October 23, 2024

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

Re: K240865
Trade/Device Name: IDS-iSYS Free Testosterone
Regulation Number: 21 CFR 862.1680
Regulation Name: Testosterone Test System
Regulatory Class: Class I, reserved
Product Code: CDZ
Dated: September 20, 2024
Received: September 20, 2024

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 (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.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

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,

Paula V. Caposino -S

Paula Caposino, Ph.D.
Deputy Director
Division of Chemistry
and Toxicology 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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
k240865

Device Name
IDS-iSYS Free Testosterone

Indications for Use *(Describe)*
The IDS-iSYS Free Testosterone assay is an in vitro diagnostic device intended for the quantitative determination of free testosterone in human serum or plasma on the IDS system. Measurement of free testosterone is used in the diagnosis and treatment of disorders involving the male sex hormones (androgens), including primary and secondary hypogonadism, impotence in male and in females; hirsutism (excessive hair) and virilization (masculinization) due to tumors, polycystic ovaries and androgenital syndromes.

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 k240865

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: 20th September 2024

Device Name

Proprietary names:	IDS-iSYS Free Testosterone
Common names:	IDS Free Testosterone
Classification:	21 CFR 862.1680 –Testosterone Test System Class 1 reserved
Product Code:	CDZ

Predicate Device Free Testosterone AccuBind® ELISA Test System (k181017)

Device Description The IDS-iSYS Free Testosterone assay consists of a reagent cartridge. The reagent cartridge contains multiple reagents:

- MP3: Magnetic particles coated with Streptavidin in a phosphate Pluronic buffer with sodium azide (NaN_3) as preservative (< 0.1%). 1 bottle, 2.5 mL.
- CONJ: Testosterone labelled with an acridinium ester derivative, in phosphate buffer containing bovine protein with ProClin 300 as preservative (< 0.0015%). 1 bottle, 3.5 mL
- Ab-BIOT: Monoclonal anti-Testosterone labelled with Biotin, in MES buffer with ProClin 300 as preservative (< 0.0015%). 1 bottle, 7.5 mL
- Cal A: Human serum matrix containing human free testosterone with sodium azide and ProClin 300 as preservatives (< 0.1% and 0.0024% respectively). 1.0 mL per bottle
- Cal B: Human serum matrix containing human free testosterone with sodium azide and ProClin 300 as preservatives (< 0.1% and 0.0024% respectively). 1.0 mL per bottle

Indications for Use

The IDS-iSYS Free Testosterone assay is an in vitro diagnostic device intended for the quantitative determination of free testosterone in human serum or plasma on the IDS system. Measurement of free testosterone is used in the diagnosis and treatment of disorders involving the male sex hormones (androgens), including primary and secondary hypogonadism, impotence in male and in females; hirsutism (excessive hair) and virilization (masculinization) due to tumors, polycystic ovaries and androgenital syndromes.

Conditions for use For in vitro diagnostic use.
Rx Only

Special instrument Requirements:

IDS-iSYS Multi-Discipline Automated System (k091849)

Comparison Tables

Similarities compared to the chosen (FDA cleared; marketed) predicate device (k181017)

Assay Performance	**Predicate Device Free Testosterone AccuBind® ELISA Test System (k181017)**	**Candidate Device IDS-iSYS Free Testosterone**
Intended Use	The direct quantitative determination of Free Testosterone	Same
Test Principle	Competitive immunoassay	Same

Differences compared to the chosen (FDA cleared; marketed) predicate device (k181017)

Assay Performance	**Predicate Device Free Testosterone AccuBind® ELISA Test System (k181017)**	**Candidate Device IDS-iSYS Free Testosterone**
Antibody	Utilizes a highly specific rabbit polyclonal antibody at a low binding capacity	Monoclonal anti-testosterone labelled with biotin
Detection Method	Microplate colorimetric reader	Chemiluminescence
Sample Type	Human serum	Human serum or plasma
Measuring range	0.11 – 60 pg/ml	0.40 – 60 pg/mL
Expected Range of Values	Males 20-39: 9.2-34.6 Males 40-59: 6.1-30.3 Males ≥60: 6.1-27.9 Females 20-39:0.2-6.1 Females 40-59: 0.3-4.4 Females ≥60: 0.5-3.4	Males 21 – 39: 4.91 – 21.64 Males 40 – 59: 3.73 – 14.96 Males ≥60: 2.25 – 11.37 Females 21 – 39: 0.46 – 2.20 Females 40 – 59: 0.40 – 1.74 Females ≥60: 0.42 – 2.20

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-A2, "Protocols for Determination of Limits of Detection and Limits of Quantitation" with three (3) IDS Free testosterone kit lots. LoB and LoD were determined with 60 replicates of 4 blank samples and 6 low concentration samples per reagent lot. LoQ was determined with 105 replicates of 7 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)	0.08
Limit of Detection (LoD)	0.17
Limit of Quantitation (LoQ)	0.40

Precision (Repeatability/Reproducibility)

Precision studies were performed with guidance from CLSI EP05 A3 "Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline".

Repeatability

A total of 10 serum samples were measured using 1 reagent lot, in duplicate, twice a day for 20 days on 1 IDS system for a total of 80 replicates per sample to assess the repeatability.

Sample ID	N	Mean Conc. (pg/mL)	Repeatability		Within Laboratory	
			SD	CV%	SD	CV%
S1	80	0.7	0.05	7.0%	0.07	9.9%
S2	80	1.1	0.05	4.3%	0.06	5.2%
S3	80	1.2	0.04	3.0%	0.06	5.0%
S4	80	3.8	0.06	1.7%	0.12	3.3%
S5	80	9.2	0.20	2.2%	0.27	2.9%
S6	80	10.8	0.15	1.4%	0.39	3.7%
S7	80	19.7	0.28	1.4%	0.44	2.3%
S8	80	32.2	0.77	2.4%	1.03	3.2%
S9	80	43.4	0.76	1.8%	1.45	3.3%
S10	80	56.0	1.24	2.2%	1.90	3.4%

Reproducibility

A total of 9 serum samples were measured using one reagent lot in 5 replicates, once a day for 5 days on 3 IDS systems by three operators (one operator per system) for a total of 75 replicates per sample to determine the reproducibility.

Sample ID	N	Mean Conc. (pg/mL)	Repeatability		Reproducibility	
			SD	CV%	SD	CV%
S2	75	1.2	0.09	7.1%	0.13	11.1%
S3	75	1.3	0.08	5.9%	0.08	6.5%
S4	75	3.8	0.16	4.2%	0.17	4.5%
S5	75	9.2	0.35	3.8%	0.35	3.8%
S6	75	10.8	0.38	3.5%	0.44	4.1%
S7	75	19.8	0.69	3.5%	0.83	4.2%
S8	75	32.6	1.66	5.1%	1.82	5.6%
S9	75	44.4	1.77	4.0%	1.94	4.4%
S10	75	57.9	1.97	3.4%	2.24	3.9%

A total of 9 serum samples were tested using three (3) reagents lot in 5 replicates, once a day for 5 days on 1 IDS system by 1 operator per system for a total of 75 replicates per sample to determine the reproducibility.

Sample ID	N	Mean Conc. (pg/mL)	Repeatability		Reproducibility	
			SD	CV%	SD	CV%
S2	75	1.2	0.09	7.8%	0.09	7.8%
S3	75	1.3	0.07	5.5%	0.07	5.8%
S4	75	3.7	0.13	3.4%	0.15	4.1%
S5	75	9.3	0.44	4.7%	0.44	4.7%
S6	75	10.9	0.44	4.0%	0.46	4.2%
S7	75	20.1	0.87	4.3%	0.89	4.4%
S8	75	33.1	2.33	7.0%	2.85	8.6%
S9	75	45.4	2.32	5.1%	2.36	5.2%
S10	75	58.9	2.80	4.7%	2.80	4.7%

Linearity

Linearity was evaluated based on CLSI EP06 Ed2, “Evaluation of Linearity of Quantitative Measurement Procedures”. For concentration by IDS Free testosterone assay, the measurement procedure shows the linearity between 0.12 pg/mL and 68.12 pg/mL, was within the allowable deviation of linearity (ADL) of ≤ ±13.6 %, or ≤+/- 0.40 pg/mL for concentrations below 1 pg/mL.

Analytical Specificity

Cross Reactivity

Cross-reactivity studies were performed in accordance with the CLSI guidance EP07-A3 "Interference testing in clinical chemistry". The study was conducted by spiking the cross-reacting compounds into 2 samples containing approximately 1.0 and 15 pg/mL concentrations of free testosterone. Results are shown in the table below:

Cross Reactant	Concentration Tested	% Cross Reactivity
11-Deoxycortisol	100000 ng/ml	< 0.01%
11-Ketotestosterone	100 ng/ml	0.02%
11-β-Hydroxytestosterone	1000 ng/ml	< 0.01%
17-Hydroxypregnenolone	1000 ng/ml	< 0.01%
17OH-Progesterone	500 ng/ml	< 0.01%
17α-Estradiol	1000 ng/ml	< 0.01%
17α-Ethinilestradiol	500 ng/ml	< 0.01%
3-EstriolGluc	1000 ng/ml	< 0.01%
3-EstriolSul	1000 ng/ml	< 0.01%
5α-Androstane-3β,17β-diol	1000 ng/ml	< 0.01%
Aldosterone	3000 ng/ml	< 0.01%
Amitriptyl HCI	1000 ng/ml	< 0.01%
Androstenedione	100 ng/ml	0.02%
Androsterone	500 ng/ml	< 0.01%
Clomiphene Citrate	1000 ng/ml	< 0.01%
Corticosterone	1000 ng/ml	< 0.01%
Cortisol	1000 ng/ml	< 0.01%
Cortisone	2000 ng/ml	< 0.01%
Cyproterone	2000 ng/ml	< 0.01%
Cyproterone acetate	1000 ng/ml	< 0.01%
D-5-Androstene-3β,17β-diol	1000 ng/ml	< 0.01%
Danazol	1000 ng/ml	< 0.01%
Desogestrel	100 ng/ml	< 0.01%
Dexamethasone	2000 ng/ml	< 0.01%
DHEA	50000 ng/ml	< 0.01%
DHEA-S	100000 ng/ml	< 0.01%
Dihydrotestosterone	500 ng/ml	< 0.01%
Epitestosterone	500 ng/ml	< 0.01%
Estradiol	1000 ng/ml	< 0.01%
Estriol	100 ng/ml	< 0.01%
Estrone	1000 ng/ml	< 0.01%
Ethisterone	1000 ng/ml	< 0.01%
Ethynodiol	1000 ng/ml	< 0.01%
Ethynodiol diacetate	50 ng/ml	< 0.01%

Flunisolide	1000 ng/ml	< 0.01%
Fluoxymesterone	1000 ng/ml	< 0.01%
Lynestrol	1000 ng/ml	< 0.01%
Medoxyprogesterone acetate	1000 ng/ml	< 0.01%
Mestranol	1000 ng/ml	< 0.01%
Methyltestosterone	100 ng/ml	0.04%
Norethindrone	50 ng/ml	< 0.01%
Norethinodrone acetate	50 ng/ml	< 0.01%
Norethynodrel	50 ng/ml	< 0.01%
Norgestimate	1000 ng/ml	< 0.01%
Norgestrel	1000 ng/ml	<0.01%
Oxymetholone	10000 ng/ml	< 0.01%
Prednisolone	1000 ng/ml	< 0.01%
Prednisone	1000 ng/ml	< 0.01%
Pregnenolone	5000 ng/ml	< 0.01%
Progesterone	1000 ng/ml	< 0.01%
Salbutamol	1000 ng/ml	< 0.01%
Spironolactone	1000 ng/ml	< 0.01%
Stanozolol	1000 ng/ml	< 0.01%
Testosterone Cypionate	12 ng/ml	< 0.01%
Testosterone enanthate	100 ng/ml	< 0.01%
Testosterone propionate	100 ng/ml	< 0.01%
Testosterone SO4	1000 ng/ml	< 0.01%
Testosterone Undecanoate	12 ng/ml	< 0.01%
Triamcinolone	50 ng/ml	< 0.01%

Interference

The interference testing of IDS Free Testosterone was evaluated following the CLSI EP07-ED3, "Interference Testing in Clinical Chemistry". The study was performed using 2 samples containing 1.0, and 45.0 pg/mL concentrations of free testosterone. No significant interference (≤±10% bias) was observed when the interfering substances were tested at the following threshold concentration:

Potentially Interfering Agent	**Threshold Concentration**
Acetylsalicylic Acid	1.67 mmol/L
Acetaminophen	1030 µmol/L
Bilirubin (Conjugated)	40 mg/dL
Bilirubin (Unconjugated)	40 mg/dL
Biotin*	500 ng/mL
Human Anti Mouse Antibody (HAMA)	1000 ng/dL
Haemoglobin	300 mg/dL
Ibuprofen	1060 µmol/L
Total Protein	10 g/dL
Red Blood Cells	0.4%

Salicylic Acid	2.07 mmol/L
Triglycerides	1500 mg/dL
Rheumatoid Factor (RhF)	1500 IU/mL

*A study was conducted to evaluate biotin interference on the IDS Free Testosterone assay. Up to 750 ng/mL biotin was spiked into serum samples containing three concentrations of free testosterone, approximately 1.5 pg/mL, 20 pg/mL, and 45 pg/mL.

No significant interference (≤±10% bias) was observed at biotin concentrations ≤ 500 ng/mL for all three concentrations of free testosterone tested.

SHBG at concentration ranging from 6.25 – 200 µg/mL was added to a charcoal-stripped human serum sample and was measured with the IDS Free Testosterone assay. All concentrations exhibited less than 10% binding. Results are tabulated below:

SHBG added (µg/mL)	Mean Relative Light Units (RLUs)	Percent B/Bo (%)
0	281560	100%
6.25	284970	101%
12.5	282335	100%
50	278307	99%
200	262790	93%

Method Comparison

The IDS Free Testosterone was compared against a commercially available quantitative free testosterone ELISA, following CLSI EP09c, "Method Comparison and Bias Estimation Using Patient Samples". A total of 241 samples, selected to represent a wide range of free testosterone concentrations, 0.41 to 55.98 pg/mL, was tested by each method. Passing-Bablok regression analysis was performed on the comparative data:

N	Slope	95% CI	Intercept (pg/mL)	95% CI	Correlation coefficient (r)
241	1.02	0.97 to 1.06	-0.02	-0.26 to 0.07	0.98

Matrix comparison

The assay should be performed using serum (standard sampling tubes or tubes containing serum separating gel) or plasma (lithium heparin, sodium heparin or potassium (K_2) EDTA) samples. Samples should be separated as soon as possible after collection.

The matrix comparison studies, based on guidance from CLSI EP35 Ed.1 "Assessment of Equivalence for Suitability of Specimen Types for Medical Laboratory Measurement Procedures", were performed to assess the equivalence between serum (serum without additives, serum gel separator tubes (SST)) and plasma (K_2 EDTA, Sodium Heparin and Lithium Heparin) sample matrices in the IDS Free Testosterone assay. Passing-Bablok regression analysis was performed on the comparative data:

Sample Type	N	Slope	95% CI	Intercept (pg/mL)	95% CI	Corr. Coeff. (r)
SST	40	0.96	0.92 to 0.98	0.08	-0.04 to 0.22	1.00
K_2 EDTA	40	0.97	0.94 to 1.01	0.08	-0.08 to 0.26	0.99
Li Heparin	40	0.97	0.92 to 1.00	0.03	-0.04 to 0.14	0.99
Na Heparin	40	0.97	0.93 to 1.00	0.00	-0.06 to 0.17	0.99

Expected Values

The following ranges were determined using the IDS Free Testosterone and are provided for information only. The 95 % reference interval for apparently healthy adults and children were calculated by a non-parametric method following guidance from CLSI C28-A3 "Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory".

Females	**21 to 39 years**	**40 to 59 years**	**≥ 60 years**
N of subjects	130	57	67
Mean (pg/mL)	1.16	0.82	0.97
SD (pg/mL)	0.44	0.35	0.43
Median (pg/mL)	1.13	0.71	0.89
Observed Range (pg/mL) (2.5^{th} to 97.5^{th} percentile)	0.46 to 2.20	0.40 to 1.74	0.42 to 2.20

Males	**21 to 39 years**	**40 to 59 years**	**≥ 60 years**
N of subjects	129	138	42
Mean (pg/mL)	12.50	8.80	7.76
SD (pg/mL)	4.03	2.71	2.17
Median (pg/mL)	12.36	8.70	7.78
Observed Range (pg/mL) (2.5^{th} to 97.5^{th} percentile)	4.91 to 21.64	3.73 to 14.96	2.25 to 11.37

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.

Conclusion

The IDS-iSYS Free Testosterone data presented and provided is complete and supports the basis for substantial equivalence to the predicate device.