December 29, 2022

Abbott Ireland Diagnostics Division
Magdalena Suszko
Associate Director Regulatory Affairs
Lisnarnuck, Longford
Co. Longford, Ireland

Re: K223324
Trade/Device Name: Total Bilirubin2
Regulation Number: 21 CFR 862.1110
Regulation Name: Bilirubin (total or direct) test system
Regulatory Class: Class II
Product Code: CIG, MQM
Dated: October 27, 2022
Received: October 31, 2022

Dear Magdalena Suszko:

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
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)*
K223324

Device Name
Total Bilirubin2

Indications for Use *(Describe)*
The Total Bilirubin2 assay is used for the quantitation of total bilirubin in human serum or plasma, of adults and neonates, on the ARCHITECT c System.
Measurement of total bilirubin, an organic compound formed during the normal and abnormal destruction of red blood cells, is used in the diagnosis and treatment of liver, hemolytic, hematological, and metabolic disorders, including hepatitis and disorders of the biliary tract. In newborn infants, the Total Bilirubin2 assay is intended to measure the levels of total bilirubin (conjugated and unconjugated) in serum or plasma to aid in the diagnosis and management of neonatal jaundice and hemolytic disease of the newborn.

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 (Summary of Safety and Effectiveness)

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

I. 510(k) Number

K223324

II. Applicant Name

Abbott Ireland
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Date Summary Prepared: December 20, 2022

III. Device Name

Trade Name: Total Bilirubin2

Device Classification: Class II
Classification Name: Bilirubin (total or direct) test system.
Governing Regulation Number: 21 CFR §862.1110
Product Code: CIG

Device Classification: Class I, reserved
Classification Name: Bilirubin (total and unbound) in the neonate test system
Governing Regulation Number: 21 CFR §862.1113
Product Code: MQM

IV. Predicate Device

ARCHITECT Total Bilirubin (k121985)

V. Description of Device

A. Principles of the Procedure

Total (conjugated and unconjugated) bilirubin couples with a diazo reagent in the presence of a surfactant to form azobilirubin. The diazo reaction is accelerated by the addition of surfactant as a solubilizing agent. The increase in absorbance at 548 nm due to azobilirubin is directly proportional to the total bilirubin concentration.

Methodology: Diazonium salt

B. Reagents

The configurations of the Total Bilirubin2 reagent kits are described below.

	List Number	
	04T0920	**04T0930**
Tests per cartridge set	225	450
Number of cartridge sets per kit	4	8
Tests per kit	900	3600
Reagent 1 (R1)	44.5 mL	85.9 mL
Reagent 2 (R2)	14.5 mL	26.7 mL

R1 Active ingredient: Brij L23 (233.333 mL/L).

R2 Active ingredients: 2,4-dichlorobenzenediazonium 1,5-naphthalenedisulfonate hydrate (1845.000 mg/L) and Brij L23 (100.000 mL/L).

VI. Intended Use of the Device

The Total Bilirubin2 assay is used for the quantitation of total bilirubin in human serum or plasma, of adults and neonates, on the ARCHITECT c System.

Measurement of total bilirubin, an organic compound formed during the normal and abnormal destruction of red blood cells, is used in the diagnosis and treatment of liver, hemolytic, hematological, and metabolic disorders, including hepatitis and disorders of the biliary tract. In newborn infants, the Total Bilirubin2 assay is intended to measure the levels of total bilirubin (conjugated and unconjugated)in serum or plasma to aid in the diagnosis and management of neonatal jaundice and hemolytic disease of the newborn.

VII. Comparison of Technological Characteristics

The Total Bilirubin2 assay (subject device) is an automated clinical chemistry assay for the quantitation of total bilirubin in human serum or plasma, of adults and neonates, on the ARCHITECT c System.

The similarities and differences between the subject device and the predicate device are presented in the following table.

Similarities and Differences Between		
Device & Predicate Device:		
	Device: **Total Bilirubin2**	**Predicate Device:** **ARCHITECT Total Bilirubin (List No. 6L45) (k121985)**
General Device Similarities		
Platform	ARCHITECT c8000 System	Same

Similarities and Differences Between		
Device & Predicate Device:		
	Device: **Total Bilirubin2**	**Predicate Device:** **ARCHITECT Total Bilirubin (List No. 6L45) (k121985)**
Intended Use and Indications for Use	The Total Bilirubin2 assay is used for the quantitation of total bilirubin in human serum or plasma, of adults and neonates, on the ARCHITECT c System. Measurement of total bilirubin, an organic compound formed during the normal and abnormal destruction of red blood cells, is used in the diagnosis and treatment of liver, hemolytic, hematological, and metabolic disorders, including hepatitis and disorders of the biliary tract. In newborn infants, the Total Bilirubin2 assay is intended to measure the levels of bilirubin in serum or plasma to aid in the diagnosis and management of neonatal jaundice and hemolytic disease of the newborn.	The ARCHITECT Total Bilirubin assay is used for the quantitation of total bilirubin in human serum or plasma on the ARCHITECT c8000 system. Measurement of total bilirubin, an organic compound formed during the normal and abnormal destruction of red blood cells, is used in the diagnosis and treatment of liver, hemolytic hematological and metabolic disorders, including hepatitis and gall bladder block. A bilirubin (total and unbound) in the neonate test system is a device intended to measure the levels of bilirubin (total and unbound) in the blood (serum) of newborn infants to aid in indicating the risk of bilirubin encephalopathy (kernicterus).
Methodology	Diazonium salt	Same
Specimen Type	Human serum or plasma	Same
Assay Principle / Principle of Procedure	Total (conjugated and unconjugated) bilirubin couples with a diazo reagent in the presence of a surfactant to form azobilirubin. The diazo reaction is accelerated by the addition of surfactant as a solubilizing agent. The increase in absorbance at 548 nm due to azobilirubin is directly proportional to the total bilirubin concentration.	Same
Standardization	Doumas method	Same
Use of Calibrators	Yes	Same
Use of Controls	Yes	Same

Similarities and Differences Between		
Device & Predicate Device:		
	Device: **Total Bilirubin2**	**Predicate Device:** **ARCHITECT Total Bilirubin (List No. 6L45) (k121985)**
Assay Range	Analytical Measuring Interval: 0.1–25.0 mg/dL Extended Measuring Interval: 25.0–125.0 mg/dL Reportable Interval: 0.1–125.0 mg/dL	Same
Tube Types	Serum: - Serum tubes - Serum separator tubes Plasma: - Dipotassium EDTA tubes - Lithium heparin tubes - Lithium heparin separator tubes - Sodium heparin tubes	Same
General Device Differences		
Lower Limits of Measurement	Limit of Blank: 0.02 mg/dL Limit of Detection: 0.04 mg/dL Limit of Quantitation: 0.07 mg/dL	Limit of Blank: 0.01 mg/dL Limit of Detection: 0.05 mg/dL Limit of Quantitation: 0.07 mg/dL

VIII. Summary of Nonclinical Performance

All performance characteristics were obtained using the ARCHITECT c8000 System.

A. Reportable Interval

Based on the limit of detection (LoD), limit of quantitation (LoQ), precision, and linearity, the ranges over which results can be reported are provided below according to the definitions from CLSI EP34, 1st ed.*

	mg/dL
Analytical Measuring Interval (AMI)[a]	0.1–25.0
Extended Measuring Interval (EMI)[b]	25.0–125.0
Reportable Interval[c]	0.1–125.0

[a] AMI: The AMI is determined by the range of values in mg/dL that demonstrated acceptable performance for linearity, imprecision, and bias. NOTE: The observed LoQ has been rounded up to the number of decimal places defined in the assay file.

[b] EMI: The EMI extends from the upper limit of quantitation (ULoQ) to the ULoQ × sample dilution.

[c] The reportable interval extends from the LoD (rounded up to the number of decimal places defined in the assay file) to the upper limit of the EMI.

NOTE: The Low Linearity value of the assay file corresponds to the lower limit of the AMI. Samples with a total bilirubin value below 0.1 mg/dL are reported as "<0.1 mg/dL".

* Clinical and Laboratory Standards Institute (CLSI). *Establishing and Verifying an Extended Measuring Interval Through Specimen Dilution and Spiking. 1st ed*. CLSI Document EP34. Wayne, PA: CLSI; 2018.

B. Within-Laboratory Precision

Within-Laboratory Precision

A study was performed based on guidance from CLSI EP05-A3.[†] Testing was conducted using 3 lots of the Total Bilirubin2 reagents, 3 lots of the Consolidated Chemistry Calibrator, 1 lot of commercially available controls, and 3 instruments. Two controls and 3 human serum panels were tested in a minimum of 2 replicates, twice per day for 20 days on 3 reagent lot/calibrator lot/instrument combinations, where a unique reagent lot and a unique calibrator lot are paired with 1 instrument. The performance from a representative combination is shown in the following table.

			Within-Run (Repeatability)		Within-Laboratory[a]	
Sample	**n**	**Mean (mg/dL)**	**SD**	**%CV**	**SD (Range[b])**	**%CV (Range[b])**
Control Level 1	80	1.1	0.02	1.9	0.04 (0.02–0.04)	3.4 (1.8–3.4)
Control Level 2	80	4.2	0.04	0.9	0.09 (0.09–0.10)	2.1 (2.0–2.2)
Panel A	80	0.3	0.00	0.0	0.00 (0.00–0.03)	0.0 (0.0–9.2)
Panel B	80	13.3	0.09	0.7	0.11 (0.09–0.12)	0.8 (0.7–0.9)
Panel C	80	22.3	0.15	0.7	0.16 (0.16–0.18)	0.7 (0.7–0.8)

[a] Includes within-run, between-run, and between-day variability.

[b] Minimum and maximum SD or %CV across the 3 reagent lot/calibrator lot/instrument combinations.

[†] Clinical and Laboratory Standards Institute (CLSI). *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition*. CLSI Document EP05-A3. Wayne, PA: CLSI; 2014.

System Reproducibility

A study was performed based on guidance from CLSI EP05-A3.[‡] Testing was conducted using 1 lot of the Total Bilirubin2 reagents, 1 lot of the Consolidated Chemistry Calibrator, 1 lot of commercially available controls, and 3 instruments. Each instrument was operated by a different technician. Two controls and 2 human serum panels were tested in a minimum of 3 replicates at 2 separate times per day on 5 different days on 2 instruments and on 4 different days on 1 instrument.

			Repeatability		**Within-Laboratory[a]**		**Reproducibility[b]**	
Sample	**n**	**Mean (mg/dL)**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Control Level 1	84	1.1	0.02	1.6	0.02	2.1	0.02	2.2
Control Level 2	84	4.5	0.03	0.6	0.06	1.5	0.16	3.5
Panel B	84	13.4	0.08	0.6	0.10	0.7	0.57	4.3
Panel C	84	22.4	0.13	0.6	0.17	0.7	1.12	5.0

[a] Includes within-run, between-run, and between-day variability.

[b] Includes within-run, between-run, between-day, and between-instrument variability.

C. Accuracy

A study was performed to estimate the bias of the Total Bilirubin2 assay relative to material standardized to the Doumas Total Bilirubin reference method. Testing was conducted using 2 concentrations of bilirubin from human serum across 3 lots of the Total Bilirubin2 reagents, 2 lots of the Consolidated Chemistry Calibrator, and 1 instrument. The bias ranged from -0.1% to 3.7%.

[‡] Clinical and Laboratory Standards Institute (CLSI). *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition*. CLSI Document EP05-A3. Wayne, PA: CLSI; 2014.

D. Lower Limits of Measurement

A study was performed based on guidance from CLSI EP17-A2.[§] Testing was conducted using 3 lots of the Total Bilirubin2 reagents on each of 2 instruments over a minimum of 3 days. The maximum observed limit of blank (LoB), limit of detection (LoD), and limit of quantitation (LoQ) values are summarized below.

	mg/dL
LoB[a]	0.02
LoD[b]	0.04
LoQ[c]	0.07

[a] The LoB represents the 95th percentile from n ≥ 60 replicates of zero-analyte samples.

[b] The LoD represents the lowest concentration at which the analyte can be detected with 95% probability based on n ≥ 60 replicates of low-analyte level samples.

[c] The LoQ is defined as the lowest concentration at which a maximum allowable precision of 20% CV was met and was determined from n ≥ 60 replicates of low-analyte level samples.

E. Linearity

A study was performed based on guidance from CLSI EP06-A.[**] This assay is linear across the analytical measuring interval of 0.1 to 25.0 mg/dL.

[§] Clinical and Laboratory Standards Institute (CLSI). *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline—Second Edition*. CLSI Document EP17-A2. Wayne, PA: CLSI; 2012.

[**] Clinical and Laboratory Standards Institute (CLSI). *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline*. CLSI Document EP06-A. Wayne, PA: CLSI; 2003.

F. Potentially Interfering Endogenous and Exogenous Substances

Potentially Interfering Endogenous Substances

A study was performed based on guidance from CLSI EP07, 3rd ed.* Each substance was tested at 2 levels of the analyte (approximately 2 mg/dL and 15 mg/dL).
No significant interference (interference within ± 10%) was observed at the following concentrations.

No Significant Interference (Interference within ± 10%)	
Potentially Interfering Substance	**Interferent Level**
Hemoglobin	1000 mg/dL
Indican	1 mg/dL
Total protein	15 g/dL
Triglycerides	1500 mg/dL

Interference beyond ± 10% (based on 95% Confidence Intervals [CI]) was observed at the concentration shown below for the following substance.

Interference beyond ± 10% (based on 95% Confidence Interval [CI])			
Potentially Interfering Substance	**Interferent Level**	**Analyte Level**	**% Interference (95% CI)**
Indican	2 mg/dL	2 mg/dL	17% (15%, 19%)

Potentially Interfering Exogenous Substances

A study was performed based on guidance from CLSI EP07, 3rd ed.* Each substance was tested at 2 levels of the analyte (approximately 2 mg/dL and 15 mg/dL).

* Clinical and Laboratory Standards Institute (CLSI). *Interference Testing in Clinical Chemistry*. 3rd ed. CLSI Guideline EP07. Wayne, PA: CLSI; 2018.

* Clinical and Laboratory Standards Institute (CLSI). *Interference Testing in Clinical Chemistry*. 3rd ed. CLSI Guideline EP07. Wayne, PA: CLSI; 2018.

No significant interference (interference within ± 10%) was observed at the following concentrations.

No Significant Interference (Interference within ± 10%)	
Potentially Interfering Substance	**Interferent Level**
4-Hydroxypropranolol glucuronide	0.2 mg/dL
Acetaminophen	160 mg/L
Acetylcysteine	150 mg/L
Acetylsalicylic acid	30 mg/L
Ampicillin-Na	80 mg/L
Ascorbic acid	60 mg/L
Biotin	4250 ng/mL
Ca-dobesilate	60 mg/L
Cefoxitin	6600 mg/L
Cyanokit (hydroxocobalamin)	2259 mg/L
Cyclosporine	2 mg/L
Doxycycline	20 mg/L
Eltrombopag	300 mg/L
Ibuprofen	220 mg/L
Indocyanine green	5 mg/L
Iron dextran	60 mg/L
Levodopa	8 mg/L
Methyldopa	25 mg/L
Metronidazole	130 mg/L
Oxytetracycline	12 mg/L
Phenylbutazone	330 mg/L
Propranolol	0.1 mg/dL

No Significant Interference (Interference within ± 10%)	
Potentially Interfering Substance	**Interferent Level**
Rifampicin	50 mg/L
Sodium heparin	4 U/mL
Theophylline (1,3-dimethylxanthine)	60 mg/L

Interference beyond ± 10% (based on 95% Confidence Intervals [CI]) was observed at the concentrations shown below for the following substance.

Interference beyond ± 10% (based on 95% Confidence Interval [CI])			
Potentially Interfering Substance	**Interferent Level**	**Analyte Level**	**% Interference (95% CI)**
Indocyanine green	10 mg/L	2 mg/dL	9% (8%, 11%)

G. Method Comparison

A study was performed based on guidance from CLSI EP09c, 3rd ed.[††] using the Passing-Bablok regression method.

Total Bilirubin2 vs Total Bilirubin on the ARCHITECT c System						
	n	**Units**	**Correlation Coefficient**	**Intercept**	**Slope**	**Concentration Range**
Serum	167	mg/dL	1.00	-0.03	1.03	0.1–22.5
Neonatal serum	163	mg/dL	1.00	0.00	1.00	0.2–22.8

[††] Clinical and Laboratory Standards Institute (CLSI). *Measurement Procedure Comparison and Bias Estimation Using Patient Samples.* 3rd ed. CLSI Guideline EP09c. Wayne, PA: CLSI; 2018.

H. Tube Type

A study was performed to evaluate the suitability of specific blood collection tube types for use with the Total Bilirubin2 assay. Samples were collected from a minimum of 40 donors and evaluated across tube types. The following blood collection tube types were determined to be acceptable for use with the Total Bilirubin2 assay:

Serum

- Serum tubes
- Serum separator tubes

Plasma

- Dipotassium EDTA tubes
- Lithium heparin tubes
- Lithium heparin separator tubes
- Sodium heparin tubes

I. Dilution Verification

A study was performed based on guidance from CLSI EP34 1st ed.* to evaluate the performance of the automated dilution protocol and manual dilution procedure of the Total Bilirubin2 assay (LN 04T09) on the ARCHITECT c8000 instrument.

Five samples were prepared to have total bilirubin concentrations within the extended measuring interval (EMI) of the Total Bilirubin2 assay by spiking total bilirubin stock into a serum pool to the target concentration values of 30.0 mg/dL, 55.0 mg/dL, 70.0 mg/dL, 90.0 mg/dL, and 110.0 mg/dL.

The performance of the automated dilution protocol (1:5) and manual dilution procedure (1:5) was considered acceptable if, for samples within the EMI, the dilution recovery was within or equal to 100% ± 10% when comparing auto-diluted or manually

* Clinical and Laboratory Standards Institute (CLSI). *Establishing and Verifying an Extended Measuring Interval Through Specimen Dilution and Spiking*. 1st ed. CLSI Guideline EP34. Wayne, PA: CLSI; 2018.

diluted samples to target or assigned concentrations and the imprecision was ≤ 7 %CV for the automated dilution protocol and ≤ 8 %CV for manual dilution procedure.

The % recovery results of 96.3% to 104.4% for the automated dilution, and 95.0% to 106.7% for the manual dilution, demonstrated acceptable performance.

The imprecision results of 1.6% to 2.5% for the automated dilution, and 2.2% to 4.9% for the manual dilution, demonstrated imprecision ≤ 7 %CV for the automated dilution protocol and ≤ 8 %CV for manual dilution procedure.

IX. Summary of Clinical Performance

This section does not apply.

X. Conclusion Drawn from Nonclinical Laboratory Studies

The results presented in this 510(k) premarket notification demonstrate that the performance of the subject device, Total Bilirubin2 (List No. 04T09), is substantially equivalent to the predicate device, Total Bilirubin (List No. 6L45, k121985).

The similarities and differences between the subject device and predicate device are presented in Section 5-VII.

There is no known potential adverse effect to the operator when using this *in vitro* device according to the Total Bilirubin2 reagent package insert instructions.