August 18, 2023

Immunodiagnostic Systems Limited
Mick Henderson
Regulatory Affairs Manager
10 Didcot Way, Boldon Business Park
Boldon, Tyne and Wear NE35 9PD
United Kingdom

Re: K223867
Trade/Device Name: IDS ACTH II
Regulation Number: 21 CFR 862.1025
Regulation Name: Adrenocorticotropic Hormone (ACTH) Test System
Regulatory Class: Class II
Product Code: CKG
Dated: July 21, 2023
Received: July 24, 2023

Dear Mick Henderson:

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
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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)*
k223687

Device Name
IDS ACTH II

Indications for Use *(Describe)*
IDS ACTH II assay is an automated in vitro diagnostic device intended for the quantitative, determination of ACTH in human K2 and K3 EDTA plasma on the IDS system. Results are to be used in conjunction with other clinical and laboratory data as an aid in the assessment of pituitary and adrenal gland function and the differential diagnosis of hyper- and hypo-cortisolism.

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

510k Number k223867

Introduction According to the requirements of 21CFR807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence.

Submitter

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Date prepared: 16 August 2023

Device Name

Proprietary names:	IDS ACTH II
Common names:	As above
Classification:	21 CFR 862.1025 Adrenocorticotropic hormone (ACTH) test system. Class 2
Product Code:	CKG

Predicate Device Roche Elecsys ACTH (k060585).

Device Description The IDS ACTH II assay consists of a reagent cartridge. The reagent cartridge contains multiple reagents:

- MP: Magnetic particles coated with mouse monoclonal anti-ACTH antibody and buffer containing phosphate with blocking proteins and ProClin 300 as preservative.
- R1: Mouse monoclonal anti-ACTH antibody labelled with an acridinium ester derivative, in buffer containing phosphate with BSA and ProClin 300 as preservative.
- R2: Buffer containing phosphate with blocking proteins and ProClin 300 as preservative.

Indications for Use

IDS ACTH II assay is an automated *in vitro* diagnostic device intended for the quantitative, determination of ACTH in human K_2 and K_3 EDTA plasma on the IDS system. Results are to be used in conjunction with other clinical and laboratory data as an aid in the assessment of pituitary and adrenal gland function and the differential diagnosis of hyper- and hypo-cortisolism.

Conditions for use For in vitro diagnostic use only.
Rx Only

Special instrument Requirements:

IDS-iSYS Multi-Discipline Automated System (k091849)

Comparison Tables

Similarities compared to the chosen predicate device (k060585)

Assay Performance	**Predicate Device ROCHE ELECSYS- ACTH (k060585)**	**Candidate Device IDS ACTH II**
Intended Use	ACTH measurements are used in the differential diagnosis and treatment of certain disorders of the adrenal glands such as Cushings syndrome, adrenocortival insufficiency, and the ectopic ACTH syndrome.	same
Method of detection (Test methodology)	Chemiluminescence	same
Assay protocol	Sandwich assay	same

Differences compared to the chosen predicate device (k060585)

Assay Performance	**Predicate Device ROCHE ELECSYS- ACTH (k060585)**	**Candidate Device IDS ACTH II**
Indications for Use	Immunoassay for the in vitro quantitative determination of adrenocorticotropic hormone (ACTH) in human EDTA plasma. The electrochemiluminescence immunoassay "ECLIA" is intended for use on the Roche Elecsys 1010/2010 and MODULAR ANALYTICS E 170 (Elecsys module) immunoassay analyzers.	IDS ACTH II assay is an automated *in vitro* diagnostic device intended for the quantitative, determination of ACTH in human K_2 and K_3 EDTA plasma on the IDS system. Results are to be used in conjunction with other clinical and laboratory data as an aid in the assessment of pituitary and adrenal gland function and the differential diagnosis of hyper- and hypo-cortisolism.
Sample type	Human plasma treated with K_3-EDTA	Human plasma treated with K_2 and K_3-EDTA
Sample Volume	50 µL	150 µL

Measuring Range	1 – 2,000 pg/mL	4 – 1,000 pg/mL

Performance Characteristics

Analytical Limits at Low levels

The limit of blank (LoB), limit of detection (LoD) and limit of quantitation (LoQ) were determined with guidance from CLSI EP17-A, "Protocols for Determination of Limits of Detection and Limits of Quantitation". LoB and LoD were determined with 60 replicates of 4 blank samples and 6 low concentration samples per reagent lot. LoQ was determined with 90 replicates of 6 low concentration samples per reagent lot. The LoQ was determined as the lowest concentration with a within-laboratory precision CV ≤ 20%".

Sensitivity	Concentration (pg/mL)
Limit of Blank (LoB)	0
Limit of Detection (LoD)	1
Limit of Quantitation (LoQ)	3

Precision (Repeatability/Reproducibility)

Precision was evaluated based on guidance from CLSI EP05-A3 3rd Edition, "Evaluation of Precision Performance of Quantitative Measurement Methods".

Repeatability

A total of 5 plasma samples were tested using 1 lot of reagents in duplicate, twice a day for 20 days on 1 system to assess the repeatability.

Results from one (1) representative reagents lot on one (1) system:

Sample	N	Mean Conc. (pg/mL)	Repeatability (Within Run)		Within Laboratory	
			SD	CV%	SD	CV
1	80	6	0.8	14.5%	1.5	26.8%
2	80	13	0.7	5.3%	1.6	12.8%
3	80	81	0.9	1.2%	2.5	3.1%
4	80	215	3.1	1.4%	5.3	2.5%
5	80	616	5.5	0.9%	10.5	1.7%

Reproducibility – between sites / systems

A total of 5 plasma sample were tested using one (1) reagents lot in 5 replicates, once a day for 5 days on 3 systems by 1 operator per system to determine the reproducibility.

Sample	N	Mean Conc. (pg/mL)	Repeatability		Reproducibility	
			SD	CV%	SD	CV%
1	75	4	0.6	14.4%	1.0	24.8%
2	75	17	0.6	3.6%	1.2	7.2%
3	75	59	1.5	2.5%	3.5	6.0%
4	75	213	2.9	1.4%	9.3	4.4%
5	75	615	7.5	1.2%	27.8	4.5%

Reproducibility - between lots

A total of 5 plasma samples were tested using three (3) reagents lot in 5 replicates, once a day for 5 days on 1 system by 1 operator per system to determine the reproducibility.

Sample	N	Mean Conc. (pg/mL)	Between-Run		Between-Day		Reproducibility	
			SD	CV%	SD	CV%	SD	CV%
1	75	4	0.8	20.8%	1.4	35.2%	2.0	50.5%
2	75	17	0.7	4.1%	0.9	5.5%	1.8	10.9%
3	75	61	0.8	1.3%	1.5	2.5%	1.9	3.2%
4	75	217	1.7	0.8%	4.1	1.9%	7.6	3.5%
5	75	645	3.8	0.6%	7.3	1.1%	31.8	4.9%

Linearity

A Linearity study was performed based on guidance from CLSI EP06 2nd Edition, "Evaluation of the Linearity of Quantitative Measurement Procedures". The IDS ACTH II is linear across the analytical measuring interval of 4 to 1000 pg/mL, within the allowable deviation of linearity (ADL) of ≤ ±16.3% or ≤ ±4 pg/mL for concentration below 20 pg/mL

Analytical Specificity

Interference

Interference and cross-reactivity studies were performed in accordance with the CLSI EP07-A3 Interference. The Interference study was performed in 2 samples containing 15 and 200 pg/mL concentrations of ACTH.

The Interference using paired-difference testing was calculated using the following equation:

$$\% \text{ Interference } = \frac{(\text{Average “spiked” concentration} - \text{ Average “control” concentration})}{\text{Average "control'' concentration}} \text{x100}$$

- The Interference using recovery testing was calculated using the following equation:

$$\% \text{ Recovery} = \frac{\text{Observed concentration}}{(\text{Expected base sample concentration } + \text{ Expected spiked sample concentration})} \text{x100}$$

- The Interference using method comparison testing was analyzed as follow:
  - Calculate the mean of candidate device.
  - Calculate the concentration difference of predicate device and mean candidate device in samples ≤ 20 pg/mL.
  - Calculate the relative difference (%bias) of predicate device and mean candidate device in samples above 20 pg/mL.

No significant interference (≤±10% bias, Cholesterol ≤±15%) was observed when the interfering agents were tested up to the following threshold concentration:

Potentially Interfering Agent	Threshold Concentration
Bilirubin, conjugated	40 mg/dL
Bilirubin, unconjugated	40 mg/dL
Biotin	3.5 µg/mL
Haemoglobin	62.5 mg/dL
Human Anti Mouse Antibody (HAMA)	1000 ng/mL
Rheumatoid Factor	324 IU/mL
Total Protein	15 g/dL
Triglyceride	1500 mg/dL
Acetaminophen	15.6 mg/dL
Acetylsalicylic acid	3 mg/dL
Ampicillin	7.5 mg/dL
Ibuprofen	21.9 mg/dL
Dexamethasone	1.2 mg/dL
Metyrapone	1.8 mg/mL

- The total Cholesterol interference study was performed in 2 samples containing 30 and 500 pg/mL concentrations of ACTH. No significant interference (≤±10% bias) was observed when total Cholesterol was tested up to 400 mg/dL.
- "The lowest Hemoglobin level that does not significantly interfere (≤±10% bias) with the assay is 62.5 mg/dL. Visual hemolysis in the sample is typically already seen in samples with hemoglobin concentration of 50 mg/dL or greater [Hemolysis_Palette_Bookmark-P.pdf (cdc.gov)]. Visibly hemolyzed samples must not be used with IDS ACTH II assay.
- "The lowest Rheumatoid Factor (RF) level that does not significantly interfere (≤±10% bias) with IDS ACTH II assay is 324 IU/mL."

Cross-Reactivity

The analytical specificity study was conducted by spiking the compounds in 2 samples containing 20 and 400 pg/mL concentrations of ACTH.

The cross reactivity was determined using the formula below:

$$\%\ \text{cross reactivity} = \frac{(\text{Mean conc. of spiked sample} - \text{mean conc. of un-spiked sample})}{\text{Final concentration of cross-reactant added}} \times 100\%$$

Results are shown in the table below:

Cross Reactant	Tested Concentration	% Cross-Reactivity
POMC	500	-2.1 %
	50 000	-0.03 %
	500 000	-0.02%
b-endorphin	500	-2.9%
	50 000	-0.01%
	500 000	<0.01%
aMSH 1-13	500	-3.7%
	50 000	-0.4%
	500 000	-0.1%
bMSH	500	-4.6%
	50 000	-0.01%
	500 000	<0.01%
ACTH 1-17	500	-1.8%
	50 000	-0.6%
	500 000	-0.1%
ACTH 1-24	500	-5.8%
	50 000	-0.5%
	500 000	-0.1%
ACTH 18-39 (CLIP)	500	-6.5%
	50 000	-0.3%

	500 000	-0.1%
ACTH 22-39	500	4.9%
	50 000	-0.4%
	500 000	-0.1%
ACTH 1-10	500	-7.5%
	50 000	-0.1%
	500 000	<0.01%
ACTH 11-24	500	-7.3%
	50 000	-0.1%
	500 000	<0.01%

Method Comparison

IDS ACTH II was compared against a commercially available quantitative automated assay, following CLSI EP-9A2, "Method Comparison and Bias Estimation Using Patient Samples". A total of 170 samples, selected to represent a wide range of ACTH concentrations [4 to 997 pg/mL], were tested by each method. Passing-Bablok regression analysis was performed on the comparative data:

N	Slope	95 % CI	Intercept (pg/mL)	95 % CI	Correlation Coeff. (r)
170	1.0	1.0 to 1.1	-0.9	-2.1 to 0.4	1.0

Matrix comparison:

The sample matrix comparison studies were performed, based on guidance from CLSI EP35 Ed1 "Assessment of Equivalence for Suitability of Specimen Types for Medical Laboratory Measurement Procedures" were performed to assess the equivalence between K_2 and K_3 EDTA plasma sample matrices in the IDS ACTH II assay. A total of 55 matched samples, with concentration ranging from 6 to 1228 pg/mL, were compared against K_3 EDTA. Passing-Bablok regression analysis was performed on the comparative data:

Sample Type	N	Slope	95% CI	Intercept (pg/mL)	95% CI	Correlation Coeff. (r)
K_2 EDTA	55	1.0	1.0 to 1.1	1.9	0.7 to 3.2	1.0

Expected Values

The following ranges were determined using the IDS ACTH II and are provided for information only. The 95 % reference interval for apparently healthy adults were calculated

by a non-parametric method following guidance from CLSI C28-A3 "Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory".

Unit	N	Mean	Median	Observed Range (2.5^{th} to 97.5^{th} percentile)
pg/mL	140	22	19	6 to 51

The above ranges should be considered as guidelines only; it is recommended that each laboratory establish its own expected range based upon its own patient population.

ACTH concentrations vary considerably depending on physiological conditions. ACTH results must be interpreted in conjunction with the patient's clinical presentation and other information available to the physician.

Conclusion

The IDS ACTH II data, presented and provided, is complete and supports the basis for substantial equivalence to the predicate device.