfilled the acceptance criteria at each time point for each condition. Based on these result, we recommend that extracted samples using the Fecal Extraction Device are stored up to 72 hours at room temperature, up to 14 days at 2-8°C and can be subjected to up to 4 freeze/thaw cycles.

Fecal Extraction Device Stability

Shelf life (Real Time Stability)

Since calprotectin is not stable in human stool for long periods of time, real time stability studies for the Fecal Extraction Device (FED) were conducted by analyzing the pH of the extraction buffer (located inside the device) of three different lots of FED every 3 to 6 months for 24 to 26 months.

Acceptance criteria: pH between 7.70 and 7.90.

Results are summarized in the table below:

pH testing Acceptance Criteria (7.70 - 790)	Reference mg/kg	1 mg/kg	2 mg/kg	3 mg/kg
time = 0 months	7.79	7.82	7.81	7.81
time = 3 months	7.78	7.81	7.81	7.80
time = 6 months	-	7.80	7.80	7.80
time = 9 months	-	7.81	7.79	7.78
time = 12 months	-	7.80	7.78	7.78
time = 18 months	-	7.79	7.78	7.78
time = 24 months	-	7.79	7.78	7.78
time = 26 months	-	-	-	7.77

Additionally, in order to test the functionality of the FED at expiration date, three lots of FED, two at expiration date (24 months) and one freshly produced, were used to perform extractions on 15 human stool samples, encompassing negative (n=11), indeterminate (n=2), around the cut-off (n=1) and a positive (n=1) samples. The calprotectin concentration of each stool extract was determined.

The results of the two lots of FED at expiration date were compared to those obtained with the freshly produced lot. Percent recovery results were calculated where possible.

Acceptance criteria: 70-130% average recovery. This acceptance criterion takes into consideration the variability between lots of FED, the extraction reproducibility (±15%) and the expected recovery on a traditional real time study (±20%).

All samples fulfilled the acceptance criteria. In conclusion, the Fecal Extraction Device will be given an expiration date of 2 years.

Stability at Room Temperature

Three independent lots of Fecal Extraction Device have been evaluated for room temperature stability. Six human stool samples, encompassing indeterminate (n=1 for lot 1 and n=2 for lots 2 and 3), around the cut-off (n=1) and positive samples (n=4 for lot 1, n=3 for lots 2 and 3) were extracted using the Fecal Extraction Device in two different conditions: using devices kept at 2-8°C and using devices kept at room temperature for at least 73 hours.

All resulting stool extracts were tested for calprotectin concentration levels using the QUANTA Flash Calprotectin assay. Results were compared to those obtained on control devices (2-8°C).

Acceptance criteria: 80-120% average recovery.

All results obtained using the three different lots of Fecal Extraction Device fulfilled the acceptance criteria. In conclusion, the Fecal Extraction Device can be kept at room temperature up to 72 hours.

Clinical performance characteristics

Same as approved in 510k submission #k170993.