DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

IMMUNODIAGNOSTIC SYSTEMS LTD
MICK HENDERSON
REGULATORY AFFAIRS OFFICER
10 DIDCOT WAY
BOLDON BUSINESS PARK
BOLDON NE35 9PD, GREAT BRITAIN

January 31, 2017

Re: K161158
Trade/Device Name: IDS-iSYS Intact PTH^{N}
Regulation Number: 21 CFR 862.1545
Regulation Name: Parathyroid hormone test system
Regulatory Class: II
Product Code: CEW
Dated: January 9, 2017
Received: January 11, 2017

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. 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 Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Katherine Serrano -S

For: Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
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: January 31, 2017

510(k) Number *(if known)*
k161158

Device Name
IDS-iSYS Intact PTH^{N}

Indications for Use *(Describe)*

IDS-iSYS Intact PTH^{N}

The IDS-iSYS Intact PTH^{N} assay is an in vitro diagnostic device intended for the quantitative determination of intact PTH in human serum or plasma on the IDS-iSYS Multi-Discipline Automated System. Results are to be used in the differential diagnosis of hypercalcemia and hypocalcemia resulting from disorders of calcium metabolism.

Type of Use *(Select one or both, as applicable)*

[X] 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
IDS-iSYS Intact PTH^{N}
Assay

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

1. 510(k) Number: k161158

2. Submitter:
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5. Date Prepared: 09 January 2017

6. Proprietary and Established Name:
IDS-iSYS Intact PTH^{N}

7. Regulatory Information:
Classification: 21CFR 862.1545
Device Class Class II
Product Code: CEW
Panel: Clinical Chemistry (75)

8. Device Descriptions:

The IDS-iSYS Intact PTH^{N} assay is based on chemiluminescence technology. 100 µL of patient sample is incubated with a biotinylated polyclonal anti-PTH (39-84) antibody and an acridinium labelled PTH (13-34) antibody. Streptavidin labelled magnetic particles are added prior to a second incubation step. The magnetic particles are captured using a magnet and a wash step performed to remove any unbound analyte. Trigger reagents are added; the resulting light emitted by the acridinium label is directly proportional to the concentration of Intact PTH in the original sample.

IDS-iSYS Intact PTH^{N} reagent kit consists of one (1) Immunoassay Cartridge, two (2) vials each of 2 concentration Calibrator levels and a mini-CD containing the Instructions For Use (IFU), CRY files and Certificate of Analysis.

IDS-iSYS Intact PTH^{N} Cartridge, sufficient for 100 tests, consists of reagents provided in individual compartment within a plastic container called the Cartridge. The IDS-iSYS Intact PTH^{N} Cartridge contains the following ready to use reagents:

- Magnetic particles coated with streptavidin in a phosphate buffer containing sodium azide as preservative (<0.1%), 1 bottle.
- Goat polyclonal antibody against 13-34 PTH labelled with an acridinium ester derivative, in buffer containing goat serum with sodium azide as preservative (<0.1%), 1 bottle.
- Goat polyclonal antibody against 39-84 PTH labelled with biotin, in buffer containing bovine and goat proteins with sodium azide as preservative (<0.1%), 1 bottle.

IDS-iSYS Intact PTH^{N} Calibrators are included in the reagent kit.

- Calibrator A: Two vials of lyophilized porcine serum matrix buffer containing low level PTH and sodium azide as preservative >1% (w/w%).
- Calibrator B: Two vials of lyophilized porcine serum matrix buffer containing high level PTH and sodium azide as preservative >1% (w/w%).

The submission is due to a new source of antibody for the assay.

9. Predicate Devices:

IDS-iSYS Intact PTH, K103325

10. Special Conditions for Use:

For in vitro diagnostic use.
Rx Only

11. Special instrument Requirements:

IDS-iSYS Multi-Discipline Automated System (K091849)

12. Intended Use:

The IDS-iSYS Intact PTH^{N} assay is an in vitro diagnostic device intended for the quantitative determination of intact PTH in human serum or plasma on the IDS-iSYS Multi-Discipline Automated System. Results are to be used in the differential diagnosis of hypercalcemia and hypocalcemia resulting from disorders of calcium metabolism.

13. Substantial Equivalence Information

A comparison of the similarities and differences between the modified IDS-iSYS Intact PTH^{N} assay and the original IDS-iSYS Intact PTH assay (K103325) are provided in the following table:

Assay Similarities and Differences		
Characteristics	**Predicate Device IDS-iSYS Intact PTH (K103325)**	**Candidate Device IDS-iSYS Intact PTH^{N}**
Intended use	intended for the quantitative determination of PTH in human serum or plasma.	Same
Measured analyte	Intact PTH	Same
Assay type	Chemiluminescence immunoassay	Same
Antibody	Goat polyclonal a) anti- PTH (13-34) b) anti-PTH (39-84)	Same
Sample matrix	Plasma (K2-EDTA, lithium heparin) and serum	Same
Sample size	100 µL	Same
Sample handling/processing	Automated IDS-iSYS Multi-Discipline Automated System	Same
Calibrator	2 levels Included with kit	Same
Calibration interval	2 point calibration curve stable for 21 days	2 point calibration curve stable for 15 days
Reagent storage	On-board or at 2-8^{O}C	Same
Measurement range	5 to 5000 pg/mL	5 to 3500 pg/mL
Reference interval	11.5 to 78.4 pg/mL	10.3 to 80.5 pg/mL

Assay Similarities and Differences		
Characteristics	**Predicate Device IDS-iSYS Intact PTH (K103325)**	**Candidate Device IDS-iSYS Intact PTH^{N}**
Interfering Substances - Bilirubin, conjugated - Bilirubin, unconjugated - Biotin - Cholesterol - HAMA - Hemoglobin - Rheumatoid Factor - Total Protein - Triglycerides - Acetaminophen - Carbamazepine - Ibuprofen	 N/A 20 mg/dL 300 nmol/L N/A 1000 ng/mL 250 mg/dL 1500 IU/mL N/A 3000 mg/dL N/A N/A N/A	 22 mg/dL 40 mg/dL Same 395 mg/dL Same 500 mg/dL 1836 IU/mL 10 g/dL Same 200 µg/mL 200 µg/mL 500 µg/mL
Specificity - PTH (1-84) - PTH (7-84) - PTH (1-34) - PTH (39-84) - PTH (53-84) - PTH (39-68) - PTH (44-68) - Human Calcitonin - CTX-1 (β CrossLaps) - Osteocalcin	 100% 60% 0.5% Not detectable 2% N/A 2% 4% 2% 2%	 Same 83.9% <0.01% <0.01% <0.01% <0.01% <0.01% <0.01% <0.01% <0.01%
Hook Effect	Not observed up to 95,000 pg/mL	Not observed up to 100,000 pg/mL
Sensitivity - Limit of Blank (LoB) - Limit of Detection (LoD) - Limit of Quantitation (LoQ)	 1.2 pg/mL 2.5 pg/mL 4.5 pg/mL	 0.9 pg/mL 2.3 pg/mL 4.5 pg/mL
Precision - Within-run - Total	in the range of 13.3 to 3807 pg/mL, n =80 1.1% to 6.3% 4.1% to 8.2%	in the range of 15.4 to 2229 pg/mL, n =80 1.5% to 9.9% 1.8% to 9.9%
Linearity	y = 1.002 x – 4.748; R^2 = 1.00	K_2 EDTA: y = 0.96 x – 0.1; R^2 = 1.00 Serum: y = 1.02x – 0.2; R^2 = 1.00

14. Performance Characteristics

Method Comparison:

The IDS-iSYS Intact PTH^N Assay was compared against a commercially available quantitative chemiluminescence Intact PTH assay, following CLSI EP-9A2, "Method Comparison and Bias Estimation Using Patient Samples". A total of 312 serum samples (291 native, 21 spiked), selected to represent a wide range of Intact PTH concentrations [6.3 – 3378.4 pg/mL], was assayed by each method. Deming regression analysis was performed on the comparative data:

n	Slope	95% CI	Intercept (pg/mL)	95% Cl	Correlation coefficient (r)
312	1.02	0.99 to 1.04	-0.7	-5.4 to 4.1	1.00

Sample Matrix:

The matrix comparison study was performed to evaluate the difference across tube types [serum without additive (red top), serum in separator tubes (SST), and lithium heparin plasma] versus the control samples (K_2 EDTA plasma) following the CLSI EP9-A3 guideline. A total of 52 samples (45 native, 7 spiked) matched samples with Intact PTH concentrations ranging from of 10.6 to 2759.0 pg/mL were tested with the IDS-iSYS Intact PTH^N assay. Passing-Bablok regression analysis was performed on the comparative data:

Sample Type	n	Slope	95% Cl.	Intercept (pg/mL)	95% Cl.	Corr. Coeff. (r)
Serum (Red Top)	52	0.94	0.92 to 0.97	2.55	0.86 to 3.16	1.00
Serum (SST)	52	0.93	0.91 to 0.96	2.38	1.25 to 3.15	1.00
Lithium Heparin	52	0.98	0.95 to 0.99	0.42	-0.43 to 1.63	1.00

The type of specimen used (serum, EDTA plasma, or Lithium Heparin plasma) may influence PTH measurement. During routine monitoring of PTH levels, use the same specimen type throughout the monitoring period to avoid bias in the results.

Reference Interval:
The 95% reference interval for the following group was calculated by a non-parametric method following the CLSI C28-A3, "How to Define and Determine Reference Intervals in the Clinical Laboratory". The K_2 EDTA plasma samples were collected from 129 individuals (67 males, 62 females; 21 to 89 years of age) with normal calcium, phosphate, and TSH values from the north, central and south regions of the United States.

No. of subjects	129
Mean (pg/mL)	35.4
SD (pg/mL)	16.6
Median (pg/mL)	32.7
Reference Interval (pg/mL)	10.3 to 80.5

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.

Sensitivity
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" using 60 blanks and 10 low level serum samples. The following limits were determined with the IDS-iSYS Intact PTH^N Assay:

Sensitivity	**Concentration (pg/mL)**
Limit of Blank (LoB)	0.9
Limit of Detection (LoD)	2.3
Limit of Quantitation (LoQ)	4.5

Precision:
Precision testing was evaluated in accordance with a modified protocol based on CLSI EP-5A2, "Evaluation of Precision Performance of Quantitative Measurement Methods". Seven (7) samples were assayed using one lot of reagent in duplicate twice per day for 20 days on one System.

Sample	**n**	**Mean (pg/mL)**	**Within run**		**Total**	
			SD	**CV%**	**SD**	**CV%**
Serum Sample 1	80	15.4	0.5	6.1	1.0	6.7
EDTA Plasma Sample 1	80	17.9	1.8	9.9	1.8	9.9
EDTA Plasma Sample 2	80	73.7	1.3	1.7	2.3	3.2
EDTA Plasma Sample 3	80	337.9	5.1	1.5	6.2	1.8
EDTA Plasma Sample 4	80	765.1	13.7	1.8	16.4	2.1
EDTA Plasma Sample 5	80	1376.6	20.4	1.5	40.7	3.0
EDTA Plasma Sample 6	80	2229.1	35.2	1.6	58.6	2.6

Linearity:
Linearity was evaluated based on CLSI EP-6A, "Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach". Samples were prepared by diluting a high patient sample with a low patient sample prior to assay. High intact PTH human K_2 EDTA plasma and serum samples were diluted with low samples prior to assay. Each sample was measured in 4 replicates.

The K_2 EDTA plasma samples with Intact PTH concentration levels above 80 pg/mL show a maximum -8.8 % deviation from linearity; samples below 80 pg/mL show a maximum deviation of -6.1 pg/mL. The weighted linear regression of the Observed versus the Expected concentrations is:

Observed = 0.96 x (Expected) – 0.1 pg/mL
Regression coefficient R^2: 1.00

The serum samples with intact PTH concentration levels above 80 pg/mL show a maximum deviation from linearity of 5.1%. The samples below 80 pg/mL show a maximum deviation of 0.6 pg/mL. The weighted linear regression of the Observed versus the Expected concentrations is:

Observed = 1.02 x (Expected) – 0.2 pg/mL
Regression coefficient R^2: 1 .00

High Dose Hook Effect:
Testing was conducted to determine if the IDS-iSYS Intact PTH^N assay is susceptible to artificially low results in the presence of very high levels of PTH (Hook Effect). Three samples (1 EDTA Plasma, 2 Serum) were spiked with 1-84 PTH to 5000 pg/mL, 25000 pg/mL, 50000 pg/mL, 75000 pg/mL and 100000 pg/mL. Each specimen was measured in four (4) replicates using 3 reagents lots.

No high dose hook effect was observed for Intact PTH concentrations measured up to 100000 pg/mL.

Interferences:
Interference studies were performed in accordance with the CLSI EP7-A2, "Interference testing in clinical chemistry; approved guideline". Two K_2-EDTA samples at a low and high Intact PTH levels were spiked with following potential interfering substances: Triglycerides, Hemoglobin, Bilirubin (conjugated and unconjugated), Red blood cells, Biotin, Acetaminophen, Ibuprofen and Carbamazepine.

Two serum samples at different Intact PTH concentrations were used to determine the potential interference of Total Protein.

% Interference was calculated using the formula below:

$$\% \text{ Interference} = \frac{(\text{Mean conc. of spiked sample} - \text{mean conc. of un-spiked sample})}{\text{Mean concentration of un-spiked sample}} \times 100\%$$

For Cholesterol (Total), Rheumatoid factor (Rf) and HAMA (human anti mouse antibodies), the interference was tested by recovery of Intact PTH from a high serum pool spiked into a serum sample with known interferent substance levels. % Recovery was calculated using the formula below:

Recovery value = Mean concentration of spiked – Mean concentration of un-spiked

% Recovery = (Recovery value / Expected recovery value) x 100

Following potential interference compounds were tested and found not to interfere significantly with the IDS-iSYS Intact PTH^N assay, based on the criteria of non-significant interference of $\leq \pm 10\%$ bias between the test (spiked) and control (un-spiked) samples:

Potentially Interfering Agent	**Highest concentration tested that demonstrated no significant interference**
Bilirubin, conjugated	22 mg/dL
Bilirubin, unconjugated	40 mg/dL
Biotin	300 nmol/L
Cholesterol, total	395 mg/dL
Haemoglobin	500 mg/dL
Human Anti Mouse Antibody (HAMA)	1000 ng/mL
Rheumatoid Factor	1836 IU/mL
Total Protein	10 g/dL
Triglyceride	3000 mg/dL
Acetaminophen	200 µg/mL
Carbamazepine	200 µg/mL
Ibuprofen	500 µg/mL

Cross Reactivity:
The potential cross-reacting substances studies were performed on the IDS-iSYS Intact PTH^N assay, based on CLSI EP-7A2. A serum sample and a zero calibrator matrix was spiked with the following substance human PTH fragments and structurally similar proteins at the concentration listed below. The cross reactivity was then determined using the following equation:

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

Analyte	Concentration tested (pg/mL)	Cross-Reactivity
PTH (1-84)	2,000	100%
PTH (7-84)	2,000	83.6%
PTH (1-34)	100,000	<0.01%
PTH (39-84)	100,000	<0.01%
PTH (53-84)	100,000	<0.01%
PTH (39-68)	100,000	<0.01%
PTH (44-68)	100,000	<0.01%
Human Calcitonin	100,000	<0.01%
CTX-1 (β CrossLaps)	100,000	<0.01%
Osteocalcin	100,000	<0.01%

15. Conclusions

The IDS-iSYS Intact PTH^N assay, after the modification in antibody source, is substantially equivalent in principle and performance to the originally submitted IDS-iSYS Intact PTH assay (K103325).