Individuals using assistive technology may not be able to fully access the information contained in this file. For assistance, please call 800-835-4709 or 240-402-8010, extension 1. CBER Consumer Affairs Branch or send an e-mail to: ocod@fda.hhs.gov and include 508 Accommodation and the title of the document in the subject line of your e-mail.

Summary Basis for Regulatory Action

Date: March 13, 2026

From: Krishna Mohan V. Ketha, Ph.D.,
Chair of the Review Committee

BLA/ STN#: 125862/0

Applicant Name: Grifols Diagnostic Solutions

Date of Submission: May 27, 2025

MDUFA Goal Date: March 27, 2026

Proprietary Name: Procleix Plasmodium

Intended Use:
The Procleix Plasmodium Assay is a qualitative *in vitro* nucleic acid amplification test for the detection of RNA from *Plasmodium* species (*P. falciparum, P. knowlesi, P. malariae, P. ovale,* and *P. vivax*) in whole blood specimens performed on the Procleix Panther System. It is intended for use in screening individual human donors, including donors of whole blood and blood components, and in screening donors of organ and tissue samples when specimens are obtained while the donor's heart is still beating. It is not intended for use on cord blood specimens. Whole blood donor samples are tested individually.

This assay is not intended for use as an aid in diagnosis of *Plasmodium* infection.

Recommended Action: The Review Committee recommends licensure of this product.

Review Office Signatory Authority: Anne Eder, M.D., Director, Office of Blood Research and Review

X I concur with the summary review.
□ I concur with the summary review and include a separate review to add further analysis.
□ I do not concur with the summary review and include a separate review.

The table below indicates the material reviewed when developing the SBRA.

Table 1: Reviews Submitted

Document Title	Reviewer Name	Document Date
Product Review (*OBRR/DETTD*)		
• *Clinical*	Krishna Mohan V. Ketha, PRB Caren Chancey, PRB Kavita Singh, PRB	February 27, 2026 February 26, 2026 March 2, 2026
• *Non-Clinical*	Ranadhir Dey, PRB Miranda Oakley, LEP	February 27, 2026 February 26, 2026
Living Organ Donor *(OTP/DHT)*	Hahn Khuu, HTRS	February 19, 2026
Statistical Review • *Clinical and Non-Clinical (OBPV/DB/DNCE)*	Ngoc Ty Nguyen	February 13, 2026
CMC Review		
• *CMC (OBRR/DETTD)*	Virginie Dujols, PRB Nitin Verma, PRB	February 24, 2026 February 24, 2026
• *Facilities Review (OCBQ/DMPQ)*	Antonia Panthiruvelil, MRB1	January 18, 2026
• *Microbiology Review (OCBQ/DMPQ)*	Brianna Davis, LMVTS	March 11, 2026
• *Inspection Waiver OCBQ/DMPQ)*	Antonia Panthiruvelil, MRB1	January 5, 2026
Labeling Review(s)		
• *APLB (OCBQ/APLB)*	Jun Lee	February 6, 2026
• *Product Office (OBRR/DETTD)*	Krishna Mohan V. Ketha	March 3, 2026
Lot Release Protocols/Testing Plans (OCBQ/DBSQC)	George Kastanis, QAB	March 2, 2026
In-support Testing (OCBQ/DBSQC)	Mathew Arnold, LBRP	March 10, 2026
Bioresearch Monitoring Review (*OCBQ/BIMO*)	Haecin Chun	February 26, 2026
Software and Instrumentation *(OBRR/DETTD)*	Hongqiang Hu, PRB Rana Nagarkatti, PRB	February 23, 2026

1. Introduction

This biologics license application (BLA) for Procleix Plasmodium assay from Grifols Diagnostic Solutions, 10804 Willow Court, San Diego, CA 92127 USA was received on May 27, 2025. The Procleix® Plasmodium Assay is manufactured at the Willow Court Facility (b) (4)

The application was assigned the number STN 125862/0 and granted a standard 10-month review status with a goal date of March 27, 2026. The application was filed July 8, 2025, and the mid-cycle meeting took place on October 28, 2025.

The BLA application was preceded by pre-submission BQ231026/0 and a supplement BQ231026/1, focused on the regulatory aspects regarding pre-clinical studies, clinical studies, and software and instrumentation for the Procleix Plasmodium assay. An investigational new drug application (IND) 30609 was submitted for all proposed clinical studies, followed by eighteen amendments; the last amendment was dated July 10, 2025.

Table 2: Chronological Summary of Submission and FDA Interaction with Grifols Diagnostic Solutions (GDS)

Date	Action	Amendment
May 27, 2025	Original BLA received	BL125862/0
July 16, 2025	Grifols proposed a new lot-to-lot variability study	
August 27, 2025	FDA IR – reanalysis of reproducibility study	
August 29, 2025	Grifols proposed new lot-to-lot variability study	BL125862/0/1
September 16, 2025	Reanalyzed Reproducibility report for Lot 1 and 2	(b) (4)
September 23, 2025	Grifols submitted Clinical Sensitivity Report v2.0	(b) (4)
October 03, 2025	IR – Clinical and Non-clinical studies	
October 14, 2025	Response to FDA IR 10/03/25	(b) (4)
October 14, 2025	IR – CMC validation	
October 15, 2025	IR – Batch Records for Lot 1 and Lot (b) (4)	
October 16, 2025	Response to FDA IR 10/14/25	(b) (4)
October 21, 2025	Response to FDA IR 10/15/25	(b) (4)
October 24, 2025	IR – Lot Release Protocol (LRP)	
October 31, 2025	Response to BIMO Inspection – Form 3454	(b) (4)
November 3, 2025	Response to FDA IR 10/24/25	(b) (4)
November 25, 2025	IR – CMC Process Qualification	
December 9, 2025	Response to FDA IR 11/25/25	(b) (4)
December 16, 2025	IR – Analyte sequences used in various assays	
December 22, 2025	Response to FDA IR 12/16/25	(b) (4)
January 13, 2026	IR – (b) (4) oligos	
January 13, 2026	IR – Manufacturing Process clarification	
January 14, 2026	Response to IR 12/13/25 – sequence info	(b) (4)
January 14, 2026	Response to IR 12/13/25 – Mfr. process	(b) (4)
January 22, 2026	IR – Status of lot-to-lot reproducibility study	
January 22, 2026	IR – CMC Bioburden	
January 23, 2026	Response to IR 1/22/26 – Status of study report	(b) (4)
January 28, 2026	Lot to Lot Reproducibility Data submitted	(b) (4)
January 29, 2026	Response to FDA IR 1/22/26 – CMC bioburden	(b) (4)
February 2, 2026	IR – (b) (4) bioburden	
February 2, 2026	Response to FDA IR 2/2/26	(b) (4)
February 11, 2026	IR – Combined real-time stability data	
February 11, 2026	IR – Software versions used for various studies	
February 13, 2026	Response to IR 2/11/26 – Stability Data	(b) (4)
February 17, 2026	Response to IR 2/11/26 – Software details	(b) (4)
February 20, 2026	IR – Details for analytical studies	
February 20, 2026	IR – Lot Release Protocol (LRP) template	
February 20, 2026	Response to IR 2/20/26 – Analytical study info	(b) (4)
February 23, 2026	Response to IR 2/20/26 – LRP template	(b) (4)

2. Background

Malaria is a globally prevalent mosquito-borne disease caused by an intraerythrocytic protozoan parasite belonging to the genus *Plasmodium*. Although predominately transmitted by mosquito bite, malaria can also be acquired via blood transfusion and organ transplantation, and from mother to fetus. Five main species of Plasmodium are known to infect humans: *P. falciparum*, *P. knowlesi*, *P. malariae*, *P. ovale,* and *P. vivax*. The most frequent and most serious infections are caused by *P. falciparum*, followed by *P. vivax*.

Clinically, symptoms may include fever, chills, headache, and malaise, and in severe cases may include hypoglycemia, convulsions, severe anemia, acute renal failure, jaundice, pulmonary edema, cerebral malaria, shock, and acidosis, and may be fatal. In some cases, infections may be chronic and/or asymptomatic for several years. In the United States, Transfusion transmitted malaria (TTM) may occur following transfusion of donated blood components from asymptomatic blood donors with dormant liver-stage or chronic, asymptomatic blood-stage parasitic infection. The fatality rate associated with TTM is higher than the fatality rate among imported clinical cases.

The Procleix Plasmodium Assay shares assay principles, manufacturing technologies and controls, and common reagents with other FDA-approved Procleix donor screening assays developed for use with the Procleix Panther System. The Panther System consists of an analyzer, associated hardware/software, assay reagents, and assay-specific software. A total of five kits are required to perform the Procleix Plasmodium Assay on the Panther System: two *Plasmodium*-specific assay kits and three ancillary kits, common to all Procleix assays (Table 3).

The Procleix Plasmodium Assay targets the 18S ribosomal RNA of the *Plasmodium* species for amplification and subsequent detection. Whole blood lysate is prepared either manually or on the Procleix Xpress System by addition of whole blood to the Parasite Transport Medium (PTM). Lysates (0.3 mL) are then analyzed as individual donations. The Procleix Plasmodium Assay involves three steps, which take place in a single tube on the Procleix Panther System: target capture, *Plasmodium* RNA amplification that utilizes transcription-mediated nucleic acid amplification (TMA) technology, involving production of cDNA by Moloney Murine Leukemia Virus (MMLV) reverse transcriptase followed by T7 promoter-driven transcription and hybridization with target-specific single-stranded luminescent nucleic acid probes. After luminescence is measured, the reactivity of the specimen is determined by calculating the signal-to-cutoff (S/CO) ratio. The assay performance is ensured through the addition of an Internal Control (IC) to each specimen tube, and the assay cutoff and run validity is determined using assay calibrators. Chemiluminescent probes that hybridize to the IC targets are discriminated from *Plasmodium*-specific probes by differential kinetics of light emission. The chemiluminescent signal produced by the hybridized probe is measured by a luminometer and reported as Relative Light Units (RLU). The Procleix Plasmodium Assay is currently marketed in 44 countries.

3. Chemistry Manufacturing and Controls (CMC)

The manufacturing of the Procleix Plasmodium assay is performed in accordance with Current Good Manufacturing Practices (cGMP) in an environmentally controlled facility.

a) Manufacturing Summary

The Procleix Plasmodium assay is manufactured at the Willow Court Facility located at 10808 Willow Court, San Diego, CA 92127 (b) (4)

i) In Vitro Substance

The *in vitro* substances (active ingredient) for the Procleix Plasmodium Assay are the (b) (4) oligonucleotides contained in the Procleix Plasmodium Assay kit. The oligonucleotides are categorized into (b) (4) distinct classes based on structure, function, and chemical composition as follows:

(b) (4)

(b) (4) of the (b) (4) Procleix Plasmodium Assay oligonucleotides are identical in structure, composition, manufacturing and control processes, specifications, and analytical methods to those of other licensed Procleix Assays. *Plasmodium*-specific oligonucleotides (capture oligonucleotides, amplification primers, and probes) target highly conserved regions of 18S ribosomal RNA for all five *Plasmodium* species. The manufacturer provided information on structure, composition, and characterization of the oligonucleotides. The in-process controls during manufacturing involved evaluation of (b) (4) and an in-process test performed to determine (b) (4) The shelf-life dating results were found to be acceptable.

ii) In Vitro Product

The BLA contained information on the common reagents and kits within the Procleix Plasmodium Assay kit. All components of the Procleix Plasmodium

Assay kit and Procleix Ancillary kits are manufactured and controlled at the Willow Court facility (WCt) (b) (4) . All manufacturing facilities are licensed and used to manufacture other Procleix commercialized products. Table 3 lists the five kits required to perform the Procleix Plasmodium Assay on the Panther System and their manufacturing locations.

Table 3: Procleix Plasmodium Assay kits, components and manufacturing locations

Kit	Plasmodium-specific or Common Kits	Reagent/Component	MFG Facility
Procleix Plasmodium Master kit	Specific	Enzyme Reagent	WCt
		Internal Control reagent	(b) (4)
		Amplification Reagent	WCt
		Probe Reagent	WCt
		Target Capture Reagent (TCR)	WCt
		Selection Reagent	WCt
Procleix Plasmodium Assay Calibrators kit	Specific	Negative Calibrator	WCt
		Positive Calibrator	(b) (4)
Procleix Assay Fluids kit	Common	Wash solution	WCt
		Oil	WCt
		Buffer for deactivation fluid	WCt
Procleix Auto Detect Reagents kit	Common	Auto Detect 1	WCt
		Auto Detect 2	WCt
Procleix Parasite Transport Medium kit	Common	Parasite Transport Medium	WCt

Manufacturing process information was provided for the Procleix Plasmodium Assay kit and Procleix Ancillary kits that included the Internal Control Reagent, Target Capture Reagent, Amplification Reagent, Probe Reagent, Selection Reagent, *Plasmodium* Positive Calibrator, Negative Calibrator, Procleix Assay Fluids kit, Procleix Auto Detect Reagents kit, and the Procleix Parasite Transport Medium kit. The information included a brief description of the reagent's function, components and composition, manufacturing process, in-process control validations, lot release specifications and analytical methods, and lot release results. Release testing for the Procleix Plasmodium Assay Calibrators kit was based on visual criteria and performance testing was not required for this kit. In-process control validations were performed using representative materials from other Procleix assays, which were found acceptable since the manufacturing process is the same.

Acceptance criteria included specifications and analytical methods to establish the identity, strength, quality, and purity, and lot-to-lot consistency of the Procleix Plasmodium Assay kit and the Procleix PTM. The ancillary kit reagents are

included as part of the master lot release testing performed on the Procleix Plasmodium Assay kit. Performance testing was not performed for the Procleix Auto Detect kit, but individual reagents were tested, and QC-released at the component level only.

b) Test Specifications

The analytical methods and their validations and/or qualifications reviewed for the Procleix Plasmodium Assay were found to be adequate for their intended use.

c) CBER Lot Release

The lot release protocol template was submitted to CBER for review and found to be acceptable after revision. A lot release testing plan was developed by CBER and will be used for routine lot release.

d) Facilities Review/Inspection

Facility information and data provided in the BLA STN 125862/0 were reviewed by CBER and found to be sufficient and acceptable. The facilities involved in the manufacture of the Procleix Plasmodium Assay are listed in the table below. The activities performed and inspectional histories are noted in Table 4 and further described in the paragraphs below.

Table 4. Summary of Manufacturing Facilities Inspection

Name/Address	FEI number	DUNS number	Inspection/ waiver	Justification/ Results
Grifols Diagnostic Solutions Inc., 10808 Willow Court, San Diego, CA 92127 Manufacturing of kit components, ancillary components, and kit packaging,	3003460312	080939915	Waiver	August 2025 Surveillance FDA/OII/OBI VAI June 2024 PAI CBER/DMPQ VAI

Acronym key: Office of Inspections and Investigations (OII); Office of Biologics Inspectorate (OBI); Voluntary Action Indicated (VAI); Pre-Approval Inspection (PAI), CBER – Center for Biologics Evaluations and Research; Division of Manufacturing Product Quality (DMPQ)

Grifols Diagnostics Solutions Inc. manufactures the Procleix Plasmodium Assay at its Willow Court site in San Diego, CA, which is composed of (b) (4) facilities. The Willow Court address includes (b) (4) facilities and are as follows: 10808 Willow Court facility manufactures kit reagents, ancillary reagents, and packages the kits (b) (4) facility conducts release testing. The (b) (4) facility manufactures the positive calibrator and internal control kit components.

A surveillance inspection of the Willow Court facilities was conducted by OII from August 19-29, 2025. A Form FDA 483 list of observations was issued at the end of the inspection. The firm responded to the observations and the corrective actions

were reviewed. All inspectional issues were resolved, and the inspection was classified as VAI.

A PAI of the (b) (4) facility was conducted by CBER/DMPQ from (b) (4) (b) (4). A Form FDA 483 list of observations was issued at the end of the inspection. The firm responded to the observations and the corrective actions were reviewed. All inspectional issues were resolved, and the inspection was classified VAI.

e) Environmental Assessment

The BLA included a request for categorical exclusion from an Environmental Assessment under 21 CFR 25.31(c). The FDA concluded that this request is justified as the manufacturing of this product will not significantly alter the concentration and distribution of naturally occurring substances and no extraordinary circumstances exist that would require an environmental assessment.

f) Container Closure System

N/A

4. Software and Instrumentation

The following is a summary overview of software, instrumentation, and risk management information provided to support a reasonable assurance that the device is safe and effective for its intended uses and conditions of use.

Versioning:

- Panther System software v7.4 .3
- Procleix Plasmodium Assay software version 1.2.5.2.
- Panther System Operational Manual version 001
- Procleix Xpress System v4.0

Device Description:

Hardware Description

The Procleix Panther System ("Panther System") is an integrated nucleic acid testing system that fully automates all steps necessary to perform Procleix assays from sample processing through amplification, detection, data reduction, and interpretation. The Panther System includes the instrument (analyzer and associated hardware), and software (system software and assay software) used to perform a specific assay such as the Procleix Plasmodium Assay. The Panther System is composed of four main areas: the Canopy, Upper Bay, Mid Bay, and Lower Bay, each containing various mechanical modules.

The Panther System detects nucleic acid from specimens using Grifols assay technology by automating the following assay processing steps:

1) Sample processing - Target Capture process isolates and purifies the target nucleic acid from specimens.

2) Amplification - Transcription-Mediated Amplification (TMA) of target produces multiple copies of RNA for easier detection of nucleic acid.
3) Detection - Hybridization Protection Assay (HPA) detection of the amplified nucleic acid using light emitting nucleic acid probes and the Dual Kinetic Assay (DKA) to differentiate the kinetic profiles between probes that have a very rapid kinetic profile vs those with a very slow kinetic profile.
4) Results Report Generation - Assay results from each sample are determined by an adjusted Relative Light Unit (RLU) based on the valid calibrators.

Software Description

There are two software components of the Panther System required to perform Procleix Plasmodium Assay:

1) Panther System Software – Manufactured by Hologic Inc.
2) Assay Software – Manufactured by Grifols Diagnostic Solutions Inc.

The Panther System Software includes the Master Controller software and instrument firmware, is 'assay-independent' and can be used for all assays on the Procleix Panther System. The assay software, also known as Assays Definition Module (ADM), contains the assay-specific parameters to perform the assay and contains all the parameters needed for the Panther System software to run the assay and generate results. The Panther System software communicates with the assay software to access assay-specific parameters.

A component of the ADM is the Assay Definition File (ADF), a text file containing all the information the Panther System needs to run a specific assay. The ADF is packaged with the data reduction modules (calculation software libraries). The ADM refers to the entire package, which includes the ADF and the data reduction modules.

The Procleix Panther System Software operates on the Microsoft Windows® (Windows 10) operating system (OS) and was developed using the (b) (4) framework, customized as per specifications developed by Hologic, Inc. specifically for use with Panther instrument, which is comprised of three main modules: Panther Graphical User Interface (GUI), the Data Manager Module, and the Instrument Control Module.

Detailed diagrams and descriptions of the Procleix Panther instrument, architecture, risk evaluation, and verification and validation (V&V) testing are provided in this submission along with the description of the Procleix Plasmodium Assay and Procleix Panther System software and cybersecurity information.

Risk Management:

Risks related to donor test results, exposure of user to infectious disease agents, chemical, physical, and environmental hazards were evaluated. Major hazards include incorrect results, i.e., false positive and false negative donor test results, and moderate hazards include delayed results and physical hazards to the user/operator.

After the implementation of risk control, the final risk profile of the Procleix Plasmodium Assay includes (b) (4) (unacceptable) risks, (b) (4) risks (that required assessment of acceptability), and (b) (4) (negligible) risks. The final risk profile of the Procleix Assay Software includes (b) (4) (unacceptable) risks, (b) (4) risks, and (b) (4) risks. The final risk profile of the Panther instrument includes (b) (4) and (b) (4) risks, and (b) (4) risks. And the final risk profile of the Procleix Xpress System v4.0 includes (b) (4) risks, (b) (4) risks and (b) (4) risks.

Of the (b) (4) risks for the Plasmodium Assay, (b) (4) are related to incorrect results (false negative/positive results) (b) (4) and (b) (4) are related to operation of the assay (due to user exposure to infectious material, personal injury leading to delays/interruption). Of the (b) (4) (b) (4) risks for the Assay Software, (b) (4) are related to incorrect results (false negative/positive results) (b) (4) and (b) (4) is related to incorrect information display. The (b) (4) risks for the Panther instrument are related to user handling with sample/reagents, contamination, and equipment errors including (b) (4) Of the (b) (4) risks for the Procleix Xpress System v4.0, (b) (4) risks are related to incorrect results (false negative/positive results) (due to (b) (4) risks are related to product user and (b) (4) risks are related delayed results.

A cybersecurity risk assessment for the Panther System installed on a customer's network was conducted. This risk assessment includes all known or foreseeable hazards related to cybersecurity, including hazardous conditions caused by (b) (4) Hazards are identified using (b) (4) The risk analysis was performed according to predefined criteria for hazard severity, probability of occurrence, residual risk and acceptance requirements. After the implementation of risk control, the final cybersecurity risk profile of the Panther System includes (b) (4) (unacceptable) risks, (b) (4) risks, and (b) (4) risks. Of the (b) (4) risks for the Panther System, (b) (4) are related to (b) (4) and (b) (4) is related to (b) (4) . The final cybersecurity risk profile of the Procleix Xpress System v4.0 includes (b) (4) (unacceptable) risks, (b) (4) risks, and (b) (4) risks. Of the (b) (4) risks, (b) (4) risks are related to (b) (4) , and (b) (4) is related to (b) (4) by a

(b) (4) . Hazards related to cybersecurity on the Panther instrument are adequately mitigated to support safety, intended use, and donor/user safety.

The applicant stated that all risk control measures are implemented and verified, and that the labeling notifies the user of residual risks. Significant risk control measures include use of barcodes/RFID tags for sample and reagent tracking, automated checks for expiry of onboard assay reagents and QC reagents, maintenance procedures, labeling and user manuals, database management with automated scheduled data backups, and access controls with individual usernames and passwords, automated lock-out after periods of inactivity, firewalls and encryption, and configuration management, among others. The applicant concluded the overall residual risk of the Panther System software is acceptable. This assessment appears to be supported by the evidence provided.
All the hazards related to the Procleix Assays Software were evaluated and implementation of all mitigations were verified. The residual risks of the identified hazards are acceptable. There are no hazards that fall within the categories of "Unacceptable" residual risk. The overall residual risk of Procleix Plasmodium Assay on the Procleix Panther System is acceptable, and the benefits provided by the assay outweigh the risks.

Unresolved Anomalies:
Grifols conducted software V&V testing to ensure that the Panther and Panther Fusion System Software, Version 7.2.7, and associated assays conforms to user needs and intended uses, and a total of 54 unresolved anomalies were reported. The reporting and assessment of anomalies was conducted in accordance with the Software Anomaly Management Work Instruction and Product Safety Risk Management Procedure. Each software anomaly was assessed for impact to donor and user safety. The assessment determined that all the 54 known software anomalies were assessed as negligible. These anomalies have an acceptable risk index as they do not pose a safety risk to the product, nor do they impact its intended use.

Testing:
Design verification was performed to confirm that the design elements meet the specified requirements and includes verification of the effectiveness of risk control measures for potential causes of failure modes. This included software verification, software validation, and system integration.

Development Management:
The software development activities included establishing detailed software requirements, linking requirements with associate verification tests, V&V testing, defect tracking, configuration management, and maintenance activities to ensure the software conforms to user needs and intended uses.

Note: During the review of the BLA submission, Grifols upgraded the Panther System Software from version 7.2 to 7.4.3. Version 7.4.3 included minor updates

with several enhancements for increased usability and bug fixes. Grifols provided risk assessment, verification, and validation data to support the use of the Procleix Plasmodium assay on Panther Systems with version 7.4.3 of the system software installed. The update does not change critical assay-specific parameters such as sample volumes, volumes of reagents used, time for incubations, time to signal readout, or assay results calculations. Thus, there is no impact of the upgraded Panter System software version 7.4.3 on the analytical and clinical data submitted for review in the BLA.

5. Analytical Studies

Based on discussions and FDA feedback (BQ231026 and IND30609), Grifols Diagnostic Solutions Inc. conducted several analytical studies to evaluate the performance of the Procleix Plasmodium Assay on the automated Procleix Panther System.

a) Precision

This study was conducted to evaluate repeatability (within-run precision) and intermediate precision (within-laboratory precision) according to CLSI guideline Evaluation *of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition (EP05-A3).*

Four positive panel members were prepared in whole blood lysate at target concentrations of approximately 0.5x limit of detection (LOD) (2.31 parasites (p)/mL), (b) (4) 3x LOD (13.86 p/mL), 10x LOD (46.2 p/mL), and 50x LOD (231 p/mL) for *P. falciparum*, along with one negative whole blood lysate panel member (0 p/mL), using *P. falciparum* as a representative species. Each panel member was tested twice per run, two runs per day, for 20 days, totaling 80 tests per panel member, using one reagent lot on one Panther system by one operator. For positive panel members with 100% agreement, within-laboratory precision ranged from 3.31% CV (3x LOD) to 3.98% CV (50x LOD). The 0.5x LOD panel member demonstrated 6.58% CV for within-laboratory precision. For the negative panel member, even though the %CV values were high, ranging between 114.77% to 459.38%, the high values are expected because these operate at the extreme lower limit of an assay's detection range, where absolute variations in signal translate to large percentage differences (Table 5).

Table 5. Intermediate (Within-Laboratory) Precision of Procleix Plasmodium Assay

Panel Member	Mean S/CO	N	Repeatability (SD/%CV)	Between Runs (SD/%CV)	Between Days (SD/%CV)	Within-Laboratory (SD/%CV)
Negative	0.00	80	0.01/422.77%	0/138.46%	0/114.77%	0.01/459.38%
Negative-IC	2.07	80	0.13/6.06%	0.04/1.90%	0.03/1.38%	0.13/6.50%
0.5x LOD	12.67	69	0.48/3.81%	0.61/4.81%	0.30/2.39%	0.83/6.58%
3x LOD	13.10	80	0.30/2.32%	0.19/1.42%	0.25/1.90%	0.43/3.31%
10x LOD	12.59	80	0.40/3.21%	0.13/1.06%	0.22/1.78%	0.48/3.82%
50x LOD	12.96	80	0.29/2.24%	0.29/2.25%	0.31/2.40%	0.52/3.98%

IC=Internal Control; LOD=Limit of Detection

b) Limit of Detection (LOD) of Procleix Plasmodium for In vitro Transcripts

This analytical sensitivity study evaluated the LOD of the Procleix Plasmodium Assay in detecting in-vitro transcripts (IVTs) of five *Plasmodium* species: *P. falciparum*, *P. malariae*, *P. vivax*, *P. ovale*, and *P. knowlesi*. The transcripts were serially diluted to concentrations of 100, 30, 10, 3, 1, and 0 copies/mL and tested with 60 replicates per concentration using two reagent lots. Detection rates at 100 and 30 copies/mL were 100% for all five species, while detection at 10 copies/mL ranged from 91.67% to 97.00% across species (Table 6). At lower concentrations (3 and 1 copies/mL), detection rates decreased as expected, ranging from 48.33% to 56.67% at 3 copies/mL and 10.00% to 35.00% at 1 copy/mL. Probit analysis determined that the 95% detection probability ranged from 8.47 copies/mL (*P. malariae*) to 11.89 copies/mL (*P. vivax*), with 95% fiducial limits ranging from 6.80-17.74 copies/mL across all species (Table 6).

Table 6: Summary of Probit Analysis of In-vitro Transcripts of *Plasmodium* Species

***Plasmodium* species**	**Detection Probabilities, copies/mL**	
	50% (95% Fiducial Limits)	**95% (95% Fiducial Limits)**
P. vivax	2.97 (2.27 - 3.70)	11.89 (9.04 - 17.74)
P. ovale	2.14 (1.51 - 2.76)	11.16 (8.15 - 18.01)
P. malariae	2.96 (2.38 - 3.57)	8.47 (6.80 - 11.45)
P. knowlesi	3.00 (2.39 - 3.63)	9.08 (7.21 - 12.58)
P. falciparum	3.35 (2.63 - 4.09)	11.37 (8.88 - 16.19)

c) Limit of Detection of *Plasmodium* parasites

P. falciparum, P. malariae, *P. vivax*, *P. ovale,* and *P. knowlesi*-infected samples were serially diluted in human whole blood at 6, 4, 2, 1, 0.5, and 0 p/mL. *P. falciparum*, and *P. ovale*- infected samples included an additional sample diluted in human whole blood at 8 p/mL with 60 replicates tested per concentration. For each panel level, lysates were created by mixing 900 µL of each infected whole blood sample with 2.7 mL of Parasite Transport Medium (PTM) and tested as an individual measurement using three reagent lots on the Procleix Panther system with the Procleix Plasmodium Assay. Detection rates varied by species and concentration, with 100% detection observed at 6 p/mL for most species, decreasing at lower concentrations. Probit analysis resulted in the 95% detection probability ranging from 2.10 p/mL (*P. knowlesi)* to 6.82 p/mL (*P. ovale*), with 95% fiducial limits ranging from 1.66 to 16.75 p/mL across species (Table 7).

Table 7: Summary of Probit Analysis of *Plasmodium* Species Parasites

***Plasmodium* species**	**Detection Probabilities, parasites/mL**	
	50% (95% Fiducial Limits)	**95% (95% Fiducial Limits)**
P. vivax	0.61 (0.08 - 1.08)	2.85 (1.66 - 16.75)
P. ovale	1.65 (1.33 - 1.96)	6.82 (5.63 - 8.75)
P. malariae	0.38 (0.21 - 0.54)	2.39 (1.85 - 3.59)
P. knowlesi	0.66 (0.50 - 0.79)	2.10 (1.72 - 2.87)
P. falciparum	0.82 (0.61 - 1.00)	3.50 (2.85 - 4.62)

d) Sensitivity of Procleix Plasmodium in Naturally Infected Specimens

Detection of *Plasmodium* in naturally infected clinical whole blood specimens was evaluated by testing individual specimen lysates. (b) (4) unique specimens were obtained, including four different *Plasmodium* species from naturally infected clinical samples (*P. falciparum, P. ovale, P. malariae*, and *P. vivax*) and cultured infected erythrocytes for *P. knowlesi*. All specimens were (b) (4) before testing. Each specimen was tested (b) (4) using (b) (4) reagent lots. The analytical sensitivity was 100% (95% CI: (b) (4) across (b) (4) reagent lots combined.

e) Internal Control Validity and Inhibition Study

Performance of the Internal Control (IC) under known inhibitory conditions was evaluated to determine if the IC adequately serves as a control for false negative results. (b) (4)

f) Analytical Specificity in Normal Whole Blood Specimens

Fresh whole blood specimens from voluntary blood donors were tested with the Procleix Plasmodium Assay to determine the specificity of the assay. A total of (b) (4) individual donor lysates (IDL) were tested at (b) (4) sites using (b) (4) reagent lots. The overall analytical specificity was 99.99% (95% CI: 99.96-100%) with

only (b) (4) false reactive result out of (b) (4) specimens that did not repeat upon (b) (4) retests, yielding a false reactive rate of (b) (4).

g) Analytical Specificity in the Presence of High-Titer Specimens (Carry-over)

High titer *P. falciparum* samples (approximately (b) (4) parasites/mL) were interspersed with negative samples in an (b) (4) on specimen processing racks to assess potential cross-contamination during automated sample processing. Lysates were prepared on (b) (4) Xpress systems and tested on (b) (4) Panther systems using (b) (4) reagent (b) (4). Each run consisted of (b) (4) negative lysates, (b) (4) high titer lysates, along with (b) (4), for a total of (b) (4) tests per run across (b) (4) runs. Out of (b) (4) negative individual donor lysates tested, (b) (4) replicates were reactive for a false positive rate of (b) (4), meeting the acceptance criteria of (b) (4) false positive rate, with an overall specificity of (b) (4) thereby demonstrating that the proximity of high titer samples did not elevate the analyte signal of neighboring negative samples.

h) Sensitivity and Specificity in Whole Blood Specimens Collected in Different Anticoagulants Study

The sensitivity and specificity of the Procleix Plasmodium assay was evaluated in whole blood specimens collected in four different anticoagulants: dipotassium EDTA (K2EDTA), tripotassium EDTA (K3EDTA), sodium citrate (NaC), and citrate phosphate dextrose adenine (CPDA). Whole blood from (b) (4) blood donors was collected in each anticoagulant type, with (b) (4) tested unspiked to evaluate specificity, and (b) (4) spiked with *P. falciparum* parasite at approximately (b) (4) LOD to evaluate sensitivity. Specimens were divided between (b) (4) reagent lots and tested as an individual measurement. The study resulted in 100% specificity (b) (4) for all unspiked specimens across all four anticoagulants, with mean analyte S/CO ratios ranging from (b) (4) and mean IC S/CO ratios ranging from (b) (4) with low variability (b) (4) CV). Sensitivity testing showed 100% reactivity (b) (4) for all *Plasmodium*-spiked specimens across all four anticoagulants, with mean analyte S/CO ratios ranging from (b) (4) with mean analyte S/CO ratios ranging from (b) (4), demonstrating that blood collection tube types have no effect on the performance of the Procleix Plasmodium assay.

i) Sensitivity and Specificity in Specimens with Autoimmune and Other Disorders

Clinical specimens from (b) (4) patients with each of eight conditions: alcoholic cirrhosis, antinuclear antibody, elevated alanine aminotransferase (ALT), multiple myeloma, multiple sclerosis, rheumatoid arthritis, rheumatoid factor, and systemic lupus erythematosus, were tested unspiked or spiked with cultured *P. falciparum*-infected erythrocytes at approximately (b) (4) LOD using (b) (4) reagent lots. Results showed 100% specificity and 100% sensitivity indicating no interference due to autoimmune or other diseases on the performance of the Procleix Plasmodium assay.

j) Specimens Infected with Microorganisms

Performance of the Procleix Plasmodium Assay was evaluated in whole blood specimens unspiked or spiked with cultured *P. falciparum*-infected erythrocytes in the presence of seven microorganisms - *Staphylococcus epidermidis, Staphylococcus aureus, Micrococcus luteus, Corynebacterium diphtheriae, Propionibacterium acnes, Candida albicans,* and *Pneumocystis carinii*. Results showed that specimens contaminated with microorganisms at concentrations up to (b) (4) do not affect the specificity or sensitivity of the Procleix Plasmodium Assay.

k) Endogenous Interference

The effect of potentially interfering endogenous substances on the Procleix Plasmodium Assay performance was evaluated by testing (b) (4) individual whole blood donor samples spiked with the potential interferents at the levels recommended by the CLSI guideline *Interference Testing in Clinical Chemistry (EP07-A2)*. The potential interferents tested were hemoglobin (5,000 mg/L), bilirubin (200 mg/L), triglycerides/intralipid (30,000 mg/L), albumin (60,000 mg/L), and human gamma globulin (60,000 mg/L). The individual donor samples spiked with *P. falciparum*-infected erythrocytes at (b) (4) LOD (no interferent) were used as positive samples for the target analyte. The results demonstrated that all donor samples containing (b) (4) LOD *P. falciparum* target generated positive results, and all target negative donor samples generated valid negative results indicating that the sensitivity and specificity of the Procleix Plasmodium Assay is not affected by the potential endogenous interfering substances tested.

l) Exogenous Interference

The purpose of this study was to evaluate the influence of potentially interfering exogenous substances on the performance of the Procleix Plasmodium assay. The effect of potential interferents was evaluated by testing whole blood samples from (b) (4) individual donors spiked *P. falciparum* infected-erythrocytes at (b) (4) LOD and with the potential interferents at levels recommended in CLSI guideline *Interference Testing in Clinical Chemistry (EP07-A2)*. The following potential interferents were tested using (b) (4) reagent lots: acetaminophen, acetylsalicylic acid, atorvastatin, loratadine, naproxen, ascorbic acid, ibuprofen, phenylephrine HCl and desloratadine. The individual donor samples spiked only with *P. falciparum*-infected erythrocytes at (b) (4) LOD (no interferent) were used as positive samples. The results showed that all donor samples containing (b) (4) LOD *P. falciparum* target generated positive results, and all target negative donor samples generated valid negative results indicating that the sensitivity and specificity of the Procleix Plasmodium assay is not affected by the potential exogenous interfering substances tested.

m) Specimens with Other Blood-borne Pathogens

The performance of the Procleix Plasmodium Assay in specimens spiked with blood-borne pathogens other than *Plasmodium* and in specimens from individuals vaccinated against HBV, SARS-CoV-2, or influenza was evaluated to

assess potential cross-reactivity or interference. The blood-borne pathogens included were: HIV-1, HIV-2, HCV, HBV, WNV, HEV, HAV, HTLV-I, HTLV-II, CMV, Dengue virus serotypes 1 – 4, Chikungunya virus, Parvovirus B19, Influenza, *Babesia microti*, Epstein Barr virus, Usutu virus, Zika virus, Yellow Fever virus, Herpes Simplex Type 1, Rubella, and *Borrelia* species (*B. burgdorferi, B. hermsii, and B. recurrentis)*. Whole blood from (b) (4) individual donors was spiked with each pathogen or obtained from vaccinees, (b) (4) unspiked to evaluate specificity and (b) (4) spiked with cultured *P. falciparum*-infected erythrocytes at approximately (b) (4) LOD, to evaluate sensitivity. Testing was performed using (b) (4) reagent lots with (b) (4) replicates tested per pathogen per reagent lot. For specificity, all (b) (4) results from specimens containing blood-borne pathogens and vaccinees were nonreactive, demonstrating 100% specificity. For sensitivity, all (b) (4) results from *Plasmodium*-spiked specimens containing pathogens/vaccinees were reactive, demonstrating 100% sensitivity. There were no invalid runs, no invalid results due to IC failure, and no false positive reactions. The study demonstrated that specimens containing other blood-borne pathogens or from HBV, SARS-CoV-2, or influenza vaccinated individuals do not affect the specificity or sensitivity of the Procleix Plasmodium Assay.

n) Specimen Stability

(b) (4) individual whole blood donors samples collected in (b) (4) anticoagulants (K2EDTA, K3EDTA, NaC, and CPDA) and spiked with cultured *P. falciparum*-infected erythrocytes at approximately (b) (4) LOD were subjected to a series of storage conditions: whole blood stored at room temperature (15-30°C) for up to (b) (4) hours and at 2 – 8°C for up to (b) (4) days before lysing in PTM, followed by lysate storage at room temperature for up to 72 hours, at 2 – 8°C for up to 7 (b) (4) days, and through three freeze/thaw cycles. Testing was performed using a (b) (4) reagent lot, with specimens tested in (b) (4) at designated time-points. For whole blood stability, 100% reactivity was observed at both Baseline (Day 0) and Day (b) (4) for individual lysates across all anticoagulants. For individual lysate stability, 100% reactivity was maintained through Day (b) (4) plus three freeze/thaw cycles for all anticoagulants, with no statistically significant differences from baseline (p=1.0000). The overall invalid rate was 0% (b) (4) with no invalid runs. The results support the whole blood specimen stability claim of 13 days at 2 – 8°C (Figure 1) and individual lysate stability for up to 7 days post-lysis followed by three freeze/thaw cycles (Figure 2).

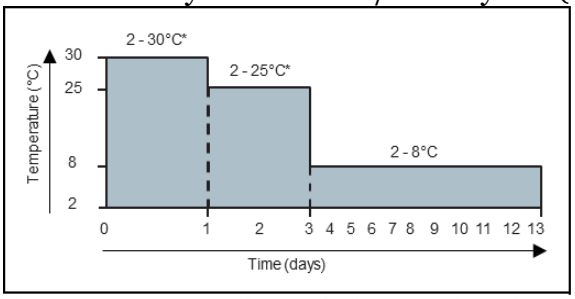

Figure 1: Storage Conditions of Whole Blood Specimens

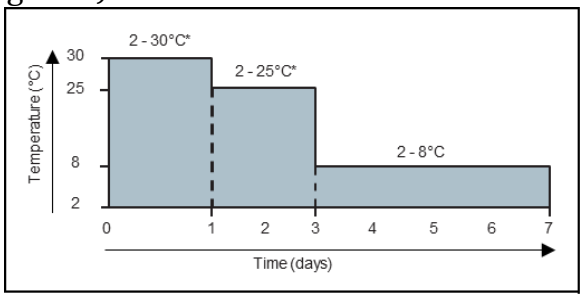

Figure 2: Storage Conditions of Individual Lysate Specimens

o) Equivalency between Manual and Automated Whole Blood Lysate Preparation

The equivalency of manual versus automated (Procleix Xpress system) whole blood lysate preparation methods for the Procleix Plasmodium Assay was evaluated to determine if the two preparation methods yielded comparable sensitivity and specificity results. A total of (b) (4) unique normal whole blood specimens were obtained, with (b) (4) used as negative samples and (b) (4) spiked with (b) (4) (b) (4) cultured *P. falciparum*-infected erythrocytes at approximately (b) (4) LOD. Each specimen was prepared using both manual lysis and automated lysis on the Xpress system, then tested as individual donor lysates in as an individual measurement. For specificity, all (b) (4) negative individual lysates prepared by both methods were nonreactive (100% specificity), with mean IC S/CO values of (b) (4) for Xpress-prepared and (b) (4) for manually prepared specimens. For sensitivity, all (b) (4) positive individual lysates prepared by both methods were reactive (100% sensitivity), with mean analyte S/CO values of (b) (4) for Xpress individual lysates, and (b) (4) for manual individual lysates. No invalid runs or invalid reactions due to IC failure were observed. The study demonstrated that manual and automated Xpress system sample preparation yield comparable results with equivalent S/CO values between the two methods with the Procleix Plasmodium Assay.

p) Long-Term Frozen Sample Stability

(b) (4) individual whole blood samples for each anticoagulant were used in this study. All samples were spiked at (b) (4) LOD of *P. falciparum*-infected erythrocytes (b) (4) in negative whole blood. After being spiked, each specimen was lysed in PTM (0.9mL whole blood in 2.7mL PTM). Multiple lysates were prepared for each specimen for testing at each time point, as well as any additional samples for any necessary retesting. All lysates were frozen at -20°C prior to time point testing (including Baseline). Specimens were tested at Baseline, 6 months, 9 months, 12 months, and (b) (4) months post-baseline. At each time point, (b) (4) replicates were tested from (b) (4) lysate for each donor for a total of (b) (4) replicates per anticoagulant. (b) (4) lots of reagents were used in this study. The results showed 100% reactivity for *Plasmodium*-spiked living donor specimens collected in each of K_3EDTA, K_2EDTA, NaC (4%), and CPDA anticoagulants/tube types, and frozen at −20°C for 13 months, supporting a claim for 12 months at −20°C.

q) Stability

The real-time, open-kit, and on-board stability studies for the Procleix Plasmodium assay evaluated reagent performance using (b) (4) independent reagent lots for up to (b) (4) months at intended storage conditions, including (b) (4) days open-kit and (b) (4) hours on-board stability. The calibrator set time, and Reagent Preparation Incubator (RPI) cycling study showed acceptable performance of reagents stored on-board for up to (b) (4) hours and at open-kit conditions for (b) (4) days, validating stability claims for open kit reagents after (b) (4) hours at (b) (4) in the RPI and 8-hour calibrator stability at room temperature. All acceptance criteria were met through (b) (4) months, supporting a 24-month shelf-life claim at −35°C to −15°C, with 30-day open-kit and 72-hour on-board stability. The stability data for the Procleix PTM was leveraged from the Procleix

Babesia assay because the (b) (4) , with data supporting 24-month shelf life with 30-day open-bottle and 48-hour open-tube claims at 15 – 30°C. Stability testing information for the Ancillary kits was established previously with the approved expiration dating of 24 months and open-kit and onboard stability of 60 days at 15 – 30°C.

6. Clinical Studies

Clinical studies were performed under the IND 30609 to evaluate the clinical specificity, sensitivity, and reproducibility of the Procleix Plasmodium assay. Clinical specificity was evaluated in a U.S. population who had no known risk of malaria exposure. Clinical sensitivity was evaluated in i) known *Plasmodium*-positive or contrived samples and ii) in a high-risk endemic population in Uganda. The reproducibility of Procleix Plasmodium Assay was evaluated for variability across lots, sites, days, runs, and operators. All clinical studies were carried out using two independent reagent lots and an additional, blended lot, that was a combination of kit constituents from Lot 1 and Lot 2.

a) Clinical Specificity

The Clinical Specificity study was performed under the IND 30609 by protocol GDSS-CSP-000011. The study was a prospective, multicenter study conducted in the U.S. at three testing sites: Creative Testing Solutions (CTS)-Charlotte, CTS-Tampa, and the American Red Cross – Scientific Support Office (ARC-SSO). To avoid disrupting the routine clinical operations of participating sites, leftover lysed whole blood samples from Procleix Babesia Assay testing of donations from U.S. blood collection centers, predominantly from *Babesia* endemic states, were used in this study. Additional whole blood donations from Southern California were included. Samples were linked to allow for donor identification, deferment, and donor follow-up if reactive. The samples were tested individually with the Procleix Plasmodium Assay.

The testing algorithm included a primary Nucleic Acid Test (NAT) comparator and serology testing on all Procleix Plasmodium Assay reactive samples. If reactive samples were not confirmed by the primary NAT comparator and/or serology, a secondary NAT comparator testing was to be performed. Donors with a reactive result with the Procleix Plasmodium Assay that were not confirmed were to be asked to participate in a donor follow-up study.

There were 11,088 individual donor samples tested in valid Procleix Plasmodium Assay runs. Of the 11,088 samples included in the study, 27 had an initial invalid result. To maintain an acceptable turnaround time, most samples with invalid results were not re-tested; the six that were retested had a final valid result. A total of 11,067 samples with valid results were included in the final specificity analysis.

Table 8. Clinical Specificity of Procleix Plasmodium Assay

Reagent Lot	Number Tested	True Negative	False Negative	True Positive	Specificity (95% CI)
Lot 1	3,835	3,835	0	0	100% (99.90 – 100.00)
Lot 2	3,545	3,545	0	0	100% (99.90 – 100.00)
Blended Lot	3,687	3,687	0	0	100% (99.90 – 100.00)
Total	**11,067**	**11,067**	**0**	**0**	**100% (99.97 – 100.00)**

The overall specificity of the Procleix Plasmodium Assay for individually tested whole blood samples was 100% (11,067/11,067) with a 95% Clopper-Pearson Confidence Interval (CI) of 99.97 – 100% (Table 8). The specificity for each clinical site and reagent lot was also 100%.

b) Clinical Sensitivity

The Clinical Sensitivity study was performed under the IND 30609 by protocol GDSS-CSP-000013 at three testing sites: CTS-Tampa, ARC-SSO, and Grifols Laboratory Solutions (GLS). The Sponsor, Grifols Diagnostic Solutions, San Diego (GDSS) provided the testing sites with known-positive whole blood lysate clinical specimens of *P. falciparum, P. vivax, P. malariae* and *P. ovale. P. knowlesi* known-positive whole blood lysates were prepared by spiking infected cultured erythrocytes in *Plasmodium*-negative whole blood.

A total of 255 neat lysate samples were tested with the Procleix Plasmodium Assay. Of the 255 lysate samples, 100 contained *P. falciparum*, ten contained *P. knowlesi*, ten contained *P. malariae*, ten contained *P. ovale* and 100 contained *P. vivax*. Twenty-five known-negative lysate samples were included for testing to mask operators to the expected results (Table 9).

Table 9. Overall Sensitivity of the Procleix Plasmodium Assay

Sample Type	Number Tested	True Positive	False Negative	Sensitivity (95% CI)
P. falciparum	100	100	0	100% (96.38 – 100.00)
P. knowlesi	10	10	0	100% (69.15 – 100.00)
P. malariae	10	10	0	100% (69.15 – 100.00)
P. ovale	10	10	0	100% (69.15 – 100.00)
P. vivax	100	100	0	100% (96.38 – 100.00)
Negative Lysates	25	0	0	-
Total	**255**	**230**	**0**	**100% (98.41 – 100.00)**

All 230 known-positive samples had true positive Procleix Plasmodium Assay results. The overall sensitivity of the assay was 100% (230/230) with a 95% CI of 98.41 – 100% in individually tested lysates.

c) Clinical Sensitivity in Subjects with Unknown Status of Infection

This study was performed under the IND 30609 by protocol GDSS-CSP-000015 to evaluate the clinical sensitivity of the Procleix Plasmodium Assay in whole

blood samples from asymptomatic donors with an unknown status of *Plasmodium* infection. Samples were collected in Uganda, a highly endemic area for malaria, to increase the probability of identifying positive specimens. The individuals tested represented the relevant blood donor population in the United States, because residents of malaria-endemic countries or former residents who return to the US after visiting these countries are currently not eligible to donate because they are at risk for malaria and are deferred for variable timeframes after returning to the U.S.

Five hundred prospectively collected whole blood specimens from individuals at high risk of *Plasmodium* infection were lysed in PTM and included in the study. A matching plasma or serum sample was collected for serology testing and a matching whole blood sample was saved for confirmatory testing. All samples were shipped frozen (≤-20°C) to the U.S. testing site (GDSS). All samples were tested individually, and reactive samples were confirmed by alternate NAT testing and/or serology.

Overall, 195 specimens were considered true positive on the Procleix Plasmodium Assay, nine were false positive, and the remaining 296 were true negative (Table 10). No specimens were considered false negative. Therefore, the clinical sensitivity of the Procleix Plasmodium Assay in specimens from subjects at high risk of malaria was 100% (195/195) with a 95% CI of 98.13% – 100%.

Table 10. Sample interpretations for the high-risk sensitivity study

N	Procleix Plasmodium result	1st Comparator Result	2nd/3rd Comparator Result*	Final interpretation
195	Reactive	Reactive	N/A	True positive
9	Reactive	Non-reactive	Non-reactive	False positive
22	Non-reactive	Reactive	Non-reactive	True negative
271	Non-reactive	Non-reactive	N/A	True negative
3	Non-reactive	Invalid	Non-reactive	True negative

*The third comparator assay was only used if the secondary comparator assay produced an invalid result. Additional results with the secondary and third comparator assays used for species determination or as controls were not included in the table.

The species detected in the study included *P. falciparum* (n=130), *P. ovale* (n=9) and *P. malariae* (n=6). One specimen was co-infected with *P. falciparum* and *P. ovale*. The infecting species could not be determined for 49 samples. There were no *P. knowlesi*- or *P. vivax*-infected specimens detected. This is expected as *P. vivax* is uncommon in eastern Uganda and *P. knowlesi* is only endemic in southeast Asia. Most specimens (92) had parasitemia of <500 p/mL; 19 specimens had parasitemia >500 p/mL. The highest level of parasitemia reported in the study was $1.1x10^8$ p/mL. All samples that were initially reactive on the Procleix Plasmodium Assay and/or the first comparator Plasmodium Assay were tested with the serology comparator. Out of the 195 true positive samples, 24 (12.31%) were seronegative, indicating a presumed window period infection.

d) Reproducibility Studies

This study was performed under the IND 30609 per the proposed protocol GDSS-CSP-000014 to evaluate the reproducibility of the Procleix Plasmodium Assay on the Procleix Panther System. The Sponsor (GDSS) provided a 5-member reproducibility panel (A-E) containing one negative panel member and four panel members that contained *Plasmodium* RNA. Panel members were comprised of lysate made from *Plasmodium*-infected human whole blood diluted in negative human whole blood and lysed in the Parasite Transport Medium (PTM). Panel members containing *Plasmodium* RNA included one high negative (approximately (b) (4) limit of detection [LOD]), one low positive ((b) (4) to (b) (4) LOD), one moderate positive ((b) (4) LOD), and one high positive ((b) (4) LOD) panel members for *P. falciparum*.

Testing was conducted at CTS-TPA, ARC-SSO, and GLS sites using a single Procleix Panther System to perform testing at each site. Two replicates of each panel members were tested in each run. At each site, a total of 36 valid runs were performed by two operators over at least (b) (4) days using two independent reagent lots (b) (4) Lot 1 and Lot 2). Because reagent (b) (4) was not independent of Lot 1 and Lot 2, the reproducibility was analyzed using results for Lot 1 and Lot 2.

The signal variability for the *Plasmodium* analyte and IC (for the negative panel member only) calculated for both lots and all sites combined is shown below in Table 11.

Table 11. Reproducibility of Procleix Plasmodium using Two Reagent Lots

Panel Member	Mean S/CO	N	Between Sites (SD/%CV)	Between Lots (SD/%CV)	Between Operators (SD/%CV)	Between Days (SD/%CV)	Within Runs (SD/%CV)	Total (SD/%CV)
A	0.02	142	0.03/ 165.31%	0/ 23.88%	0/0%	0.01/56.37%	0.02/ 113.44%	0.04/ 209.63%
A-IC	1.72	142	0.04/ 2.04%	0.22/ 12.9%	0/0%	0/0%	0.12/6.7%	0.25/ 14.68%
B	5.51	144	0.27/ 4.89%	0/ 0%	0/ 0%	0/ 0%	5.2/ 94.26%	5.2/ 94.39%
C	11.93	143	0.24/ 2.04%	0/ 0%	0.12/ 1.02%	0.1/ 0.81%	0.59/ 4.92%	0.65/ 5.48%
D	12.33	144	0.27/ 2.17%	0.11/ 0.87%	0/ 0%	0.14/ 1.13%	0.4/ 3.27%	0.51/ 4.18%
E	11.99	144	0.44/ 3.64%	0.1/ 0.85%	0.12/ 1.01%	0/ 0%	0.49/ 4.05%	0.67/ 5.6%

CV=coefficient of variation, N=number of samples with valid Procleix Plasmodium assay results, SD=standard deviation; Panel member: A=Negative, B=High Negative, C=Low Positive, D=Moderate Positive, E=High Positive. SD and CV are shown as 0 if variability is numerically negative.

For all panel members, within-run variability was the greatest contributor to total variability. The low, moderate and high positive panel members all had total %CVs of <10%. The %CVs for the high negative and negative panel members were higher, as expected. The signal variability results overall for both lots and all sites combined were acceptable.

Lot-to-Lot Variability

To address lot-to-lot variability of the Procleix Plasmodium assay, Grifols performed an additional study using three independent reagent lots of the Procleix Plasmodium assay. The study was conducted at one site with two operators per site across six days of testing using two replicates per panel member.

Table 12. Signal variability for each panel member for all lots combined.

Panel Member	Mean S/CO	N	Between Lots (SD/%CV)	Between Operators (SD/%CV)	Between Days (SD/%CV)	Within Runs (SD/%CV)	Total (SD/%CV)
A	0	72	0/0%	0/0%	0/0%	0/667.98%	0/667.98%
A-IC	1.94	72	0.02/1.29%	0/0%	0.03/1.58%	0.08/4.21%	0.09/4.68%
B	7.16	72	0.39/5.42%	0/0%	1.03/14.39%	4.97/69.44%	5.09/71.12%
C	12.99	71	0.21/1.58%	0/0%	0.21/1.65%	0.63/4.87%	0.7/5.38%
D	12.94	72	0.2/1.53%	0/0%	0.32/2.44%	0.55/4.22%	0.66/5.11%
E	12.81	72	0.27/2.12%	0/0%	0.24/1.85%	0.6/4.69%	0.7/5.47%

CV=coefficient of variation, N=number of samples with valid Procleix Plasmodium assay results, SD=standard deviation; Panel member: A=Negative, B=High Negative, C=Low Positive, D=Moderate Positive, E=High Positive. SD and CV are shown as 0 if variability is numerically negative.

For all panel members, within-run variability was the greatest contributor to total variability. The low, moderate and high positive panel members all had total %CVs of <10%. The %CVs for the high negative and negative panel members were higher, as expected. The signal variability results overall with three independent lots were acceptable.

e) BIMO – Clinical/Statistical/Pharmacovigilance

BIMO inspection assignments were issued for the sponsor and a clinical investigator that participated in the conduct of study Protocols GDSS-CSP 000011, GDSS-CSP-000013 and GDSS-CSP-000014. The sponsor inspection also included Protocol GDSS-CSP-000015. The inspections did not reveal substantive issues that impact the data submitted in this Biologics License Application (BLA).

f) Pediatrics

N/A

g) Other Special Populations

N/A

7. Advisory Committee Meeting

N/A

8. Other Relevant Regulatory Issues

N/A

9. Labeling

The Advertising and Promotional Labeling Branch (APLB) reviewed the proposed package insert and package and container labels on February 06, 2026, and found them acceptable from a promotional and comprehension perspective.

10. Recommendations and Risk/ Benefit Assessment

a) Recommended Regulatory Action

The Review Committee reviewed the original submission and related amendments. All review issues have been resolved and therefore the Review Committee recommends licensure of the Procleix Plasmodium Assay.

b) Risk/ Benefit Assessment

The risk/benefit analysis demonstrates that the benefit of the Procleix Plasmodium Assay outweighs any risk to the blood donor and the safety of the nation's blood supply. The clinical studies with the Procleix Plasmodium Assay demonstrate a sensitivity of 100% (95% CI of 98.41% – 100.00%), indicating a low probability of a false negative result. Among 11,067 whole blood donors tested with the Procleix Plasmodium Assay, the assay specificity of 100% (95% CI of 99.97 – 100%) in clinical trials suggests a low probability of a false positive result.

c) Recommendation for Post-Marketing Activities

No post-marketing activities have been proposed for this application.