September 14, 2021

DiaSorin Inc.
% Mari Meyer
Vice President, Regulatory and Clinical Affairs, North America
1951 Northwestern Ave
Stillwater, Minnesota 55082

Re: K193650
Trade/Device Name: LIAISON Ferritin
Regulation Number: 21 CFR 866.5340
Regulation Name: Ferritin Immunological Test System
Regulatory Class: Class II
Product Code: DBF
Dated: March 16, 2021
Received: March 17, 2021

Dear Mari Meyer:

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,

Ying Mao, Ph.D.
Chief, Immunology and Flow Cytometry Branch
Division of Immunology
and Hematology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

# Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
*See PRA Statement below.*

510(k) Number *(if known)*
K193650

Device Name
LIAISON® Ferritin

Indications for Use *(Describe)*
The DiaSorin LIAISON® Ferritin assay is a quantitative automated chemiluminescent immunoassay (CLIA) for the in vitro detection of ferritin in human serum, serum separator tubes (SST), or lithium (Li) heparin plasma to aid in the diagnosis of iron deficiency anemia and iron overload.

This assay must be performed on the LIAISON® XL Analyzer.

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.

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# 510(k) Summary

**1. 510(k) Number:** K193650

**2. Applicant:** Mari Meyer
DiaSorin Inc.
1951 Northwestern Avenue, P.O. Box 285, Stillwater, MN 55082-0285
Office Number: 651-439-9710; Fax Number: 651-351-5669
Email: mari.meyer@diasorin.com

**3. Date:** September 13, 2021

**4. Proprietary and Established Names:**

LIAISON® Ferritin

**5. Regulatory Information:**

Regulation Section: 21 CFR 866.5340
Classification: Class II
Product Code: DBF
Panel: Subpart F - Immunological Test Systems

**6. Predicate Device(s):**

Roche Elecsys® Ferritin assay previously FDA cleared under (K971833).

**7. Device Description:**

The method for the quantitative determination of ferritin is a sandwich chemiluminescence immunoassay.
A specific mouse monoclonal antibody is coated on the magnetic particles (solid phase); another monoclonal antibody (mouse) is linked to an isoluminol derivative (isoluminol-antibody conjugate).
During the incubation, ferritin present in calibrators, samples or controls binds to the solid phase monoclonal antibody, and subsequently the antibody conjugate reacts with ferritin already bound to the solid phase.
After incubation, the unbound material is removed with a wash cycle.
Subsequently, the starter reagents are added and a flash chemiluminescence reaction is thus induced. The light signal, and hence the amount of isoluminol-antibody conjugate, is measured by a photomultiplier as relative light units (RLU) and is indicative of ferritin concentration present in calibrators, samples or controls.

## 8. Intended Use:

The DiaSorin LIAISON® Ferritin assay is a quantitative automated chemiluminescent immunoassay (CLIA) for the *in vitro* detection of ferritin in human serum, serum separator tubes (SST), or lithium (Li) Heparin plasma to aid in the diagnosis of iron deficiency anemia and iron overload.
This assay must be performed on the LIAISON® XL Analyzer.

## 9. Indication(s) for Use:

Same as Intended Use

## 10. Substantial Equivalence Information:

A comparison of the similarities and differences between the LIAISON® Ferritin assay and the predicate Roche Elecsys® Ferritin assay is provided in the following table:

| **Assay Similarities and Differences** | | |
|---|---|---|
| **Characteristic** | **Candidate Device LIAISON® Ferritin** | **Predicate Device Roche Elecsys® Ferritin (K971833)** |
| **Intended Use** | The DiaSorin LIAISON® Ferritin assay is a quantitative automated chemiluminescent immunoassay (CLIA) for the in vitro detection of ferritin in human serum, serum separator tubes (SST), or lithium (Li) plasma to aid in the diagnosis of iron deficiency anemia and iron overload. This assay must be performed on the LIAISON® XL Analyzer. | Immunoassay for the in vitro quantitative determination of ferritin in human serum and plasma. The electrochemiluminescence immunoassay "ECLIA" is intended for use on Elecsys and cobas e immunoassay analyzers. |
| **Measured Analyte** | Ferritin | Same |
| **Assay Type** | Chemiluminescence immunoassay (CLIA) | Electrochemiluminescence immunoassay (ECLIA) |
| **Results** | Quantitative | Same |
| **Sample Type** | Human serum, SST serum, and lithium heparin plasma | Serum collected using standard sampling tubes (SST) or tubes containing separating gel; Li-, Na-heparin, K3-EDTA, and sodium citrate plasma. |
| **Sample Size** | 10 µL | 10 µL |
| **Storage** | 2-8°C | same |
| **Operating Principle** | Automated Chemiluminescent Immunoassay (CLIA) | Electrochemiluminescence immunoassay (ECLIA) |
| **Solid Phase** | Magnetic particles, coated with mouse monoclonal anti-ferritin antibody | Streptavidin-coated microparticles |
| **Conjugate** | Mouse monoclonal anti-ferritin antibody labelled with isoluminol | Mouse Monoclonal anti-ferritin antibody labeled with ruthenium complex |

| | | |
|---|---|---|
| **Analytical Measuring Range** | 0.46 – 2,200 ng/mL | 0.500 – 2,000 ng/mL. |
| **Calibrators** | 2 Levels, on board | 4 Levels (not provided with the kit) |

## 11. Standard/guidance Document Reference:

- CLSI Guideline EP5-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline.
- CLSI Guideline EP15-A3, User Verification of Precision and Estimation of Bias; Approved Guideline.
- CLSI Guideline EP EP07-A2, Interference Testing in Clinical Chemistry, Approved Guideline.
- CLSI Guideline EP06-A2, Evaluation of the Linearity of Quantitative Measurement Procedures; A Statistical Approach; Approved Guideline.
- CLSI Guideline EP 17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline.
- CLSI Guideline EP28-A3C, Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline.

## 12. Performance Characteristics:

Method Comparison

A total of 173 samples spanning the assay range, were tested by the LIAISON® Ferritin and by another commercially available method following CLSI EP09-A3, and yielded the following Passing & Bablok regression analysis:

LIAISON® Ferritin = 0.965x (Reference Method) - 1.12; $R^2$=0.99

| Passing & Bablok Fit | | | | | |
|---|---|---|---|---|---|
| n | Slope | 95% Confidence Interval (slope) | Intercept | 95% Confidence Interval (Intercept) | $R^2$ |
| 173 | 0.965 | 0.95 - 0.98 | -1.12 | -2.13 to -0.32 | 0.995 |

Sample Matrix Comparison

Thirty-seven (37) matched patient sets of serum, SST serum, and Lithium Heparin plasma samples and six (6) contrived matched patient samples to cover the full assay range were tested to determine if these sample types provide equivalent results on the LIAISON® Ferritin assay.

The results of the regression analysis (slope, intercept and correlation coefficient) of the 43 samples are reported in the following table.

**Sample matrix equivalence-summary**

| Sample Matrix | Slope (95% CI) | Intercept (95% CI) |
|---|---|---|
| **Serum versus SST** | 1.002 (0.9727 to 1.038) | 0.0179 (-0.7744 to 0.6374) |
| **Serum versus Li Heparin** | 0.984 (0.9413 to 0.9905) | -1.732 (-2.137 to -0.5159) |

Expected values/Reference Range

To determine the expected values of ferritin in an apparently normal population, a study was performed on a total of 78 human serum samples; 39 collected from apparently healthy female subjects, and 39 collected from apparently healthy male subjects, age 18 years or greater. The expected values study was conducted according to CLSI Approved Guideline EP28-A3C, "Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline-Third Edition".

It is recommended that each laboratory establish its own range of expected values for the population taken into consideration.
Reference range median value and observed range 5th to 95th percentile for each population, female and male, are reported here below:

Observed reference ranges:

| Gender | Population (N) | Median | Observed Range 5th to 95th Percentile |
|---|---|---|---|
| Female | 39 | 52.15 ng/mL | 6.29 – 317.1 ng/mL |
| Male | 39 | 124.3 ng/mL | 3.55 – 362.4 ng/mL |

Precision

Two kit controls and 6 samples containing concentrations of analyte prepared to span the range of the assay were assayed twice per day in duplicate, over twenty operating days on two LIAISON® XL Analyzer at DiaSorin GmbH using two reagent lots to determine reproducibility of the LIAISON® Ferritin assay. The testing was performed according to CLSI EP5-A3.

| Sample ID | n | Mean (ng/mL) | Repeatability | | Between Run | | Between Day | | Between Lot | | Between Instrument | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | SD | %CV | SD | %CV | SD | %CV | SD | %CV | SD | %CV | SD | %CV |
| Kit control 1 | 320 | 32.81 | 0.608 | 1.9 | 0.697 | 2.1 | 0.966 | 2.9 | 0.000 | 0.0 | 0.473 | 1.4 | 1.419 | 4.3 |
| Kit control 2 | 320 | 300 | 5.807 | 1.9 | 8.507 | 2.8 | 10.972 | 3.7 | 5.773 | 1.9 | 0.000 | 0.0 | 16.119 | 5.4 |
| Panel 1 | 320 | 5.84 | 0.148 | 2.5 | 0.146 | 2.5 | 0.173 | 3.0 | 0.139 | 2.4 | 0.119 | 2.0 | 0.326 | 5.6 |
| Panel 2 | 320 | 18.26 | 0.349 | 1.9 | 0.501 | 2.7 | 0.450 | 2.5 | 0.019 | 0.1 | 0.344 | 1.9 | 0.833 | 4.6 |
| Panel 3 | 320 | 178 | 2.584 | 1.5 | 4.600 | 2.6 | 4.040 | 2.3 | 2.895 | 1.6 | 0.000 | 0.0 | 7.248 | 4.1 |
| Panel 4 | 320 | 1093 | 18.77 | 1.7 | 32.103 | 2.9 | 30.696 | 2.8 | 38.051 | 3.5 | 0.000 | 0.0 | 61.426 | 5.6 |
| Panel 5 | 320 | 404.9 | 6.672 | 1.6 | 10.966 | 2.7 | 8.564 | 2.1 | 10.166 | 2.5 | 0.000 | 0.0 | 18.479 | 4.6 |
| Panel 6 | 320 | 1883 | 35.83 | 1.9 | 49.448 | 2.6 | 51.353 | 2.7 | 89.412 | 4.7 | 0.000 | 0.0 | 119.83 | 6.4 |

Linearity

Linearity studies were conducted according to CLSI EP06-A. A dilution series of four (4) samples with ferritin concentrations distributed throughout the assay range (0.46 – 2200 ng/mL) were prepared by diluting a serum pool spiked with ferritin (2000, 1500, 500 and 50 ng/mL) with a low serum pool (<1.5 ng/mL) or Specimen Diluent. Samples were analyzed with one replicate on a LIAISON® XL Analyzer using one (1) reagent lot.
The resulting linear regression equation for the sample with 2000 ng/mL ferritin is:

Observed Ferritin [ng/mL] = -1.402 + 1.006 *(Expected Ferritin [ng/mL]), $R^2$=1.000

Recovery Study

Four (4) representative human serum samples with low concentration of Ferritin were analyzed neat. Recovery samples were then prepared by addition of Ferritin antigen stock solution to obtain high and low Ferritin concentrations

**Recovery Results**

| Sample ID | Neat concentration [ng/mL] | Expected concentration [ng/mL] | Observed concentration [ng/mL] | Recovery (%) |
|---|---|---|---|---|
| Sample 1 | 31.11 | 90.86 | 91.43 | 101% |
| Sample 2 | 22.45 | 283.14 | 303.45 | 100% |
| Sample 3 | 17.20 | 76.95 | 79.06 | 104% |
| Sample 4 | 31.97 | 312.97 | 307.35 | 98% |
| Average Recovery | | | | 101% |

Cross Reactivity

| | |
|---|---|
| human liver ferritin | >100.0% |
| human spleen ferritin | 78.8% |

Interference Studies - Endogenous substances. exogenous substances

Controlled studies of potentially interfering substances performed in a human serum sample at a Ferritin level of approximately 20 ng/mL, 200 ng/mL and 2000 ng/mL showed no interference in the LIAISON® Ferritin assay at the highest concentration for each listed below. The testing was based on CLSI-EP07-A2.

| Drug / Substance | Concentration Tested |
|---|---|
| **Human Albumin** | 60 mg/mL |
| **Triglyceride** | 30 mg/mL |
| **Hämoglobin** | 10 mg/mL |
| **Conjugated Bilirubin** | 0.2 mg/mL |
| **Unconjugated Bilirubin** | 0.2 mg/mL |
| **Acetominophen** | 0.2 mg/mL |
| **Acetylsalicylic acid** | 0.5 µg/ml |
| **Ampilicin** | 0.05311 mg/mL |
| **L-Ascorbin acid** | 1.76 mg/mL |

| Drug / Substance | Concentration Tested |
|---|---|
| **Dobesilate Calcium Monohydrate** | 0.0333 mg/mL |
| **Ferrous sulfate** | 0.1519 mg/mL |
| **Ibuprofen** | 0.5 mg/mL |
| **Levodopa** | 0.256 mg/mL |
| **Methotrexate hydrate** | 0.909 mg/mL |
| **Metronidazole** | 0.119 mg/mL |
| **N-Acety-L cysteine** | 2.87 mg/mL |
| **Phenylbutazone** | 0.2 mg/mL |
| **Prednison** | 0.18 mg/mL |
| **Rifampicin** | 0.06427 mg/mL |
| **Theophylline** | 0.03999 mg/mL |
| **Valproinacid** | 0.505 mg/mL |

Limit of Blank, Limit of Detection and Limit of Quantitation

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined according to CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline June 2012- Second Edition.

The following limits were determined with the LIAISON® Ferritin assay:

| LoB | LoD | LoQ |
|---|---|---|
| 0.004 ng/mL | <0.073 ng/mL | <0.046 ng/mL |

Stability

| Product | Storage Conditions | | Claimed stability |
|---|---|---|---|
| Reagent Integral | Open vial | on system | 8 weeks |
| Reagent Integral | Open vial | 2-8°C | 8 weeks |
| Calibration curve | N/A | N/A | 8 weeks |

Traceability

The LIAISON® Ferritin Calibrators are traceable to an internal reference standard oriented at the 2nd reference standard NIBSC 94/572.

## 13. Conclusion:

The LIAISON® Ferritin assay is substantially equivalent in principle and performance to the Roche Elecsys® Ferritin assay.