January 15, 2021

Siemens Healthcare Diagnostics Products Ltd.
Malgorzata Robak
Regulatory Affairs Supervisor
Glyn Rhonwy, Llanberis
Caernarfon, Gwynedd LL55 4EL
UK

Re: K203270
Trade/Device Name: IMMULITE/IMMULITE® 1000 Cortisol
Regulation Number: 21 CFR 862.1205
Regulation Name: Cortisol (Hydrocortisone And Hydroxycorticosterone) Test System
Regulatory Class: Class II
Product Code: CGR
Dated: November 3, 2020
Received: November 5, 2020

Dear Malgorzata Robak:

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,

Kellie B. Kelm, Ph.D.
Director
Division of Chemistry and Toxicology 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)*
K203270

Device Name
IMMULITE/IMMULITE® 1000 Cortisol

Indications for Use *(Describe)*
For in vitro diagnostic use with the IMMULITE® and IMMULITE 1000 Analyzers — for the quantitative measurement of cortisol (hydrocortisone, Compound F) in serum, as an aid in the clinical assessment of adrenal status.

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 of Safety and Effectiveness for IMMULITE/IMMULITE® 1000 Cortisol

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

A. 510(k) Number: k203270

B. Purpose of the Submission
Modified Device – new supplier of the antibody

C. Applicant:

Contact: Malgorzata Robak
Regulatory Affairs Supervisor
Address: Siemens Healthcare Diagnostics Products Limited
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Llanberis, Caernarfon
LL55 4EL
United Kingdom
Phone: +44 7921 882559
E-mail: malgorzata.robak@siemens-healthineers.com

Date: **January 8, 2021**

D. Proprietary and Established Name:

IMMULITE/IMMULITE® 1000 Cortisol

E. Measurand

Cortisol

F. Regulatory Information

Trade Name:	IMMULITE/IMMULITE® 1000 Cortisol
Common Name:	Chemiluminescence Immunoassay, for the determination of Cortisol
Classification Name:	Cortisol Test System
FDA Classification:	Class II
Review Panel:	Clinical Chemistry
Product Code:	CRG
Regulation Number:	21 CFR 862.1205

G. Predicate Device:

Device Name: IMMULITE/IMMULITE® 1000 Cortisol

510(k) Number: K931409

H. Intended Use:

Same as Indication for Use

I. Indications for Use:

For in vitro diagnostic use with the IMMULITE® and IMMULITE 1000 Analyzers — for the quantitative measurement of cortisol (hydrocortisone, Compound F) in serum, as an aid in the clinical assessment of adrenal status.

J. Special Conditions for Use statement(s):

For Prescription Use Only

K. Special Instrument Requirements

For use with IMMULITE/IMMULITE® 1000

L. Device Description

The IMMULITE/IMMULITE® 1000 Cortisol assay is comprised of the following components:

Component	Volume	Ingredients
Cortisol Test Unit (solid phase)	1 bead/Test unit	Polyclonal rabbit anti-cortisol antibody.
Cortisol Reagent Wedge (liquid phase)	7.5 mL	Alkaline phosphatase (bovine calf intestine) conjugated to cortisol in buffer, with preservative.
Cortisol Adjustors (Low and High)	3 mL	Cortisol in processed human serum, with preservative.

M. Substantial Equivalence Information

The following table demonstrates substantial equivalence between the IMMULITE/IMMULITE® 1000 Cortisol (Candidate Device) with an antibody from a new supplier and the currently marketed IMMULITE/IMMULITE® 1000 Cortisol (Predicate Device) that was cleared under 510 (k) K931409.

Trade name	Candidate Device (Modified) IMMULITE/IMMULITE® 1000 Cortisol	Predicate device (Unmodified) IMMULITE/IMMULITE® 1000 Cortisol
Intended Use	For in vitro diagnostic use with the IMMULITE® and IMMULITE 1000 Analyzers — for the quantitative measurement of cortisol (hydrocortisone, Compound F) in serum, as an aid in the clinical assessment of adrenal status.	For in vitro diagnostic use with the IMMULITE® and IMMULITE 1000 Analyzers — for the quantitative measurement of cortisol (hydrocortisone, Compound F) in serum, as an aid in the clinical assessment of adrenal status.
Analyte	Cortisol	Same

Trade name	Candidate Device (Modified) IMMULITE/IMMULITE® 1000 Cortisol	Predicate device (Unmodified) IMMULITE/IMMULITE® 1000 Cortisol
Automated	Automated Assay	Same
Measurement	Quantitative	Same
Sample Type	Human serum	Same
Detection Limit	LoB: 0.008µg/dL (0.22nmol/L)	Analytical Sensitivity: 0.20 µg/dL (5.5 nmol/L)
	LoD: 0.053µg/dL (1.46nmol/L)	Not Applicable
	LoQ: 0.2µg/dL (5.52nmol/L)	Not Applicable
Calibration Range	1-50 µg/dL (28 to 1380 nmol/L)	Same
Operating Principle	Competitive	Same
Technology	Chemiluminescent enzyme immunoassay	Same
Instrument	IMMULITE/MMULITE 1000	Same
Sample Volume	10 µL	10 µL
Calibrator	Two levels (low & high) cortisol adjustor	Same
Controls	Commercial	Commercial
Detection Enzyme conjugate	Alkaline phosphatase (bovine calf intestine) conjugated to cortisol	Same
Capture Antibody	Polyclonal rabbit anti-cortisol	Same

N. Test Principle

IMMULITE/IMMULITE 1000 Cortisol is a solid-phase, enzyme-labeled chemiluminescent competitive immunoassay. The solid phase (bead) is coated with polyclonal rabbit anti-cortisol antibody. The liquid phase consists of alkaline phosphatase (bovine calf intestine) conjugated to cortisol. The patient sample and the reagent are incubated together with the coated bead for 30 minutes. During this time, cortisol in the sample competes with enzyme-conjugated cortisol in the reagent for a limited number of antibody binding sites on the bead. Unbound patient sample and enzyme conjugate are then removed by centrifugal washes. Finally, chemiluminescent substrate is added to the test unit containing the bead and the signal is generated inversely proportion to the bound enzyme.

O. Performance Characteristics

The assay principle, design and reagent formulation has not changed from the original device. Substantial equivalence was demonstrated by testing several performance characteristics including detection limits, linearity, precision, spike recovery, method comparison, interfering and cross-reactive substances. All the studies evaluated produced acceptable results when compared to the Predicate device and were deemed verified.

1. Detection Limits

LoB, LoD, and LoQ were determined in accordance with *Clinical and Laboratory Standards Institute (CLSI) EP17-A2*: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline—Second Edition The LoB/LoD/LoQ estimates are summarized below:

Limit of Blank (LoB)	0.008µg/dL (0.22nmol/L)
Limit of Detection (LoD)	0.053µg/dL (1.46nmol/L)
Limit of Quantitation (LoQ)	0.2µg/dL (5.52nmol/L)

The reportable range of the IMMULITE/IMMULITE 1000 Cortisol assay is 1 to 50 µg/dL (28 to 1380 nmol/L).

2. Linearity

The Linearity study was conducted in accordance with the principles described in *CLSI EP06-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline*. Samples spanning the assay range were prepared by combining a high human serum pool with a low human serum pool for a total of 9 levels of dilutions prepared by mixing the high and low serum pools. The high serum pool consisted of a human serum pool sample spiked with cortisol to obtain a desired cortisol concentration at the upper end of the working range of the assay (observed concentration: 50.98µg/dL). The low serum pool consisted of a low-level human serum pool diluted with charcoal-adsorbed human serum in order to achieve a cortisol concentration at the approximate LoQ (observed concentration: 0.18 µg/dL). The modified IMMULITE/IMMULITE 1000 Cortisol assay has been shown to be linear from 0.18 – 50.98 µg/dL. The Linearity information provided in the Instruction for Use for modified IMMULITE/IMMULITE 1000 Cortisol has not changed and are as per K931409.

3. Repeatability and Within-Lab Precision

The repeatability and within-lab precision information provided in the Instruction for Use for modified IMMULITE/IMMULITE 1000 Cortisol has not changed and are as per K931409.

4. Spike Recovery

The spike and recovery information provided in the Instruction for Use for modified IMMULITE/IMMULITE 1000 Cortisol has not changed and are as per K931409.

5. Method Comparison with predicate device

A method comparison study was performed by comparing the modified device to the currently-marketed predicate device (unmodified IMMULITE/IMMULITE 1000 Cortisol Assay) in accordance with *CLSI EP09c Measurement Procedure Comparison and Bias Estimation Using Patient Samples, 3rd Edition.* A total of 152 native patient samples covering the full range of the assay were assayed in duplicate split across 4 runs, with each run on a different instrument (41 patients on instrument 1-3, and 30 patients on instrument 4).

Sample Category	**N**	**Range**	**Regression equation**
Serum	152	2.01 – 48.3 µg/dL	IMM 1000 = 0.951 (IMMULITE 1000 commercial) - 0.155 µg/dL. r=0.991

6. Specificity (Cross-Reactivity)

Specificity (cross-reactivity) of the modified IMMULITE/IMMULITE 1000 Cortisol assay to the various compounds listed in the Table below were evaluated. Cross-reactant solutions were prepared by dissolving each cross-reactant into an appropriate solvent (ethanol, methanol or NaOH). Each cross-reactant was then spiked at a ratio of 1:19 into an aliquot of a blank sample (charcoal-absorbed human serum) such that the final concentration in the sample was equal to that outlined in Table below. Blank samples were also prepared which consisted of charcoal-adsorbed human serum spiked 1:19 with the solvents used to prepare the cross-reactants. In addition to the cross reactants evaluated in K931409 the following cross reactants were evaluated: Allotetrahydrocortisol, α-Cortol, α-Cortolone, β-Cortol' β-Cortolone, Dehydrocorticosterone 20α-Dihydrocortisol, 20β-Dihydrocortisol, 20α-Dihydrocortisone, Estradiol, Fludrocortisone. Complete summary of the results are summarized below.

Compound	Cross-Reactant added concentration (µg/dL)	% Cross- Reactivity
Blank (Methanol)	N/A	N/A
Blank (Ethanol)	N/A	N/A
Blank (NaOH)	N/A	N/A
Aldosterone	1,000	ND
Androstenedione	10,000	ND

Compound	Cross-Reactant added concentration (µg/dL)	% Cross- Reactivity
Betamethasone	1,000	ND
Corticosterone	400	0.92%
Cortisone	400	1.77%
11-Deoxycorticosterone	400	ND
11-Deoxycortisol	100	4.05%
21-Deoxycortisone	500	ND
Dexamethasone	400	ND
DHEA-SO4	10,000	ND
Estriol	100	ND
Estrone	500	ND
Fludrocortisone	1,000	ND
Fluticasone	22	ND
17α-hydroxyprogesterone	400	ND
Methotrexate	100	ND
Methylprednisolone	200	1.12%
Prednisolone	8	16.01%
Prednisone	16	ND
Pregnanediol	2,000	ND
Progesterone	400	ND
Spironolactone	1,000	ND
Tetrahydrocortisol	1,000	ND
Tetrahydrocortisone	400	ND
Triamcinolone	5,000	ND
Allotetrahydrocortisol	100	2.06%
α-Cortolone	1,000	ND
a-Cortol	1000	ND
β-Cortol	1,000	ND
β-Cortolone	1,000	ND
11-Dehydrocorticosterone	1000	ND
20α-dihydrocortisol	1,000	0.28%
20β-dihydrocortisol	1000	ND
20α-dihydrocortisone	1,000	ND
Estradiol	1,000	ND

7. Interference

Interference with the modified IMMULITE/IMMULITE 1000 Cortisol assay was determined for the following substances: conjugated and unconjugated bilirubin, hemolysate, hemoglobin, intralipid and biotin. The paired difference approach was employed for this study as per CLSI EP07: Interference Testing in Clinical Chemistry, 3rd Edition. Working stock solutions of the interfering substance were prepared and spiked into 5 patient samples such that the final interferent concentration in the sample was equal to that found in Table below. The 5 patient samples ranged from 3.3 – 23.1 µg/dL. The interference information for Bilirubin, Hemolysis and Lipemia provided in the Instruction for Use for modified IMMULITE/IMMULITE 1000 Cortisol has not changed and are as per K931409. Information regarding Biotin interference are summarized below:

Interfering Substance	Interfering substance spiking concentration	Observed Mean % Recovery
Biotin	3500ng/mL	96.0%

8. Clinical Evaluation

Not applicable

P. Conclusion

Based on the results of comparative testing, the modified IMMULITE/ IMMULITE 1000 Cortisol is substantially equivalent to the currently marketed predicate device, IMMULITE/IMMULITE 1000 Cortisol.