December 13, 2023

Siemens Healthcare Diagnostics Products GmbH
Dr. Sanja Matern
Regulatory Affairs Manager, Head of Product Group, Regulatory Affairs Marburg
Emil-von-Behring-Str. 76
Marburg, Hesse 35041
Germany

Re: K233663
Trade/Device Name: N Antisera to Human Immunoglobulins (IgG, IgA, and IgM)
Regulation Number: 21 CFR 866.5510
Regulation Name: Immunoglobulins A, G, M, D, and E Immunological Test System
Regulatory Class: Class II
Product Code: CFN
Dated: November 15, 2023
Received: November 15, 2023

Dear Sanja Matern:

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 and Part 809); 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,

Ying Mao -S

Ying Mao, Ph.D.
Branch Chief
Division of Immunology and Hematology Devices
OHT7: Office of In Vitro Diagnostics
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: 07/31/2026
*See PRA Statement below.*

510(k) Number *(if known)*
K233663

Device Name
N Antisera to Human Immunoglobulins (IgG, IgA, and IgM)

Indications for Use *(Describe)*
In-vitro diagnostic reagents for the quantitative determination of immunoglobulins (IgG, IgA and IgM) in human serum, heparinized and EDTA plasma, and IgG in human urine and cerebrospinal fluid (CSF) by means of immunonephelometry on the BN II and BN ProSpec® System. Measurements of IgG aid in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.

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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# Special 510(k) Summary K233663

This summary of the special 510(k) safety and effectiveness information is submitted in accordance with the requirements of 21 CFR §807.92, the Safe Medical Act of 1990, and follows the FDA guidance 'The Special 510(k) Program: Guidance for Industry and Food and Drug Administration Staff', issued September 13, 2019.

## 1. Applicant


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35041 Marburg, Germany

| | |
|---|---|
| Contact Person: | Dr. Sanja Matern |
| Email: | sanja.matern@siemens-healthineers.com |
| Phone: | +49 (173) 3239008 |
| Date Prepared: | December 13, 2023 |


## 2. Device

| | |
|---|---|
| Name of Device: | N Antisera to Human Immunoglobulins (IgG, IgA, and IgM) |
| Regulation Number: | 21 CFR 866.5510 |
| Regulation Description: | Immunoglobulins A, G, M, D, and E immunological test system. |
| Product Code: | CFN |
| Device Classification Name: | Method, Nephelometric, Immunoglobulins (G, A, M) |
| Regulatory Class: | Class II |
| 510(k) Review Panel | Immunology (82) |

## 3. Predicate Device

| | |
|---|---|
| Name of Device / 510(k): | N Antisera to Human Immunoglobulins (IgG, IgA, and IgM) / K083445 |
| Regulation Number: | 21 CFR 866.5510 |
| Regulation Description: | Immunoglobulins A, G, M, D, and E immunological test system. |
| Product Code: | CFN |
| Device Classification Name: | Method, Nephelometric, Immunoglobulins (G, A, M) |
| Regulatory Class: | Class II |
| 510(k) Review Panel | Immunology (82) |

A Class 2 Device Recall N Antisera to Human Immunoglobulins (IgG, IgA, and IgM) was issued on August 30, 2022. Despite there was no High Dose Hook (HDH) Effect claim for the determination of Immunoglobulin G in cerebrospinal fluid (CSF) samples, customer expectations were not met. Therefore, we now would like to introduce a HDH claim for CSF samples.

## 4. Device Description / Test Principle

The Intended Use, Composition and test principle for the device N Antisera to Human Immunoglobulins (IgG, IgA, and IgM) as stated in the Package Insert:

In-vitro diagnostic reagents for the quantitative determination of immunoglobulins (IgG, IgA and IgM) in human serum, heparinized and EDTA plasma, and IgG in human urine and cerebrospinal fluid (CSF) by means of immunonephelometry on the BN II and BN ProSpec® System. Measurements of IgG aid in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.

The N Antiserum to Human IgG reagent containing animal serum, produced by immunization of rabbits with highly purified human immunoglobulin (< 3.5 g/L). The reagent is a ready-to-use liquid containing preservatives.

There are two product variants available. One variant (REF OSAS11) contains 1 x 2 mL vial / box, and the other variant (REF OSAS19) contains 1 x 5 mL vial / box.

Proteins contained in human body fluids form immune complexes in an immunochemical reaction with specific antibodies. These complexes scatter a beam of light passed through the sample. The intensity of the scattered light is proportional to the concentration of the relevant protein in the sample. The result is evaluated by comparison with a standard of known concentration.

## 5. Intended Use / Indications for Use

In-vitro diagnostic reagents for the quantitative determination of immunoglobulins (IgG, IgA and IgM) in human serum, heparinized and EDTA plasma, and IgG in human urine and cerebrospinal fluid (CSF) by means of immunonephelometry on the BN II and BN ProSpec® System. Measurements of IgG aid in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.

(Comment: The outer box label presents the symbol 'RxOnly' instead of a written statement 'and intended for prescription use')

## 6. Special instrument requirements:

BN II System (K943997)

BN ProSpec System (K001647)

Both analyzers together are summarized as BN Systems (nephelometry)

## 7. Purpose of Submission

The purpose of this submission is a special 510(k) premarket notification for a modified device: N Antisera to Human Immunoglobulins (IgG, IgA, and IgM). This device was modified by enclosing a HDH effect claim for CSF samples (IgG).

A special 510(k) Premarket Notification is the requested pathway because of the following:

- The change is to the manufacturer's own legally marketed device.
- There is no change to the intended use or indications for use.
- There is no change in the fundamental scientific technology.

- There is no change to the principle of operation.
- There is no change to the formulation.
- There is no change to the instrument parameters related to sample volume, reagent volume, mix speed, wavelengths, or read times.

## 8. Comparison of Technological Characteristics with the Predicate Device

The following table presents a comparison of the similarities and differences between the proposed device N Antisera to Human Immunoglobulins (IgG, IgA, and IgM) and the predicate device N Antisera to Human Immunoglobulins (IgG, IgA, and IgM) (K083445). Enclosing a HDH effect claim for CSF samples for IgG. This is the only difference between the modified device and predicate device.

| **Similarities and differences between the predicate and the proposed device** | | |
|---|---|---|
| **Item** | **<u>Predicate Device</u><br>Siemens Healthineers<br>N Antisera to Human Immunoglobulins (IgG, IgA, and IgM) (K083445)** | **<u>Proposed Device</u><br>Siemens Healthineers<br>N Antisera to Human Immunoglobulins (IgG, IgA, and IgM)** |
| **Regulation Number**<br>**Regulation Description**<br><br>**Regulatory Class**<br>**510(k) Review Panel** | 21 CFR 866.5510<br>Immunoglobulins A, G, M, D, and E immunological test system<br>Class II<br>Immunology (82) | Same<br>Same<br><br>Same<br>Same |
| **Product Code**<br><br>**Device Classification Name** | CFN<br><br>Method, Nephelometric, Immunoglobulins (G, A, M) | Same<br><br>Same |
| **Indications for Use / Intended Use** | In-vitro diagnostic reagents for the quantitative determination of immunoglobulins (IgG, IgA and IgM) in human serum, heparinized and EDTA plasma, and IgG in human urine and cerebrospinal fluid (CSF) by means of immunonephelometry on the BN II and BN ProSpec® System. Measurements of IgG aid in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents. | Same |
| **Sample Type** | Human serum, heparinized and EDTA plasma, urine and cerebrospinal fluid (CSF) | Same |

| Similarities and differences between the predicate and the proposed device | | |
|---|---|---|
| **Item** | **Predicate Device**<br>**Siemens Healthineers N Antisera to Human Immunoglobulins (IgG, IgA, and IgM) (K083445)** | **Proposed Device**<br>**Siemens Healthineers N Antisera to Human Immunoglobulins (IgG, IgA, and IgM)** |
| **Analyte** | Immunoglobulin (IgG) | Same |
| **Units** | g/L | Same |
| **Measurement** | Quantitative | Same |
| **Test Principle**<br>biochemical principle of reagent | Proteins contained in human body fluids form immune complexes in an immunochemical reaction with specific antibodies. These complexes scatter a beam of light passed through the sample. The intensity of the scattered light is proportional to the concentration of the respective protein in the sample. The result is evaluated by comparison with a standard of known concentration. | Same |
| **Reagent Composition** | N Antisera are liquid animal sera and are produced by immunization of rabbits with highly purified human immunoglobulin (IgG). As preservative sodium azide is used. | Same |
| **Form** | Liquid suspension | Same |
| **Calibrator** | N Protein Standard SL | Same |
| **Traceability/Standardization** | Traceable to ERM-DA470k/IFCC | Same |
| **Calibrator Levels** | One level (one standard diluted to either six concentration levels (serum and CSF samples) or five concentrations levels (urine samples) | Same |

| Similarities and differences between the predicate and the proposed device | | |
|---|---|---|
| **Item** | **Predicate Device**<br>**Siemens Healthineers N Antisera to Human Immunoglobulins (IgG, IgA, and IgM) (K083445)** | **Proposed Device**<br>**Siemens Healthineers N Antisera to Human Immunoglobulins (IgG, IgA, and IgM)** |
| **Storage** | Stability:<br>Until expiration date (indicated on the box label) when stored at 2 – 8°C<br>Stability once opened:<br>four weeks stored at 2 – 8°C | Same |
| **Sample stability** | Serum and Plasma samples:<br>- Fresh samples up to 8 days when stored at 2 – 8°C<br>- Frozen samples up to 3 months when stored at -20°C<br>Urine samples:<br>- Only fresh samples up to 3 days when stored at 2 – 8°C<br>CSF samples:<br>- Only fresh samples up to 7 days when stored at 2 – 8°C | Same |
| **Antigen excess**<br>**(High Dose Hook Effect)** | Serum and Plasma samples:<br>- n/a<br>Urine samples:<br>- 998 mg/L<br>CSF Samples:<br>- n/a | Serum and Plasma samples:<br>- same<br>Urine samples:<br>- Same<br>CSF Samples:<br>- 1130 mg/L |
| **Analytical Measuring Range** | Serum and Plasma samples:<br>1.4 – 46.0 g/L<br>Urine samples:<br>3.6 – 58.0 mg/L | Same |

| Similarities and differences between the predicate and the proposed device | | |
|---|---|---|
| **Item** | **Predicate Device**<br>**Siemens Healthineers N Antisera to Human Immunoglobulins (IgG, IgA, and IgM) (K083445)** | **Proposed Device**<br>**Siemens Healthineers N Antisera to Human Immunoglobulins (IgG, IgA, and IgM)** |
| | CSF samples:<br>3.6 – 115 mg/L | |
| **Expected Values** | Serum and Plasma samples: 7 – 16 g/L<br><br>Urine samples: in second morning urine < 9.6 mg/L<br><br>CSF Samples: < 34 mg/L3 | Same |

The difference between the predicate device and proposed device does not result in a change to the intended use, the indications for use, or to safety and efficacy when used according to the product labeling.

## 9. Summary of Design Control Activities

A risk analysis according to ISO 14971 was performed with risks identified. No new risks were introduced. Further mitigation of risk to acceptable level was achieved through verification activities summarized below and proposed change in instructions for use to inform the user about the HDH CSF limit concentration.

The risk analysis supports that the modification of N Antiserum to Human IgG assay does not introduce any new risk to the performance of the assay.

Enclosing a High Dose Hook effect claim for CSF samples for the N Antiserum to Human IgG assay is the only change. The reagent, packaging and instruments used for analysis remain unchanged.

### 9.2. Verification Activities

Based on the results of the risk analysis, a High Dose Hook study was identified as verification activity and acceptance criteria established.

### 9.3. Performance Studies

A High Dose Hook study was performed for the establishment of High Dose Hook limit.

### 9.3.1 High Dose Hook Study

A High Dose Hook study was designed based on a previous High Dose Hook study performed within K083445. A CSF high sample pool was measured within a dilution scheme with twelve (12) individual dilution levels, including the neat sample with a concentration of 1130 mg/L. The study was performed with three (3) independent lots of N Antiserum to Human IgG assay on the BN II System. An acceptance

criteria of a minimum High Dose Hook limit of up to 412 mg/L was defined. High Dose Hook limit was shown for all three lots up to the maximum measured concentration of 1130 mg/L.

## 10. Comments on Substantial Equivalency

The Siemens Healthcare Diagnostics Products GmbH confirms that the data presented in this special 510(k) premarket notification as well as the descriptions of similarities and differences support a decision of substantial equivalence between the modified (proposed) N Antisera to Human Immunoglobulins (IgG, IgA, and IgM) and the predicate device, N Antisera to Human Immunoglobulins (IgG, IgA, and IgM) (K083445). These two medical devices have the same intended uses, technology and performance specifications. Therefore, a premarket clearance is supported based on the performance testing data provided in this submission.

## 11. Conclusion

The presented data supports FDA's substantial equivalence decision for enclosing a High Dose Hook effect claim for CSF samples of the N Antisera to Human Immunoglobulins (IgG, IgA, and IgM) IgG assay on the BN systems compared to the predicate device, N Antisera to Human Immunoglobulins (IgG, IgA, and IgM) (K083445).

The data submitted for this premarket notification demonstrates that the device raises no concerns regarding safety and effectiveness.