September 29, 2023

Miris AB
% John Smith, Partner
Hogan Lovell US LLP
555 13th Street NW
Washington, District of Columbia 20004

Re: K223085
Trade/Device Name: Miris Human Milk Analyzer (HMA)
Regulation Number: 21 CFR 862.1493
Regulation Name: Breast Milk Macronutrients Test System
Regulatory Class: Class II
Product Code: QEI
Dated: August 23, 2023
Received: August 23, 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 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,

Marianela Perez-torres -S

Marianela Perez-Torres, Ph.D
Acting Director
Division of Chemistry
and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
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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: 06/30/2023
See PRA Statement below

510(k) Number *(if known)*
K223085

Device Name

Miris Human Milk Analyzer (HMA)

Indications for Use *(Describe)*

The Miris Human Milk Analyzer (HMA) quantitatively measures the concentration of fat, protein, and carbohydrate in human milk. The Miris HMA also provides calculated values for total solids and energy. These measurements, in conjunction with other clinical assessments, may be used to aid in the nutritional management of newborns, including preterm, and infants. This device is intended for use in healthcare by trained healthcare personnel at clinical laboratories. The Miris HMA is also intended for use by personnel trained in the use of the device at Human Milk Banking Association of North America (HMBANA) accredited human milk banks, for the purpose of labeling milk donations and in the processing of milk donations.

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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510(k) SUMMARY

Miris AB's Miris Human Milk Analyzer

510(k) Number
K223085

Submitter

Miris AB
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Phone: +46 18 14 69 07
Contact Person: John Smith
Contact phone: 202-637-3638

Date Prepared: September 19, 2023

Name of Device: Miris Human Milk Analyzer (HMA)

Common or Usual Name: Breast milk macronutrient test system

Classification Name: Breast milk macronutrient test system

Regulatory Class: Class II

Regulation Number: 21 CFR 862.1493

Product Code: QEI

Predicate Devices

Miris Human Milk Analyzer DEN180007

Device Description

The Miris Human Milk Analyzer (HMA) includes a mid-infrared (mid-IR) spectroscopy system and a man-machine interface (MMI). The user is guided by the interactive MMI, via the screen, through the measurement process by use of the six-button controlled menu system. Milk samples are injected into the measuring unit (cuvette) via the instrument inlet using a syringe (sample volume 3 mL), excess sample and waste exiting via the outlet.

The device consists of the following components and accessories: an instrument casing with sample inlet and outlet holding a measurement unit and electronics mainboard, with AC/DC adapter, syringes for injection of sample, zero-setting solution, quality control solutions, and cleaning agent, waste container (not provided by the manufacturer), and outlet tubes.

Intended Use / Indications for Use

The Miris Human Milk Analyzer (HMA) quantitatively measures the concentration of fat, protein, and carbohydrate in human milk. The Miris HMA also provides calculated values for total solids and energy. These measurements, in conjunction with other clinical assessments, may be used to aid in the nutritional management of newborns, including preterm, and infants. This device is intended for use in healthcare by trained healthcare personnel at clinical laboratories. The Miris HMA is also intended for use by personnel trained in the use of the device at Human Milk Banking Association of North America (HMBANA) accredited human milk banks, for the purpose of labeling milk donations and in the processing of milk donations.

Summary of Technological Characteristics

Mid-infrared (mid-IR) spectroscopy is the technological principle for both the subject and predicate devices. The subject and predicate devices are based on the following identical technological elements:

- The Miris HMA device is comprised of a sample cuvette and assisting hardware components. The cuvette is a mid-infrared measurement cell with an inlet and an outlet. Liquids are injected via the inlet and pass between two CaF_2 (calcium fluoride) windows separated by a spacer (50 µm). On one side of the windows is an infrared radiation source (emitter) and on the other side is a four-channel detector receiving the radiation transmitted through the liquid. The filters in the detector are selected to absorb only mid-infrared radiation correlated to fat, protein and carbohydrates, respectively. The fourth filter acts as a reference filter.

- The radiation from an IR-source penetrates the transparent cuvette containing the liquid sample. After passing through the cuvette chamber the quantities of radiation absorbed by specific functional groups of fat, protein and carbohydrate, respectively, are evaluated. The quantitative determination of fat, protein and carbohydrate is performed according to Beer's law - the absorbance is proportional to concentration. The Miris HMA software processes the measurement data by the internal calibration and the results are presented to the user.

There are no technological differences between the subject and predicate device.

A table comparing the key features of the subject and predicate devices is provided below.

Miris AB's

Miris Human Milk Analyzer (HMA)

Substantial Equivalence Chart

	Miris HMA (K223085)	**Miris HMA De novo (DEN180007)**
Intended Use	The Miris Human Milk Analyzer (HMA) quantitatively measures the concentration of fat, protein, and carbohydrate in human milk. The Miris HMA also provides calculated values for total solids and energy. These measurements, in conjunction with other clinical assessments, may be used to aid in the nutritional management of newborns, including preterm, and infants. This device is intended for use in healthcare by trained healthcare personnel at clinical laboratories. The Miris HMA is also intended for use by personnel trained in the use of the device at Human Milk Banking Association of North America (HMBANA) accredited human milk banks, for the purpose of labeling milk donations and in the processing of milk donations.	The Miris Human Milk Analyzer (HMA) quantitatively measures the concentration of fat, protein, and carbohydrate in human milk. The Miris HMA also provides calculated values for total solids and energy. These measurements, in conjunction with other clinical assessments, may be used to aid in the nutritional management of newborns, including preterm, and infants. This device is intended for use in healthcare by trained healthcare personnel at clinical laboratories.
Indications for Use	See above	See above
User Population	Newborns, including preterm, and infants	Same
Technological Characteristics	Mid-infrared transmission spectroscopy system	Same
Major Components	A sample cuvette, hardware consisting of a mainboard and CPU (Central Processing Unit) board, a display, touch button, fan, case, and accessories. The hardware electronics consists of a mainboard with a CPU-board, detector board and emitter board.	Same
Accessories	AC/DC adapter (Input 100-240 VA, 2.3 A, output 18 V, 5.6 A) Power cable USB optical mouse Zero-setting solution: Miris Check Quality control solution: Miris Calibration Control Kit Cleaning agent: Miris Cleaner Syringes for injection of sample and solutions Outlet tubes Spare parts kit for in- and outlet	Same

	Miris HMA (K223085)	Miris HMA De novo (DEN180007)
	USB flash memory USB hub Sample tubes Heating bath Ultrasonic processing device	
Dimensions (l x w x h)	11 x 26 x 31 cm	9 x 26 x 31 cm
Weight	3.8 kg	3.1 kg
Power Source	AC/DC adapter (Input 100-240 VA, 2.3 A, output 18 V, 5.6 A	Same
Software	Application software, version 3.10	Application software, version 3.09
Standards with which the Device Complies	IEC 61010-1:2010 IEC 61010-2-101:2015	IEC 61010-1:2001
Components tested	Fat, Crude Protein, True Protein, Carbohydrate [g/100mL]	Same
Components calculated	Total solids (TS) [g/100 mL], Energy [kcal/100 mL]	Same
Measuring range	Fat 0.6 - 6 g/100 mL Crude protein 0.8 - 3 g/100 mL True protein 0.6 - 2.4 g/100 mL Carbohydrate 6.6 - 8.7 g/100 mL	Fat 0.6 - 4 g/100 mL Crude protein, True protein and Carbohydrate measuring ranges are the Same.
Measurement performance	Repeatability (CV): Fat, Crude protein, True protein ≤5% at concentration <1 g/mL, ≤3% at concentration >1 g/mL; Carbohydrate, Total solids, Energy ≤3% Accuracy: Fat, Crude protein, True protein, Total solids, Energy ±10%; Carbohydrate ±13%	Same

Performance Data

Precision Study

Repeatability and reproducibility of the Miris HMA for measuring fat, CP, TP, and CHO content in a human milk sample was evaluated following the CLSI EP05-A3 guideline. The calculated parameters TS and E were also evaluated.

The study was performed at three US human donor milk bank sites (one main site, two secondary sites) in February and March 2022. The Main site (E:) was the Mothers' Milk Bank (San José, USA).

The Secondary site (F) was Mid-Atlantic Mothers' Milk Bank 'Three Rivers' (Pittsburgh, USA). The Secondary site (G) was The New York Milk Bank, Inc., (New York, USA).

Study design, precision and reproducibility

Site type	Number of sites	Number of samples	Number of days	Runs/day	Replicates/sample/ run
Main (E)	1	5	20	2	2
Secondary (F, G)	2	5	5	2	3

At the main site (E), 5 human milk samples were tested on 1 device by 1 operator over 20 days, with 2 runs per day, and 2 replicates of each sample per run (i.e., planned 400 observations).

At each of the two secondary sites (F, G), the same 5 samples were tested on 1 device by 2-3 operators over 5 days, with 2 runs per day, and 3 replicates of each sample per run (i.e., planned 150 observations per site).

The results of the precision study show that Miris HMA demonstrated acceptable results for the intended use of the device similar to the predicate device.

These results confirm earlier results included in the Miris HMA DEN180007 and support use of Miris HMA in human donor milk banks.

Detection Capability

Data concerning the Miris HMA detection capabilities were included in DEN180007. These studies demonstrated the following:

- LoB was below 0.1 g/100 mL for fat, crude protein, true protein and carbohydrate.
- LoB ≤ LoD < LoQ.
- LoQ was below the low end of the Miris HMA measuring range for all variable within an acceptable deviation.

Interference

Data concerning potential interfering substances for the Miris HMA were included in DEN180007.

Based on testing of 30 substances and results from this testing the User Manual states the following:

Interference with the Miris HMA measurement results was found from the following substances: Citalopram, Sertraline, Ampicillin, Vancomycin, Clindamycin, Cephalexin, Pseudoephedrine, and Hemoglobin. Macronutrient analysis by Miris HMA is not recommended on milk that may contain any of these drugs, i.e. milk from mothers taking the drug.

Human milk may be contaminated with hemoglobin, from whole blood. If the milk is visibly pink, presumed from blood contamination, macronutrient analysis by HMA is not recommended.

Carry Over

Data concerning the Miris HMA potential carry over were included in DEN180007.

Results indicated that carry-over occurred in <2% of all samples tested at 3 mL sample injections, which is the required sample listed in the User Manual.

Linearity

Data from a linearity study for a measuring range of fat up to 4 g/100 mL was included in de novo DEN180007, a new study for a measuring range of fat up to 6 g/100 mL is included in this 510(k) submission Specifically, the linear range of the Miris HMA method for measuring Fat, CP, TP, and CHO content in a normal human milk sample following the CLSI EP06-A guideline. The calculated variables TS and E were also evaluated.

Results output Miris HMA linearity study, linear intervals of the HMA.

Variable	Linear interval	Unit	Intercept	Slope	R^2
Fat	0.4 - 7.0	g/100 mL	-0.1122	1.0284	0.9981
Crude protein	0.4 - 3.8	g/100 mL	0.0364	0.9925	0.9964
True protein	0.3 - 3.1	g/100 mL	0.0647	0.9811	0.9967
Carbohydrate	6.1 - 8.9	g/100 mL	0.5095	0.9457	0.9854
Total solids	0.7 - 20.8	g/100 mL	0.2079	0.9890	0.9974
Energy	8 - 143	kcal/100 mL	0.0135	1.0067	0.9982

Linearity was demonstrated in intervals corresponding to the Miris HMA measuring range of fat, crude protein, true protein, carbohydrate, total solids and energy, with a deviation from linearity within 10%.

Trueness, Method Comparison Testing

The objective of this study was to compare the Miris HMA analysis to analysis by biochemical standard methods, estimating the bias for measuring fat, CP, TP, and CHO in human milk samples following the CLSI EP09c guideline. The calculated variables TS and Energy were also evaluated.

The study on the Miris HMA included 112 samples (and 1 extra sample to replace a partly spilled-out sample) tested in two replicates on one device. Bias was estimated both from first replicate results only, and from means of duplicates. As many Miris HMA users only have sample availability to run a single analysis, bias estimation based on first replicate results was the primary outcome. Bias estimation based on means was done to see whether duplicate analysis would reduce bias compared to single analysis.

The comparative methods used were biochemical standard methods, validated for analysis on human milk:

- Röse Gottlieb (ISO 1211) for fat,
- Kjeldahl (ISO 8968-1) for crude protein,
- Kjeldahl crude protein*0.8 for true protein,

- Total CHO content calculated by difference, from values obtained by the comparative methods,
- Drying oven for total solids (ISO 6731),
- Bomb calorimetry for energy (ISO 1928)

The following ranges were assessed this study.

- Fat 0.6 - 6.4 g/100 mL
- Crude protein 0.9 - 3.5 g/100 mL
- True protein 0.7 - 2.8 g/100 mL
- Carbohydrate 6.1 - 8.8 g/100 mL
- Total solids 9.8 - 15.6 g/100 mL
- Energy 44 - 111 kcal/100 mL

Overall, the results indicated a Miris HMA bias < 7% (95% CI) for all variables. Point estimates showed acceptable biases (±10%) at low, medium, and high levels of fat, protein, and carbohydrate, respectively.

The analytical performance characteristics of the Miris HMA device for the milk bank use demonstrated that the method comparison, precision and linearity functions met all expected performance acceptance criteria. There were no changes to the device and all other analytical characteristics were demonstrated in DEN180007.

In all instances, the Miris HMA functioned as intended and the precision in the milk bank setting, and the linearity and method comparison observed was as expected.

Stability of the Miris HMA and Reagents

The stability studies and acceptance criteria have been reviewed and found to be acceptable. The stability data supports the claims as reported in the package labeling.

Conclusions

The Miris HMA expanded indication for use to the milk bank setting is as safe and effective as the Miris HMA granted a de novo under DEN180007. The Miris HMA 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 diagnostic use of measuring the concentration of fat, protein, and carbohydrates in human milk and do not affect its safety and effectiveness when used as labeled. In addition, the minor technological differences between the Miris HMA and its predicate device raise no new issues of safety or effectiveness. Precision, linearity and method comparison performance data demonstrate that the Miris HMA is as safe and effective as the Miris HMA granted a de novo under DEN180007. Thus, the Miris HMA is substantially equivalent.