



July 31, 2024

Axis-Shield Diagnostics Ltd.
Claire Dora
Associate Director, Regulatory Affairs
Luna Place, The Technology Park
Dundee, DD2 1XA, Scotland, UK

Re: K233541

Trade/Device Name: ARCHITECT Active-B12 (Holotranscobalamin)
Regulation Number: 21 CFR 862.1810
Regulation Name: Vitamin B12 test system
Regulatory Class: Class II
Product Code: CDD
Dated: June 28, 2024
Received: July 1, 2024

Dear Claire Dora:

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.

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

Indications for Use

510(k) Number (if known)
K233541

Device Name
ARCHITECT Active-B12 (Holotranscobalamin)

Indications for Use (Describe)

The ARCHITECT Active-B12 (Holotranscobalamin) assay is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of Holotranscobalamin in human serum on the ARCHITECT i System. Active-B12 (Holotranscobalamin) is used as an aid in the diagnosis and treatment of vitamin B12 deficiency

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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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510(k) Summary

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:

K233541

B. 510(k) Preparation Date:

31st July 2024

C. Applicant and Correspondent:

Axis-Shield Diagnostics Ltd.

The Technology Park

Dundee, DD2 1XA,

Scotland, UK

Establishment # 8032314

Dr Claire Dora

Associate Director, Regulatory Affairs

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D. Device Name:

ARCHITECT Active-B12 (Holotranscobalamin) Reagents



E. Regulatory Information:

Trade Name: ARCHITECT Active-B12 (Holotranscobalamin)
Common Name: Vitamin B12 Radioassay
Classification Name: Vitamin B12 test system
Governing Regulation: 21CFR 862.1810
Product Code: CDD
Device Classification: Class II
Classification Panel: Clinical Chemistry

F. Legally marketed device to which equivalency is claimed:

ARCHITECT Active-B12 (Holotranscobalamin), K112443.

G. Description of Device:

The ARCHITECT Active-B12 (Holotranscobalamin) assay is a two-step immunoassay for the quantitative determination of Holotranscobalamin in human serum using CMIA technology, with flexible assay protocols, referred to as Chemiflex.

In the first step, sample and anti-holotranscobalamin coated paramagnetic microparticles are combined. Holotranscobalamin present in the sample binds to the anti-holotranscobalamin coated microparticles. After washing, anti-transcobalamin acridinium-labeled conjugate is added to create a reaction mixture in the second step. Following another wash cycle, pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of Holotranscobalamin in the sample and the RLUs detected by the ARCHITECT i System optics.



H. Intended Use of Device:

The ARCHITECT Active-B12 (Holo transcobalamin) assay is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of Holo transcobalamin in human serum on the ARCHITECT i System. Active-B12 (Holo transcobalamin) is used as an aid in the diagnosis and treatment of vitamin B12 deficiency.

I. Comparison with Predicate Device:

The modified (candidate) ARCHITECT Active-B12 (Holo transcobalamin) assay is substantially equivalent to the predicate device previously cleared under 510(k) premarket notification, K112443. The function and intended use of the device are equivalent to the predicate device. The table below provides a comparison of the technological characteristics of the proposed and predicate devices.

Attribute	Original Device (Predicate) ARCHITECT Active-B12 (Holo transcobalamin), K112443	Candidate Device (New) ARCHITECT Active-B12 (Holo transcobalamin)
SIMILARITIES		
FDA Product Code	CDD	Same
Intended Use	The ARCHITECT Active-B12 (Holo transcobalamin) assay is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of Holo transcobalamin in human serum on the ARCHITECT iSystem. Active-B12 (Holo transcobalamin) is used as an aid in the diagnosis and treatment of vitamin B12 deficiency.	Same
Intended Use Environment	Rx Only	Same



Attribute	Original Device (Predicate) ARCHITECT Active-B12 (Holotranscobalamin), K112443	Candidate Device (New) ARCHITECT Active-B12 (Holotranscobalamin)
Instrument	ARCHITECT i 2000SR system	Same
Assay Technology	Chemiluminescent microparticle immunoassay (CMIA)	Same
Units of Measure	pmol/L	Same
Measuring Interval (Reportable Range)	5.0 – 128.0 pmol/L	Same
Sample type	Serum (serum and SST)	Same
Storage Requirements for reagents, calibrators and controls	2-8°C until expiration date	Same
Onboard Storage	System temperature up to 30 days	Same
Stored Calibration	Calibration frequency 30 days	Same
Expected values	Central 95%: 25.1 to 165.0 pmol/L	Same
Limit of Quantitation (LoQ)	5.0 pmol/L	Same
Linear range	Across the measuring interval, 5.0 to 128.0 pmol/L	Same
Cross-reactivity	≤ 10% Cross-reactivity observed in presence of; <ul style="list-style-type: none"> • Apotranscobalamin at 500 pmol/L • Haptocorrin at 5000 pmol/L 	Same
Interference	≤10% bias in the presence of the following substances; <ul style="list-style-type: none"> • Triglycerides 850 mg/dL • Rheumatoid Factor 70 IU/mL 	Same



DIFFERENCES		
Sample volume	110µL	70µl with 40µL buffer chase
Calibrator value assignment	Calibrator values: 0.0, 8.0, 16.0, 32.0, 64.0, 128.0 pmol/L	Calibrator Values: 0.0, 7.4, 16.8, 35.7, 73.5, 149.1 pmol/L
Lot-to-Lot	No Lot-to-lot data	Maximum % difference from target to observed concentration was 9.1%
Precision	Total %CV ≤ 5.8 % Within-run %CV ≤ 4.4 %	For samples with holotranscobalamin concentrations ≥ 20 pmol/L: <ul style="list-style-type: none"> • Total %CV ≤ 6.2 % • Within-run %CV ≤ 5.8 % For samples with holotranscobalamin concentrations <20 pmol/L: <ul style="list-style-type: none"> • Total SD observed was 0.62 and 1.50 • Within-run SD observed was 0.49 and 1.37
Interference	≤10% bias in the presence of the following substances; <ul style="list-style-type: none"> • Bilirubin 20 mg/dL • Hemoglobin 200 mg/dL • Total Protein 10 g/dL • Biotin -Not tested 	≤10% bias in the presence of the following substances; <ul style="list-style-type: none"> • Bilirubin (unconjugated) 40 mg/dL • Bilirubin (conjugated) 40 mg/dL • Hemoglobin 1000 mg/dL • Total Protein 15 g/dL • Biotin 4250 mg/dL

J. Summary of Non-Clinical Performance:

The ARCHITECT Active-B12 (Holotranscobalamin) assay demonstrated substantially equivalent performance to the predicate, ARCHITECT Active-B12 (Holotranscobalamin) assay, K112443. A summary of the non-clinical performance data included in this 510(k) submission has been presented below for the candidate device, ARCHITECT Active-B12 (Holotranscobalamin) assay.

Precision

Precision was evaluated according to the CLSI guideline EP05-A3, 3rd Ed.

The candidate device demonstrated a $\leq 8\%$ within-laboratory (total) %CV for samples with HoloTC concentrations ≥ 20.0 pmol/L and a total standard deviation (SD) of ≤ 1.6 pmol/L for samples with HoloTC concentrations < 20.0 pmol/L.

Detection Capability

Limit of Quantitation was evaluated according to the CLIS guideline EP17-A2, 2nd Ed.

10 low-level HoloTC samples at concentration levels ranging from 0.6 to 5.5 pmol/L were prepared. These samples were tested over 3 days using 2 reagent lots and 1 instrument. The LoQ was determined to be 0.7 pmol/L.

In the same study, the Limit of Blank (LoB) and Limit of Detection (LoD) were determined. The LoB was 0.1 pmol/L and the LoD was 0.2 pmol/L.

Linearity

Linearity was evaluated according to the CLSI guideline EP06-Ed2:2020, 2nd Ed.

One dilution series was prepared as follows: a high HoloTC sample was combined in specific ratios with a low HoloTC sample. The dilution series, including the low level and high-level sample, was tested using the ARCHITECT Active-B12 (Holotranscobalamin) assay. The ARCHITECT Active-B12 (Holotranscobalamin) assay demonstrated linearity across the measuring interval from 5.0 to 128.0 pmol/L (actual range observed: 2.26 to 134.17 pmol/L).

High Sample Dilution Verification

High Sample dilution capabilities (Autodilution and manual dilution) was evaluated using the 1:2 assay protocol using human serum samples diluted with assay specific multi-diluent.

The observed percent recovery for individual samples for when comparing manual to auto dilution met the study design as defined as 90 – 110% recovery for auto vs manual.

Reactivity

Reactivity was evaluated following according to the CLSI guideline EP07, 3rd Ed.

No reactivity was observed as defined by $\leq 10\%$ reactivity for B₁₂ binding proteins apotranscobalamin at 500 pmol/L and haptocorrin at 5000 pmol/L.

Interference

Interference was evaluated following according to the CLSI guideline EP07, 3rd Ed.

No interference was observed as defined by $\leq 10\%$ bias $\leq 10\%$ in the presence of the following substances;

- Bilirubin (conjugated and unconjugated), 40 mg/dL
- Hemoglobin, 1000 mg/dL
- Total Protein, 15 g/dL
- Triglycerides, 850 mg/dL
- Rheumatoid Factor, 70 IU/mL
- Biotin, 4250 ng/mL

On-Board Stability

On-Board stability and Calibration Interval were evaluated based on guidance from the CLSI guideline EP25-A, 1st Ed.

For the on-board stability study, three native serum pools targeted at the medical decision points of the assay were assessed in fresh and reference reagent kits (stored at intended storage of 2-8°C) and test reagent kits (stored on-board the instrument) over a period of 31 days. Ten testing time-points were spread out over this testing period. All samples demonstrated suitable stability through linear regression analysis detailing delta values

(pmol/L) versus Test Day over the 31 days; therefore supporting reagent on-board stability of 30 days.

For calibration interval, 3 testing time-points were performed up to 31 days. All samples demonstrated % difference <10% to Day 0 over the 31 days; therefore supporting reagent calibration interval of 30 days.

K. Comparison Studies

The ARCHITECT Active-B12 (Holotranscobalamin) assay demonstrated substantially equivalent performance to the predicate, ARCHITECT Active-B12 (Holotranscobalamin) assay as indicated by a method comparison.

Method Comparison

A correlation study was performed based on guidance from the CLSI EP09c.

Using two candidate lots and one predicate lot, 108 samples ranging from 5.4 to 128.0 pmol/L were evaluated using the Pearson correlation coefficient (r) and the Passing-Bablok regression method where by a slope of 0.9 and r value of 0.95 was demonstrated.

L. Conclusion:

Based on the performance characteristics, the ARCHITECT Active-B12 (Holotranscobalamin) assay is substantially equivalent to the predicate device cleared in K112443. The modifications to the assay have not changed the intended use, as described in the labelling, nor have the changes altered the fundamental assay technology of the device.