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.

Procleix® Plasmodium Assay

For *In Vitro* Diagnostic Use

IVD

Rx Only

1000 Test Kit, 5000 Test Kit

CONTENTS

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 living donors of organ and tissue samples when specimen 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.

SUMMARY AND EXPLANATION OF THE TEST

Malaria is a disease caused by intraerythrocytic protozoan parasites from the genus *Plasmodium*. It is most often transmitted to humans through the bite of an infected *Anopheles* mosquito.[1] In addition to vector-borne transmission, the parasite is known to be transmitted from mother to fetus due to preferential accumulation of parasites in the placental intervillous space[2] and from transfusion of infected blood products.[3] There are five main species of *Plasmodium* that are known to infect humans: *P. falciparum*, *P. knowlesi*, *P. malariae*, *P. ovale,* and *P. vivax*.[4]

Of the five species of *Plasmodium* infecting humans, *P. falciparum* is the most frequent and most serious, followed by *P. vivax*.[5] Symptoms of malaria 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.[6] In some cases, infections may be chronic and/or asymptomatic for several years.[7]

In non-endemic areas, imported cases of malaria have become more common due to increasing population movement via travelers to, and residents from, endemic areas, with the West Africa region accounting for the majority of imported cases.[8] Most recently, in 2023, several locally acquired cases of *Plasmodium* infection were reported in the United States (US).[9] After 20 years without locally acquired mosquito-transmitted malaria (autochthonous) in the United States, nine cases were reported to CDC during May–August 2023. In September 2023, a 10th U.S. case of locally acquired malaria was diagnosed, in Arkansas[10].

To exclude the risk of current or previous malaria infections that can be transmitted by a blood transfusion, many countries use donor questionnaires to either defer donors[11,12] or selectively screen donors for antibodies.[13] These methods result in donor loss, negatively impacting blood availability. [14]

The Procleix Plasmodium Assay, which detects the 18S ribosomal RNA of *P. falciparum*, *P. knowlesi*, *P. malariae*, *P. ovale*, and *P. vivax*, uses the same target capture, transcription-mediated amplification (TMA), and hybridization protection assay (HPA) using chemiluminescent technology as other Procleix blood screening assays.

PRINCIPLES OF THE PROCEDURE

The Procleix Plasmodium Assay is performed on the fully automated Procleix Panther System.

The Procleix Plasmodium Assay requires a whole blood sample lysis step that can be performed manually or on the Procleix Xpress System. During sample lysis on the Procleix Xpress System, whole blood is added to Parasite Transport Medium (PTM), allowing the rupture of the red blood cell (RBC) membranes as well as the release of the parasites and the liberation and stabilization of the RNA into the lysis solution. The Procleix Xpress System pipettes 2.7 mL of PTM into empty individual lysate tubes. Following the prefilling of the lysate tubes with PTM, whole blood sample tubes are loaded onto the worktable. The pipettor mixes the whole blood sample and then 0.9 mL of whole blood is transferred to the lysate tube containing 2.7 mL of PTM, followed by a lysate mixing step. Upon completion of lysis, individual donor lysate tubes are loaded onto the Procleix Panther System. For manual lysis, follow the same volumes and steps as the automated lysis procedure. Refer to SPECIMEN PREPARATION for instructions to create lysates for use with the Procleix Plasmodium Assay.

After the lysates are made, the Procleix Plasmodium Assay involves three main steps, which take place in a single tube on the Procleix Panther System: target capture, *Plasmodium* RNA target amplification by TMA,[15] and detection of the amplification products (amplicon) by the HPA.[16]

During sample preparation, RNA is isolated from the lysate via a target capture system. Oligonucleotides (capture oligonucleotides) that correspond to highly conserved regions of *Plasmodium* RNA are hybridized to the *Plasmodium* RNA target, if present, in the test specimen. The target sequence for the Procleix Plasmodium Assay is the 18S ribosomal RNA of *P. falciparum*, *P. knowlesi*, *P. malariae*, *P. ovale*, and *P. vivax*. The hybridized target is then captured onto magnetic microparticles that are separated from the specimen in a magnetic field. Wash steps use magnetic separation to remove extraneous components from the reaction tube.

Target amplification occurs via TMA, which is a transcription-based nucleic acid amplification method that utilizes two enzymes, Moloney Murine Leukemia Virus (MMLV) reverse transcriptase and T7 RNA polymerase. The reverse transcriptase is used to generate a DNA copy (containing a promoter sequence for T7 RNA polymerase) of the target RNA sequence. The T7 RNA polymerase produces multiple copies of RNA amplicon from the DNA copy template. The Procleix Plasmodium Assay uses the TMA method to amplify conserved regions of *Plasmodium* 18S ribosomal RNA.

Detection is achieved by HPA using single-stranded nucleic acid probes with chemiluminescent labels that are complementary to the amplicon. The labeled nucleic acid probes hybridize specifically to the amplicon. The Selection Reagent differentiates between hybridized and unhybridized probes by inactivating the label on unhybridized probes. During the detection step, the chemiluminescent signal produced by the hybridized probe is measured by a luminometer and is reported as Relative Light Units (RLU).

Internal Control is added to each test specimen, control, and assay calibrator via the working Target Capture Reagent. The Internal Control in the Procleix Plasmodium Assay controls for specimen processing, amplification, and detection steps. Internal Control signal is discriminated from the *Plasmodium* signal by the differential kinetics of light emission from probes with different labels.[17] Internal Control-specific amplicon is detected using a probe with rapid emission of light (flasher signal). Amplicon specific to *Plasmodium* is detected using probes with relatively slower kinetics of light emission (glower signal). The Dual Kinetic Assay (DKA) is a method used to differentiate between the signals from flasher and glower labels.[17]

The Procleix Plasmodium Assay Calibrators are used to determine the analyte and internal control cutoff values and establish run validity, see QUALITY CONTROL PROCEDURES.

REAGENTS

Procleix Plasmodium Assay Reagents

Internal Control Reagent
A HEPES buffered solution containing detergent and an RNA transcript.
Contains <0.0001% non-infectious internal control transcript, 10% lithium lauryl sulfate.
*Store **unopened reagent** at –35° to –15°C.*

Target Capture Reagent
A HEPES buffered solution containing detergent, capture oligonucleotides, and magnetic microparticles.
***Note**: Internal Control Reagent must be added to Target Capture Reagent before use in the assay.*
Contains <0.0001% Plasmodium and internal control capture oligos, <1% magnetic particles, 10% lithium lauryl sulfate.
Store at 2° to 8°C. (Do not freeze)

Amplification Reagent
Primers, dNTPs, NTPs, and cofactors in TRIS buffered solution containing ProClin 300 preservative.
Contains <0.001% Plasmodium and internal control primer oligos, <11% nucleoside trisphosphates, <3% magnesium, <0.02% ProClin 300 preservative.
*Store **unopened reagent** at –35° to –15°C.*

Enzyme Reagent
MMLV Reverse Transcriptase and T7 RNA Polymerase in HEPES/TRIS buffered solution containing 0.05% sodium azide as preservative.
Contains <2% RT and T7 enzymes, 0.05% sodium azide.
*Store **unopened reagent** at –35° to –15°C.*

Probe Reagent
Chemiluminescent oligonucleotide probes in succinate buffered solution containing detergent.
Contains <0.4% acridinium ester-labeled probes for Plasmodium and internal control, <4% lithium lauryl sulfate, <5% lithium chloride.
*Store **unopened reagent** at –35° to –15°C.*
Probe Reagent is light-sensitive. Protect from light during storage.

Selection Reagent
Borate buffered solution containing surfactant.
Contains <4% boric acid, <1% sodium hydroxide, 1% Triton X-100.
Store at 15° to 30°C.

Procleix Plasmodium Assay Calibrators

C0

Procleix Negative Calibrator
A HEPES buffered solution containing detergent.
Contains 10% lithium lauryl sulfate.
Store at –35° to –15°C.

C1

Procleix Plasmodium Assay Positive Calibrator
A HEPES buffered solution containing detergent and a Plasmodium RNA transcript.
Contains <0.08% non-infectious Plasmodium transcript, 10% lithium lauryl sulfate.
Store at –35° to –15°C.

Procleix Panther System Reagents

R1

Auto Detect 1

Aqueous solution containing hydrogen peroxide and nitric acid.

Contains 32 mM hydrogen peroxide, 1 mM nitric acid.

*Store **unopened reagent** at 15° to 30°C.*

R2

Auto Detect 2

1.6 N sodium hydroxide.

*Store **unopened reagent** at 15° to 30°C.*

W

Wash Solution

HEPES buffered solution.

Contains <1% sodium chloride, <0.03% methyl and propyl paraben.

*Store **unopened reagent** at 15° to 30°C.*

O

Oil

Silicone oil.

*Store **unopened reagent** at 15° to 30°C.*

DF

Buffer for Deactivation Fluid

Sodium bicarbonate buffered solution.

Contains <7.0% sodium bicarbonate, <2% sodium hydroxide.

*Store **unopened reagent** at 15° to 30°C.*

Additional Reagent

Parasite Transport Medium (PTM)

A TRIS buffered solution containing detergent

Contains <0.6% magnesium, 6% lithium lauryl sulfate.

Store at 15° to 30°C.

STORAGE AND HANDLING INSTRUCTIONS

A. Room temperature is defined as 15° to 30°C.

B. The Probe Reagent is light-sensitive. Protect this reagent from light during storage.

C. Do not use reagents or fluids after the expiration date.

D. Do not use assay-specific reagents from any other Procleix assay.

E. If a precipitate forms in the Target Capture Reagent (TCR) during storage, see instructions under REAGENT PREPARATION. DO NOT VORTEX. DO NOT FREEZE TCR.

Note: If after removing the TCR from storage at 2° to 8°C, the precipitate is allowed to settle to the bottom of the container, the likelihood of the formation of a gelatinous precipitate is increased substantially.

F. Do not refreeze Internal Control, Amplification, Enzyme, and Probe Reagents after the initial thaw.

G. Calibrators are single-use vials and must be discarded after use. Do not refreeze Calibrators after initial thaw.

H. To reduce the possibility of reagent cross-contamination, it is recommended to use new reagent caps when unloading reagent bottles from the Panther instrument and storing them.

I. If precipitate forms in the Wash Solution, Selection Reagent, Probe Reagent, Negative Calibrator, or Positive Calibrator, see instructions under REAGENT PREPARATION.

J. Changes in the physical appearance of the reagent supplied may indicate instability or deterioration of these materials. If changes in the physical appearance of the reagents are observed (for example, obvious changes in reagent color or cloudiness are indicative of microbial contamination), they should not be used.

K. For instructions on preparation of reagents, see instructions under REAGENT PREPARATION and the *Procleix Reagent Preparation Incubator 250 Operator's Manual,* or *Procleix Reagent Equilibration System Operator's Manual,* as applicable.

L. Consult the following table for storage information.

Reagent/Fluids	**Unopened Reagent**	**Opened Reagent (Opened/Thawed Stability)**		
	Storage Temperature	**Room Temperature**	**Onboard Stability**	**Storage Temperature**
Internal Control Reagent (IC)	–35° to –15°C	Up to 8 hours at RT prior to combining with TCR		
Target Capture Reagent (TCR)	2° to 8°C			
working Target Capture Reagent (wTCR)		84 hours	72 hours	30 days at 2° to 8°C
Amplification Reagent	–35° to –15°C	84 hours	72 hours	30 days at 2° to 8°C
Enzyme Reagent	–35° to –15°C	84 hours	72 hours	30 days at 2° to 8°C
Probe Reagents	–35° to –15°C	84 hours	72 hours	30 days at 2° to 8°C
Selection Reagent	RT	30 days	72 hours	30 days at RT
Calibrators	–35° to –15°C	8 hours, single-use reagent		
Parasite Transport Medium (PTM)	RT	90 days*		90 days at RT
Auto Detect Reagents	RT	60 days at RT		
Buffer for Deactivation Fluid	RT	60 days at RT		
Oil	RT	60 days at RT		
Wash Solution	RT	60 days at RT		

RT = Room Temperature (15° to 30°C)

RT stability includes onboard stability time on the Procleix Panther System.

- The RT stability period starts as soon as the reagents are removed from the Procleix Reagent Preparation Instrument 250 (RPI 250) or Procleix Reagent Equilibration System (RES) after the preparation program is completed.
- If opened reagents are placed in the RPI 250 or RES at the room temperature program, the time duration is included in the total RT stability.
- For reagents with 30 days open bottle/thawed stability, the RT stability time must occur within 30 days, which includes onboard stability. See REAGENT PREPARATION, Item C for more information.

If using RPI 250 File 3 or RES Room Temperature program for thawing unopened reagents (TCR and Amplification, Enzyme, and Probe Reagents), reagents must remain in the RPI 250 or RES for 4 to 20 hours. Refer to the *Procleix RPI 250 Operator's Manual* or the *Procleix Reagent Equilibration System Operator's Manual* for additional information.

Caution: Only the reagent onboard stability is tracked by the Procleix Panther System Software. The time reagents remain at RT when not onboard the Procleix Panther System MUST be manually tracked by the user to ensure maximum allotted RT time is not exceeded.

Maintain reagents at the appropriate storage condition when not in use. Return reagents to their appropriate storage conditions without delay unless they are on the RPI 250, the RES, or the Procleix Panther System. Deviations from storage may impact the performance of the assay.

*Pre-filled tubes with PTM can be stored for up to 48 hours at RT.

SPECIMEN COLLECTION, STORAGE, AND HANDLING

Warning: Handle all specimens as if they are potentially infectious agents.

Note: Take care to avoid cross-contamination during the sample handling steps. For example, discard used material without passing over open tubes.

LIVING DONOR WHOLE BLOOD SPECIMENS

A. Only blood specimens collected in plastic tubes may be used. Do not freeze whole blood specimens.

B. Whole blood collected in K_2EDTA, K_3EDTA, Sodium Citrate, and CPDA may be used. Follow sample tube manufacturer's instructions.

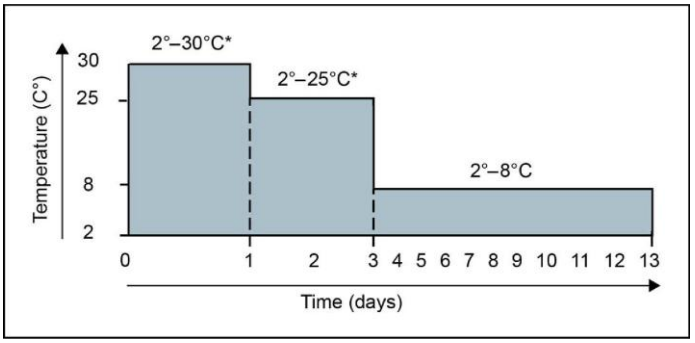
Whole blood from individual donor specimens may be stored for a total of 13 days from the time of collection to the time of testing with the following conditions:

For storage above 8°C, specimens may be stored for 72 hours up to 25°C, and up to 30°C for any 24 hour period during the 72 hours. Other than noted above, specimens are stored at 2° to 8°C.

Refer to Figure 1 below for the example storage temperature chart.

Stability in frozen/thawed whole blood has not been evaluated.

Figure 1: Living Donor Whole Blood Specimen Stability



***The cumulative time spent at the elevated temperatures cannot exceed these limits.**

C. Individual donor lysates from whole blood collected in K_2EDTA, K_3EDTA, Sodium Citrate, and CPDA may be stored for a total of 7 days from the time of the lysis to the time of testing under the following conditions:

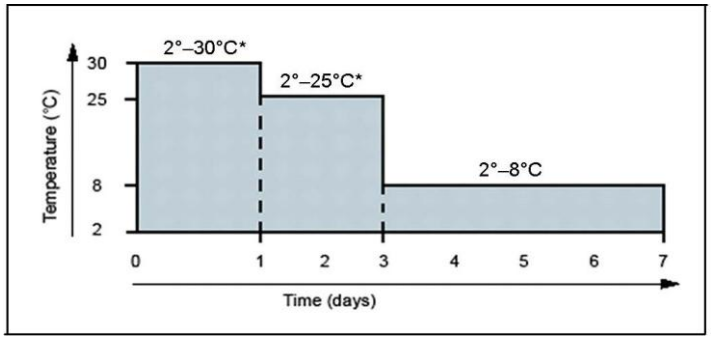
For storage above 8°C, individual donor lysates may be stored for 72 hours up to 25°C, and up to 30°C for any 24 hour period during the 72 hours.

Other than noted above, specimens are stored at 2° to 8°C.

In addition, individual donor lysates may be stored at ≤ –20°C for up to 12 months before testing.

Refer to Figure 2 below for the example storage temperature chart.

Figure 2: Living Donor Individual Donor Lysate Stability



***The cumulative time spent at the elevated temperatures cannot exceed these limits.**

D. Specimen Stability may be affected by elevated temperature.

E. No adverse effect on assay performance was observed when individual donor lysates were subjected to 3 freeze-thaw cycles.

Note: When testing frozen lysates, allow specimens to reach room temperature prior to processing by following these steps:

1. **Warm the frozen lysate specimens to a temperature between 28°C and 30°C**. This can be achieved by using either a water bath or a dry incubator.
    - If using a water bath, place the specimens in a 30°C water bath for at least 30 minutes and no more than 2 hours.
    - Alternatively, warm the specimens in a dry incubator set to 28°C - 30°C for at least 1 hour and no more than 2 hours.
2. **Mix and homogenize**

    Every 10 minutes during incubation, remove the specimens from the water bath or dry incubator. Gently invert them 10 times to mix and homogenize the contents. Check for any precipitates. Make sure they are completely dissolved before proceeding.
3. **Final Homogenization**

    Prior to loading on the Panther, gently invert the sample 10 more times to ensure complete homogenization.

F. Ensure that all whole blood samples are at room temperature before loading onto the Procleix Xpress System.

G. Ensure that all whole blood samples have been mixed preferably on a tube mixer for at least 5 minutes or by inversions for at least 15 times immediately before loading onto the Procleix Xpress System. Ensure that the whole blood is mixed gently and thoroughly and is homogenous.

H. If testing previously centrifuged samples, or blood with visibly separated plasma and red blood cells, ensure that they are thoroughly mixed until they are homogenous prior to performing the run.

Note: A higher rate of pipetting errors or an increased risk of False Negatives may be encountered when using non-homogenous or previously centrifuged samples.

I. Individual donor lysates should be mixed by inversion if stored for extended periods of time prior to retesting, which may require up to 10 inversions to homogenize the samples.

J. Do not test more than 4 replicates from an individual donor lysate tube.

K. Other collection and storage conditions should be validated by the user. If specimens are to be shipped, they should be packaged and labeled in compliance with applicable federal and international regulations covering the transport of clinical specimens and etiologic agents.

L. False positive results may occur if cross-contamination of specimens is not adequately controlled during specimen handling and processing.

MATERIALS REQUIRED AND PROVIDED IN ASSAY KITS

Component	Part Number / Quantity	Part Number / Quantity
Procleix Plasmodium Assay Kit	**9052707** (1000 Test Kit)	**9052708** (5000 Test Kit)
Box 1		
Internal Control Reagent	4 x 2.8 mL	20 x 2.8 mL
Amplification Reagent	4 x 26 mL	20 x 26 mL
Enzyme Reagent	4 x 13.4 mL	20 x 13.4 mL
Probe Reagent	4 x 34.7 mL	20 x 34.7 mL
Box 2		
Target Capture Reagent	4 x 161 mL	20 x 161 mL
Box 3		
Selection Reagent	4 x 91 mL	20 x 91 mL
Calibrators Box		
Negative Calibrator	15 x 2.2 mL	75 x 2.2 mL
Positive Calibrator	15 x 2.2 mL	75 x 2.2 mL

MATERIALS REQUIRED BUT NOT PROVIDED IN ASSAY KITS

These catalog numbers can be ordered separately as needed in order to meet individual site testing requirements

Component	Part Number/Quantity	Part Number / Quantity
Procleix Assay Fluids Kit	**303344** (1000 tests)	
Wash Solution	1 x 2.9 L	
Oil	1 x 260 mL	
Buffer for Deactivation Fluid	1 x 1.4 L	
Procleix Auto Detect Reagents Kit	**303345** (1000 tests)	**9053575** (4000 tests)
Auto Detect 1	1 x 245 mL	4 x 245 mL
Auto Detect 2	1 x 245 mL	4 x 245 mL
Procleix Parasite Transport Medium (PTM)	**9051577** (200 tests)	
	1 x 1.6 L	

Disposables *(Disposables are single use only, do not reuse. Use of other disposables is not recommended.)*	**Part Number**	**Quantity**
Multi-Tube Units (MTUs)	104772	1 case of 100
Waste Bag Kit	902731	1 box of 10
1 MTU Waste Cover	504405	1 box of 10
Reagent Spare Caps (TCR and Selection Reagents)	CL0039	1 bag of 100
Reagent Spare Caps (Amplification and Probe Reagents)	CL0042	1 bag of 100
Reagent Spare Caps (Enzyme Reagents)	501619	1 bag of 100

Instruments

Procleix Panther System and operator's manual
Procleix Reagent Preparation Incubator 250 (RPI 250) with Independent Temperature Monitor (ITM) and operator's manual, or
Procleix Reagent Equilibration System (RES) and operator's manual

Panther System Maintenance	**Part Number**	**Quantity**
Advanced Cleaning Solution	PRD-04550	1 bottle (255 mL)

MATERIALS REQUIRED BUT NOT PROVIDED

Bleach (for use in final concentrations of 5 to 8.25% sodium hypochlorite and 0.5 to 0.7% sodium hypochlorite)
Alcohol (70% ethanol, 70% isopropyl alcohol solution, or 70% isopropyl alcohol wipes)
Disposable 1000 µL conductive filter tips (DiTis) with filter in rack approved for use with the Procleix Panther System Contact Grifols Technical Service for approved tips.
For Manual lysis:
Lysate tubes or 12–16 x 75 mm polypropylene plastic or siliconized glass tubes
50 mL graduated conical tube for decanting Parasite Transport Medium (PTM)
Calibrated pipettes and 1000 µL pipette tips with filter

ADDITIONAL MATERIALS AVAILABLE FROM GRIFOLS

These catalog numbers can be ordered separately as needed in order to meet individual site testing requirements.

Component	Part Number / Quantity	Part Number / Quantity
Procleix Plasmodium Assay Calibrators Kit*	**9052709** (15 Sets)	**9052710** (75 Sets)
Negative Calibrator	15 x 2.2 mL	75 x 2.2 mL
Positive Calibrator	15 x 2.2 mL	75 x 2.2 mL

***This kit is also included within the Procleix Plasmodium Assay Kit when you order Part Number 9052707 or 9052708. Procleix Plasmodium assay kits are master lotted. If these part numbers are purchased separately, they must be purchased from the same master lot as the Procleix Plasmodium Assay kit to ensure that only reagents belonging to a specific master lot are run together on the Procleix Panther System.

OPTIONAL MATERIALS AVAILABLE FROM GRIFOLS

Instruments/Software

For preparation of individual lysates using automated system:

- Procleix Xpress System and operator's manual

For data management:

- Bloodstream software and operator's manual

For instrument and software specifics and ordering information, contact Grifols Customer Service.

A. For *in vitro* diagnostic use.

B. When performing testing with different Procleix Assays using shared instrumentation, ensure appropriate segregation is maintained to prevent mix-up of samples during processing. In addition, verify that the correct set of reagents is being used for the assay that is being run.

C. To reduce the risk of invalid results, carefully read the entire package insert for the Procleix Plasmodium Assay and the *Procleix Panther System Operator's Manual* prior to performing an assay run.

D. Specimens may be infectious. Use Universal Precautions [18,19] when performing the assay. Proper handling and disposal methods should be established according to local, state, and federal regulations[20]. Only personnel adequately qualified and proficient in the use of the Procleix Plasmodium Assay and trained in handling infectious materials should perform this procedure.

E. Use routine laboratory precautions. Do not pipette by mouth. Do not eat, drink, or smoke in designated work areas. Wear disposable gloves and laboratory coats when handling specimens and kit reagents. Wash hands thoroughly after handling specimens and kit reagents.

F. The Enzyme Reagent contains sodium azide as a preservative. Do not use metal tubing for reagent transfer. If solutions containing azide compounds are disposed of in a plumbing system, they should be diluted and flushed with generous amounts of running water. These precautions are recommended to avoid accumulation of deposits in metal piping in which explosive conditions could develop.

G. Avoid contact of Auto Detect Reagents 1 and 2 with skin, eyes, and mucous membranes. Wash with water if contact with these reagents occurs. If spills of these reagents occur, dilute with water before wiping dry, and follow appropriate site procedures.

H. Dispose of all materials that have come in contact with specimens and reagents according to local, state, and federal regulations[19]. Thoroughly clean and disinfect all work surfaces.

I. Use only specified disposables.

J. Do not use kit after expiration date.

K. DO NOT interchange, mix, or combine reagents from kits with different master lot numbers.

L. Avoid microbial and nuclease contamination of reagents. Use of filtered disposable pipette tips is required on the Procleix Panther System.

M. Store all assay reagents at specified temperatures. The performance of the assay may be affected by use of improperly stored assay reagents. See STORAGE AND HANDLING INSTRUCTIONS and REAGENT PREPARATION.

N. Store all specimens at specified temperatures. The performance of the assay may be affected by use of improperly stored specimens. See SPECIMEN COLLECTION, STORAGE, AND HANDLING for specific instructions.

O. To reduce the risk of invalid results when testing frozen lysates, ensure specimens are brought to room temperature. See SPECIMEN COLLECTION, STORAGE, AND HANDLING for specific instructions.

P. Ensure that precipitates are dissolved. Do not use a reagent if gelling, precipitate, or cloudiness is present. See REAGENT PREPARATION for specific instructions.

Q. Do not combine any assay reagents or fluids without specific instructions. Do not top off reagent or fluids. The Procleix Panther System verifies reagent levels.

R. Only the reagent onboard stability is tracked by the Procleix Panther System Software. The time reagents remain at room temperature when not onboard the Procleix Panther System MUST be tracked by the user to ensure maximum allotted room temperature time is not exceeded.

S. Some reagents of this kit are labeled with risk and safety symbols per US and international regulations and should be handled accordingly. Safety Data Sheets (SDS) are accessible from the manufacturer's website. For information on which codes are applicable per local regulations, please consult the corresponding SDS.

Procleix Selection Reagent

Boric Acid 1–5 Weight-%
Sodium Hydroxide 0.5–1.5 Weight-%
Octyl phenyl polyethylene glycol ether 0.1-1 Weight-%

DANGER

H315 - Causes skin irritation
H319 - Causes serious eye irritation
H360 - May damage fertility or the unborn child

P201 - Obtain special instructions before use.
P202 - Do not handle until all safety precautions have been read and understood.
P203 - Obtain, read and follow all safety instructions before use.
P264 - Wash hands thoroughly after handling.
P264+P265 - Wash hands thoroughly after handling. Do not touch eyes.
P280 - Wear protective gloves, protective clothing, eye protection, face protection.
P302+P352 - IF ON SKIN: Wash with plenty of soap and water.
P305+P351+P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P308+P313 - IF exposed or concerned: Get medical advice/attention.
P318 - IF exposed or concerned, get medical advice.
P332+P317 - If skin irritation occurs: Get medical help.
P332+P313 - If skin irritation occurs: Get medical advice/attention.
P337+P317 - If eye irritation persists: Get medical help.
P337+P313 - If eye irritation persists: Get medical advice/attention.
P362+P364 - Take off contaminated clothing and wash it before reuse.
P405 - Store locked up.
P501 - Dispose of contents and container to hazardous or special waste collection point, in accordance with local, regional, national and/or international regulation.

Procleix Internal Control Reagent

Lithium dodecyl sulphate 5 - <10 Weight-%

DANGER

H318 - Causes serious eye damage.
H316 - Causes mild skin irritation
H402 - Harmful to aquatic life

P264+P265 - Wash hands thoroughly after handling. Do not touch eyes.
P273 - Avoid release to the environment
P280 - Wear protective gloves, eye protection, face protection.
P305+P351+P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P305+P354+P338 - IF IN EYES: Immediately rinse with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P310 - Immediately call a POISON CENTER or doctor.
P317 - Get medical help.
P332+P317 - If skin irritation occurs: Get medical help.
P332+P313 - If skin irritation occurs: Get medical advice or attention.
P501 - Dispose of contents and container to hazardous or special waste collection point, in accordance with local, regional, national and/or international regulation.

Procleix Probe Reagent

Lithium dodecyl sulphate 1-5 *Weight-%*
Lithium Chloride 1-5 weight-%
Ethanol 1-5 weight-%

DANGER

H318 - Causes serious eye damage.
H227 - Combustible liquid.
H316 - Causes mild skin irritation
H402 - Harmful to Aquatic Life

P210 - Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking

P264+P265 - Wash hands, forearms and face thoroughly after handling. Do not touch eyes
P273 - Avoid release to the environment
P280 - Wear protective gloves, protective clothing, eye protection, face protection.
P305+P351+P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P305+P354+P338-IF IN EYES: Immediately rinse with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P310 - Immediately call a POISON CENTER or a doctor.
P317 - Get medical help.
P332+P317 - If skin irritation occurs: Get medical help.
P332+P313 - if skin irritation occurs: Get medical advice or attention.
P370+P378 - In case of fire: Use Dry chemical, CO2, alcohol-resistant foam or waterspray to extinguish.
P403 - Store in a well-ventilated place.
P403+P235 - Store in a well-ventilated place. Keep cool.
P501 - Dispose of contents/container to hazardous or special waste collection point, in accordance with local, regional, national and/or international regulation

Procleix Target Capture Reagent

Lithium dodecyl sulphate 5-<10 Weight-%

DANGER

H318 - Causes serious eye damage.
H316 - Causes mild skin irritation
H402 - Harmful to aquatic life

P264+P265 - Wash hands thoroughly after handling. Do not touch eyes.
P273 - Avoid release to the environment.
P280 - Wear protective gloves, eye protection, face protection.
P305+P351+P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P305+P354+P338 - IF IN EYES: Immediately rinse with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P310 - Immediately call a POISON CENTER or doctor.
P317 - Get medical help.
P332+P313 - If skin irritation occurs: Get medical advice or attention
P332+P317 - If skin irritation occurs: Get medical help.
P501 - Dispose of contents and container to hazardous or special waste collection point, in accordance with local, regional, national and/or international regulation.

Procleix Calibrators

Lithium dodecyl sulphate 5 – <10 Weight-%

DANGER

H318 - Causes serious eye damage
H316 - Causes mild skin irritation.
H402 - Harmful to Aquatic Life

P264+P265 - Wash hands thoroughly after handling. Do not touch eyes
P273 - Avoid release to the environment.
P280 - Wear protective gloves, protective clothing, eye protection, face protection
P305+P351+P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P305+P354+P338 - IF IN EYES: Immediately rinse with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P310 - Immediately call a POISON CENTER or a doctor.
P317 - Get medical help.
P332+P313 - If skin irritation occurs: Get medical advice or attention.
P332+P317 - If skin irritation occurs: Get medical help.
P501 - Dispose of contents and/or container to hazardous or special waste collection point, in accordance with local, regional, national and international regulations.

Procleix Enzyme Reagent

Glycerol 10-30 Weight-%
Octyl phenyl polyethylene glycol ether 5-<10 Weight-%
Sodium Azide 0.01-0.1 Weight-%

H412 - Harmful to aquatic life with long lasting effects.

P273 - Avoid release to the environment
P501 - Dispose of contents/container to hazardous or special waste collection point, in accordance with local, regional, national and/or international regulation.

Procleix Amplification Reagent

5-chloro-2-methyl-1,2-thiazol-3(2H)-one and 2-methyl-1,2-thiazol-3(2H)-one <0.001Weight %.

EUH208 - May produce an allergic reaction.

Procleix Auto Detect 2

Sodium Hydroxide 5 –10 Weight-%

DANGER

H314 - Causes severe skin burns and eye damage
H318 - Causes serious eye damage

P260 - Do not breathe mist, spray, vapors
P264 - Wash hands, forearms and face thoroughly after handling
P264+P265 - Wash hands , forearms and face thoroughly after handling. Do not touch eyes.
P280 - Wear protective gloves, protective clothing, eye protection, face protection
P301 + P330 + P331 - IF SWALLOWED: Rinse mouth. Do NOT induce vomiting
P302+P361+P354 - IF ON SKIN: Take off immediately all contaminated clothing. Immediately rinse with water for several minutes.
P303 + P361 + P353 - IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water or shower
P304 + P340 - IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing
P305+P351+P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P305+P354+P338 - IF IN EYES: Immediately rinse with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P310 - Immediately call a POISON CENTER or doctor.
P316 - Get emergency medical help immediately.
P363 - Wash contaminated clothing before reuse.
P405 - Store locked up.
P501 - Dispose of contents and container to hazardous or special waste collection point, in accordance with local, regional, national and/or international regulation.

Procleix Buffer for Deactivation Fluid

Sodium Bicarbonate 5-10 Weight-%
Sodium Hydroxide 0.5-1.5 Weight-%
Sodium Hypochlorite 0.1-0.5 Weight-%

WARNING

H315 - Causes skin irritation
H319 - Causes serious eye irritation
H401 - Toxic to aquatic life
H412 - Harmful to aquatic life with long lasting effects

P264 - Wash hands thoroughly after handling
P264+P265 - Wash hands thoroughly after handling. Do not touch eyes.
P273 - Avoid release to the environment
P280 - Wear protective gloves, eye protection
P302 + P352 - IF ON SKIN: Wash with plenty of water.
P305 + P351 + P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing
P332+P313 - If skin irritation occurs: Get medical advice/attention.
P332+P317 - If skin irritation occurs: Get medical help.
P337+P313 - If eye irritation persists: Get medical advice/attention.
P337+P317 - If eye irritation persists: Get medical help.
P362+P364 - Take off contaminated clothing and wash it before reuse.
P501 - Dispose of contents and container to hazardous or special waste collection point, in accordance with local, regional, national and/or international regulation.

Procleix Parasite Transport Medium

Lithium dodecyl sulphate 3 – 7 Weight-%

WARNING

H316 - Causes mild skin irritation.
H318 - Causes serious eye damage.
H402 - Harmful to Aquatic Life

P264+P265 - Wash hands thoroughly after handling. Do not touch eyes
P273 - Avoid release to the environment.

	P280 - Wear protective gloves, protective clothing, eye protection, face protection P305+P351+P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P305+P354+P338 - IF IN EYES: Immediately rinse with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P310 - Immediately call a POISON CENTER or a doctor. P317 - Get medical help. P332+P313 - If skin irritation occurs: Get medical advice or attention. P332+P317 - If skin irritation occurs: Get medical help. P501 - Dispose of contents and/or container to hazardous or special waste collection point, in accordance with local, regional, national and international regulations.

T. The Procleix Panther System groups a kit of reagents into a matched set the first time that it scans their barcodes during the inventory process. These reagents are required to be run as a set in all subsequent worklists. Bottles belonging to a matched set cannot be swapped with bottles in other matched sets of reagents. Refer to the *Procleix Panther System Operator's Manual* for more information.

U. Refer to precautions within this package insert and the *Procleix Panther System Operator's Manual*.

V. DO NOT heat the Probe Reagent above 35°C when using the RPI 250 or RES. Refer to the *Procleix RPI 250 Operator's Manual* or the *Procleix Reagent Equilibration System Operator's Manual*, as applicable.

W. Each calibrator is designed to be run in triplicate; any excess material in each vial is to be appropriately discarded.

A. Room temperature is defined as 15° to 30°C.

B. Choose a new or opened matched set of reagents. An open set of reagents must be used on either the same Procleix Panther System as used previously or a Procleix Panther System that is connected to that system via Data Sharing. Do not use reagents that have been used outside the Procleix Panther System, as the instrument verifies reagent volumes.

C. Verify that the reagents have not exceeded the expiration date and/or storage stability times, including onboard stability. Refer to STORAGE AND HANDLING INSTRUCTIONS.

The Procleix Panther System tracks the number of hours each reagent and fluid is loaded onboard the instrument. The Procleix Panther System will not start pipetting specimens if reagents have expired or exceeded their onboard stability. Consult the following table for onboard stability information.

Reagent/Fluid	Onboard Stability
wTCR, Probe Reagent, Enzyme Reagent, Amplification Reagent, Selection Reagent	72 hours
Wash Solution, Oil, Buffer for Deactivation Fluid, Auto Detect Reagents	60 days

D. Remove a bottle of Selection Reagent from room temperature storage.

Note: The Selection Reagent must be at room temperature before use.

1. Selection Reagent may form precipitate if it is inadvertently stored at 2° to 8°C or if the room temperature falls between 2° to 15°C.
2. If cloudiness or precipitate is present, perform Selection Reagent recovery as described in the *Procleix RPI 250 Operator's Manual* or the *Procleix Reagent Equilibration System Operator's Manual*. Do not use if precipitate or cloudiness persists.
3. If foam is present, carefully remove it with sterile swabs or sterile pipettes. Use a new swab or pipette for each vial.
4. Record the date that it was first opened (OPEN DATE) on the space provided on the label.

E. Precipitate will form in the Probe Reagent when stored at 2° to 8°C. To facilitate dissolution of precipitate, use the RPI 250 or the RES to thaw Probe Reagent at an average temperature of 32° ± 2°C not to exceed 35°C. Refer to the *Procleix Reagent Preparation Incubator 250 Operator's Manual* or the *Procleix Reagent Equilibration System Operator's Manual*. Ensure that precipitates in Probe Reagent are dissolved. Do not use if precipitate or cloudiness is present.

F. Refer to the *Procleix RPI 250 Operator's Manual* if using the RPI 250, or the *Procleix Reagent Equilibration System Operator's Manual* if using the RES, to prepare the following reagents: TCR, Probe Reagent, Enzyme Reagent, and Amplification Reagent.

Note: If precipitate is still present after thawing, Probe Reagent can be incubated with RPI 250 File 3 (room temperature) or RES Room Temperature program to facilitate complete dissolution of precipitate. The Probe Reagent may also be warmed in a water bath to facilitate dissolution of precipitate, but temperature in the water bath should not exceed 30°C. If thawing is conducted on the lab bench, probe reagent may take up to 4 hours with periodic mixing to allow complete dissolution of precipitate.

G. Ensure that precipitates are dissolved. Do not use a reagent if gelling, precipitate, or cloudiness is present (refer to instructions in steps H.4, I, and J below).

Record the date of thaw (THAW DATE) for each reagent on the space provided on the label.

H. Prepare working Target Capture Reagent (wTCR):

1. Remove TCR from 2° to 8°C storage. IMMEDIATELY upon removing from storage, mix vigorously (at least 10 inversions). DO NOT VORTEX.
2. Place TCR into the RPI 250 or RES and refer to the applicable *Procleix RPI 250 Operator's Manual* or *Procleix Reagent Equilibration System Operator's Manual* for instructions.

   Note: If a gel is observed after performing this procedure, a new bottle must be used according to the handling recommendations above. Return the bottle with gel back to 2° to 8°C storage for subsequent use.
3. Thaw one vial of Internal Control (IC) Reagent up to 24 hours at 2° to 8°C or up to 8 hours at room temperature. Do not use the RPI 250 or RES to thaw Internal Control Reagent.
4. Mix the Internal Control Reagent thoroughly by gentle manual inversion or mechanical inversion using a laboratory rocker.

   Note: If gelling occurs, gel must be dissolved prior to use and within the 8 hour thaw period at room temperature. To expedite the dissolution of gel, warm the Internal Control Reagent at 25° to 30°C in a water bath. Periodically remove Internal Control Reagent from water bath to gently invert until gel is dissolved. Dry the exterior of the vial prior to opening.
5. Unload TCR from the RPI 250 or RES.
6. Pour the entire vial of Internal Control Reagent into the TCR bottle. This is now the working Target Capture Reagent (wTCR).
7. Mix thoroughly.
8. Record the date Internal Control Reagent was added, wTCR expiration date (date Internal Control Reagent was added plus 30 days), and lot number used (IC LOT) in the space indicated on the TCR bottle.
9. Retain the IC Reagent vial to scan the barcode label into the system.

I. Thaw calibrators at room temperature. **Do not use the RPI 250 or RES to thaw Procleix Plasmodium Assay Calibrators.**

Note: These are single-use vials which must be thawed prior to each run.

1. Mix calibrators gently by inversion to avoid foaming.
2. If foam is present, remove it with sterile swabs or sterile pipettes. Use a new swab or pipette for each vial.

Note: If gelling occurs, gel must be dissolved prior to use and within the 8 hour thaw period at room temperature. To expedite the dissolution of gel, warm the calibrators at 25° to 30°C in a water bath. Periodically remove calibrators from water bath to gently invert until gel is dissolved.

J. Record the date Wash Solution, Buffer for Deactivation Fluid, Oil, Auto Detect 1, and Auto Detect 2 were first opened and loaded onto the Procleix Panther System (OPEN DATE) in the space provided on the label.

SPECIMEN PREPARATION

AUTOMATED LYSIS INSTRUCTIONS

A. Refer to the *Procleix Xpress System Operator's Manual* for instructions to prepare individual donor lysate samples using the Procleix Xpress System.

MANUAL LYSIS INSTRUCTIONS

A. Work Area Preparation

1. Wipe down bench top and pipettes with freshly made 0.5–0.7% sodium hypochlorite and leave in contact with the surface for 15 minutes. Do not allow the sodium hypochlorite solution to dry.
2. Remove sodium hypochlorite by wiping down the bench with deionized water.
3. Cover the work area with a plastic-backed absorbent laboratory bench cover.

B. Manual Lysis Preparation

1. Prepare the number of lysate tubes required (1 per blood sample for individual donor testing) and label as per laboratory protocol.
2. Decant the approximate volume of Parasite Transport Medium (PTM) required into the conical tube.
3. Using a single pipette tip, retrieve 2.7 mL of PTM from the conical tube and dispense into each pre-labeled lysis tube.
4. When dispensing the PTM is complete, discard the pipette tip and any remaining PTM.

Note: It is acceptable to use a calibrated repeat pipettor attached to a secondary container to dispense PTM under the following conditions:

- HDPE or PP are acceptable materials for the secondary container.
- PTM that was poured into a secondary container must not be poured back into the original container for reuse.
- Open bottle stability of the PTM primary container must not be exceeded.

C. Preparation of the Individual Donor Lysate

1. Ensure that all whole blood samples have been mixed preferably on a tube mixer for at least 5 minutes or by inversions for at least 15 times immediately before loading onto the Procleix Xpress System. Ensure that the whole blood is mixed gently and thoroughly and is homogenous.
2. Remove the cap from the whole blood specimen and transfer 900 µL of whole blood into the pre-labeled lysate tube containing PTM. Following the dispense of the blood sample into the lysate tube, homogenize the whole blood and PTM by gently aspirating and dispensing the solution at least 5 times. Avoid creating bubbles or aerosols.
3. Dispose of the pipette tip into the container of 0.5–0.7% sodium hypochlorite.
4. Recap the whole blood specimen.
5. Repeat steps C. 2 to C. 4 for each separate lysate being prepared.
6. The lysate tube(s) are now ready to be placed into Panther Sample Racks and loaded on the Procleix Panther System for testing.

PROCEDURAL NOTES

Note: Refer to the *Procleix Panther System Operator's Manual* for operating instructions.

A. The operator must ensure that the Procleix Plasmodium Assay Calibrators are used with the corresponding master lot of kit reagents as indicated on the master lot barcode sheet enclosed with each shipment of Procleix Plasmodium Assay Calibrators.

B. Replace bottles in the Universal Fluids Drawer when notified by the system. Refer to the *Procleix Panther System Operator's Manual*.

Note: Auto Detect Reagents and Assay Fluids may be used with any master lot of Procleix Assay Reagents that are run on the Procleix Panther System.

C. Wash Solution is shipped at ambient temperature and stored at room temperature. Precipitates may form in the Wash Solution during shipment or during storage when temperatures fall to between 2° and 15°C. Wash Solution may be warmed to facilitate dissolution of precipitate. **Do not use the RPI 250 or RES to warm the Wash Solution.** Temperature should not exceed 30°C. Ensure that precipitates in the Wash Solution are dissolved prior to use. Do not use if precipitate or cloudiness is present.

D. To reduce the risk of invalid results, carefully read the entire package insert for the Procleix Plasmodium Assay prior to performing an assay run. This package insert must be used with the Procleix *Panther System Operator's Manual*, *Procleix RPI 250 Operator's Manual* or *Procleix Reagent Equilibration System Operator's Manual*, and any applicable technical bulletins.

E. RUN SIZE

For the Procleix Plasmodium Assay, each worklist may contain up to 250 tests, including Procleix Plasmodium Assay Calibrators.

F. EQUIPMENT PREPARATION

See the *Procleix Panther System Operator's Manual*.

G. RUN CONFIGURATION

1. Each run must have a set of Procleix Plasmodium Assay Calibrators.
2. For the Procleix Plasmodium Assay, a set of calibrators consists of one vial each of Negative Calibrator and Positive Calibrator. The Negative and Positive Calibrators are run in triplicate.

H. WORK FLOW

1. Prepare reagent in clean area.
2. The sample loading area must be amplicon-free.

I. DECONTAMINATION

1. The extremely sensitive detection of analytes by this test makes it imperative to take all possible precautions to avoid contamination. Laboratory bench surfaces must be decontaminated daily with 0.5 to 0.7% sodium hypochlorite in water (diluted bleach). Allow bleach to contact surfaces for at least 15 minutes, then follow with a water rinse. Chlorine solutions may pit equipment and metal. Thoroughly rinse bleached equipment to avoid pitting.
2. Follow instructions provided in the *Procleix Panther System Operator's Manual* for instrument decontamination and maintenance procedures.

ASSAY PROCEDURE

Procleix Plasmodium Assay Calibrators are to be used with the corresponding master lot of the Procleix Plasmodium Assay. The operator must check to ensure that the Procleix Plasmodium Assay Calibrators are used with the corresponding master lot of kit reagents as indicated on the Procleix Plasmodium Assay master lot sheet in use.

For equipment preparation, rack setup, and assay procedure information, see instructions in the *Procleix Panther System Operator's Manual*.

QUALITY CONTROL PROCEDURES

Note: All Quality Control procedures described below are performed by the Procleix Plasmodium Assay software.

ACCEPTANCE CRITERIA FOR THE PROCLEIX PLASMODIUM ASSAY

A. Run validity:

A run (also identified as a worklist) is valid if the minimum number of calibrators meet their acceptance criteria and are valid.

1. In a Procleix Plasmodium Assay run, at least four of the six calibrator replicates must be valid. At least two of the three Negative Calibrator replicates and two of the three Positive Calibrator replicates must be valid.
2. Calibrator acceptance criteria are automatically verified by the Procleix Panther System Software. If less than the minimum number of calibrator replicates is valid, the Procleix Panther System Software will automatically invalidate the run.
3. In a valid run, cutoff values will be automatically calculated for Internal Control (flasher) and analyte (glower).
4. If a run is invalid, sample results are reported as invalid and all specimens must be retested.

B. Sample validity:

1. In a valid run, a sample result is valid if the IC signal is equal to or above the IC cutoff, with the following exceptions:
    a. Specimens with an analyte signal (glower signal) greater than the analyte cutoff are not invalidated even if the Internal Control (IC) signal is below the cutoff.
    b. Specimens with RLU values outside software limits are invalidated by the software and their reactive status cannot be assessed. The software also automatically invalidates Positive Calibrators with RLU values outside software limits.
2. A sample may also be invalidated due to instrument and/or results processing errors. Refer to the *Procleix Panther System Operator's Manual* for details.
3. All individual specimen results that are invalid in a valid run must be retested.

INTERPRETATION OF RESULTS

Two cutoffs are determined by the Procleix Panther System Software for each assay using calibrator RLU values: one for the Analyte Signal (glower signal) termed the Analyte Cutoff and one for the Internal Control Signal (flasher signal) termed the Internal Control Cutoff. For each sample, an Analyte Signal RLU value and Internal Control Signal RLU value are determined. Analyte Signal RLU divided by the Analyte Cutoff is abbreviated as the Analyte Signal/Cutoff (S/CO) on the report.

Summary of Specimen Interpretation:

Specimen Interpretation	Criteria
Nonreactive	RLU values within limits set by software and Analyte S/CO < 1.00 and IC RLU ≥ IC Cutoff
Reactive	RLU values within limits set by software and Analyte S/CO ≥ 1.00
Invalid	RLU values outside limits set by software and Analyte S/CO < 1.00 and IC RLU < IC Cutoff

A. Any specimen with an interpretation of Invalid or Error in the Procleix Plasmodium Assay must be retested in singlet.

B. If at any point in the testing algorithm there is insufficient volume to complete the testing, an alternate lysate from the index donation may be used as long as the storage criteria in the package insert are met.

C. Lysates with a valid Internal Control value and with an Analyte S/CO less than 1.00 in the Procleix Plasmodium Assay are considered Nonreactive for *Plasmodium*. No further testing of a *Plasmodium* Nonreactive specimen is required.

D. Specimens with an Analyte S/CO greater than or equal to 1.00 with IC Signal less than or equal to 750,000 RLU are considered Reactive.

1. If an individual donor lysate tests Reactive with the Procleix Plasmodium Assay, then the individual donor lysate is considered Reactive for *Plasmodium*.
2. Further clarification of the Reactive lysates for informational purposes may be obtained by testing an alternate lysate from the index donation with the Procleix Plasmodium Assay and/or by follow-up testing. Results of testing obtained for clarification do not replace test results for purposes of donor eligibility.
3. Any Reactive result should be resolved according to the resolution algorithm for reactive specimens, as explained in this section.

LIMITATIONS OF THE PROCEDURE

A. This assay has been developed and intended for use with the Procleix Panther System only.

B. This assay has not been approved for use with pooled samples.

C. This assay has not been approved for use with cadaveric samples.

D. Though rare, mutations within the highly conserved regions of the genome covered by the primers and/or probes in the Procleix Plasmodium Assay may result in failure to detect the parasite.

E. Certain substances may interfere with the performance of the assay. See the SPECIFICITY AND SENSITIVITY OF THE PROCLEIX PLASMODIUM ASSAY IN THE PRESENCE OF DONOR AND DONATION FACTORS section.

F. Test results may be affected by improper specimen collection, storage, or specimen processing.

G. Cross-contamination of samples can cause false positive results.

H. Assays must be performed, and results interpreted, according to the procedures provided. Deviations from these procedures, adverse shipping and/or storage conditions, or use of outdated calibrators and/or reagents may produce unreliable results.

I. Failure to achieve expected results is an indication of an invalid run. Possible sources of error include test kit deterioration, operator error, faulty performance of equipment, specimen deterioration, or contamination of reagents.

PERFORMANCE CHARACTERISTICS

PERFORMANCE CHARACTERISTICS IN LIVING DONOR BLOOD SPECIMENS

CLINICAL PERFORMANCE

CLINICAL REPRODUCIBILITY OF THE PROCLEIX PLASMODIUM ASSAY

Reproducibility was evaluated on the Procleix Panther System at 3 US sites. Two operators performed testing using 1 Procleix Panther System at each site. Each operator performed 3 runs per day on each of 6 days, using 2 independent reagent kit lots, equally over the course of testing. Each run had 2 replicates of each panel member.

The negative panel members were made from *Plasmodium*-negative lysed human whole blood. The positive panel members were created by spiking the whole blood with *P. falciparum*. High negative, low positive, moderate positive, and high positive concentrations were prepared for testing.

Agreement values were 100% in the negative, low, moderate, and high positive panel members and 56.94% in the high negative panel member.

Table 1 shows the percent agreement with expected results and reproducibility and precision of assay results for each panel member between sites/ instruments, between operators, between lots, between days, within run, and overall.

Table 1. Reproducibility of the Procleix Plasmodium Assay on the Procleix Panther System using Two Reagent Lots

Panel Member*	Mean S/CO	% Agreement	Between Sites/Instrument		Between Lots		Between Operators		Between Days		Within Runs		Total	
			SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Negative	0.02	100	0.03	165.31	0	23.88	0	0	0.01	56.37	0.02	113.44	0.04	209.63
High Negative**	5.51	56.94	0.27	4.89	0	0	0	0	0	0	5.2	94.26	5.2	94.39
Low Positive	11.93	100	0.24	2.04	0	0	0.12	1.02	0.1	0.81	0.59	4.92	0.65	5.48
Moderate Positive	12.33	100	0.27	2.17	0.11	0.87	0	0	0.14	1.13	0.4	3.27	0.51	4.18
High Positive	11.99	100	0.44	3.64	0.1	0.85	0.12	1.01	0	0	0.49	4.05	0.67	5.6

S/CO = Analyte signal to cutoff ratio, SD = Standard Deviation, CV = Coefficient of variation
Note: Variability from some factors may be numerically negative. This can occur if the variability due to those factors is very small. In these cases, SD and %CV are shown as 0.

*n = 142 for the negative panel member, 143 for the low positive panel member, and 144 for the high negative, moderate, and high positive panel members.
Estimated target concentration in parasites/mL (p/mL) for each panel member: Negative = 0 p/mL, High Negative = 1.75 p/mL, Low Positive = 10.50 p/mL, Moderate Positive = 35 p/mL, High Positive = 175 p/mL
**The high negative panel member was expected to have <100% reactive results, as it had a concentration targeted below the assay's 95% limit of detection.

An additional study was performed to demonstrate lot-to-lot variability using three independent reagents lots of the Procleix Plasmodium assay. The same panel members that were used for the reproducibility study were included in this study. Testing was performed at a single site with two operators per site across six days of testing using two replicates per panel.

Agreement values were 100% in the negative, low, moderate, and high positive panel members and 70.83% in the high negative panel members.

Table 2 shows the percent agreement with expected results and lot-to-lot variability of assay results for each panel member between lots, between operators, between days, within run, and overall.

Table 2. Lot-to-Lot Reproducibility of the Procleix Plasmodium Assay on the Procleix Panther System using Three Reagent Lots

Panel Member*	Mean S/CO	% Agreement	Between Lots		Between Operators		Between Days		Within Runs		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Negative	0	100	0	0	0	0	0	0	0	667.98	0	667.98
High Negative**	1.94	70.83	0.02	1.29	0	0	0.03	1.58	0.08	4.21	0.09	4.68
Low Positive	7.16	100	0.39	5.42	0	0	1.03	14.39	4.97	69.44	5.09	71.12
Moderate Positive	12.99	100	0.21	1.58	0	0	0.21	1.65	0.63	4.87	0.7	5.38
High Positive	12.94	100	0.2	1.53	0	0	0.32	2.44	0.55	4.22	0.66	5.11
Negative	12.81	100	0.27	2.12	0	0	0.24	1.85	0.6	4.69	0.7	5.47

S/CO = Analyte signal to cutoff ratio, SD = Standard Deviation, CV = Coefficient of variation
Note: Variability from some factors may be numerically negative. This can occur if the variability due to those factors is very small. In these cases, SD and %CV are shown as 0.

*n = 72 for the negative, high negative, moderate, and high positive panel members and 71 for the low positive panel members.
Estimated target concentration in parasites/mL (p/mL) for each panel member: Negative = 0 p/mL, High Negative = 1.75 p/mL, Low Positive = 10.50 p/mL, Moderate Positive = 35 p/mL, High Positive = 175 p/mL
**The high negative panel member was expected to have <100% reactive results, as it had a concentration targeted below the assay's 95% limit of detection.

CLINICAL SPECIFICITY OF THE PROCLEIX PLASMODIUM ASSAY SPECIFICITY IN NORMAL BLOOD DONORS

A prospective, multicenter clinical study was conducted to estimate specificity of the Procleix Plasmodium Assay on the Procleix Panther System. Whole blood samples from voluntary whole blood donors were lysed and tested individually. Three (3) US blood testing laboratories performed testing. Two (2) independent reagent kit lots and one (1) blended reagent kit lot (comprising components of the two independent lots) were used over the course of the study at each testing laboratory.

Of the 69 Procleix Plasmodium Assay runs, 68 runs (98.55%, 68/69) were valid, and 1 run (1.45%, 1/69) was invalid due to operator error.

Of the 11,088 individual donations included in the study, 27 individual donations (0.24%, 27/11,088) had an invalid result (16 hardware errors, 9 IC failures and 2 specimen issues), of which 6 were re-tested, all with a valid result.

A total of 11,067 individual donations had final outcomes for the specificity analyses. Procleix Plasmodium Assay specificity was 100% (11,067/11,067; 95% CI: 99.97% to 100%) in individual donations. Table 2 shows the specificity of the Procleix Plasmodium Assay on the Procleix Panther System in individual donations.

Table 2. Clinical Specificity of the Procleix Plasmodium Assay on the Procleix Panther System in Individual Donations

Sample Type	n	True Negative	True Positive	False Positive	% Specificity	95% CI
Individual donations	11,067	11,067	0	0	100	99.97-100

n = number of specimens
CI = Clopper-Pearson confidence interval

CLINICAL SENSITIVITY OF THE PROCLEIX PLASMODIUM ASSAY IN KNOWN-POSITIVE SAMPLES

One hundred (100) *P. falciparum*, 100 *P. vivax*, 10 *P. malariae*, and 10 *P. ovale* unique, known-positive whole blood specimens, and 10 *P. knowlesi* from cultured erythrocytes were used to prepare lysates neat (i.e., undiluted). Known-positive status was verified by testing neat samples with a NAT. The samples were tested with the Procleix Plasmodium Assay at three (3) laboratories.

Two (2) independent reagent kit lots and one (1) blended reagent kit lot (comprising components of the two independent lots) were used at each site. Results were compared to the known-positive status and clinical sensitivity was calculated (Table 3). All samples had valid results. Procleix Plasmodium Assay sensitivity was 100% (230/230; 95% CI: 98.41% to 100%) in neat known-positive samples.

Table 3. Clinical Sensitivity of the Procleix Plasmodium Assay in Known-Positive Samples

Sample Type	n	True Positive	False Negative	% Sensitivity	95% CI
Neat	230	230	0	100	98.41-100

n = number of specimens
CI = Clopper-Pearson confidence interval

CLINICAL SENSITIVITY OF THE PROCLEIX PLASMODIUM ASSAY IN SAMPLES WITH AN UNKNOWN STATUS OF INFECTION COLLECTED IN A MALARIA ENDEMIC AREA FROM ASYMPTOMATIC BLOOD DONORS

Five hundred (500) specimens were prospectively collected between November and December 2024 from asymptomatic whole blood donors in Uganda, a highly malaria endemic area. Whole blood lysates were prepared at the Makarere University - Johns Hopkins University (MU-JHU) and shipped frozen to the U.S.

Two (2) independent reagent kit lots and one (1) blended reagent kit lot (comprising components of the two independent lots) were used at 1 internal site. The same lysate tube tested was used in a comparator NAT for *Plasmodium* species detection and discrepant results were further investigated by a third and a fourth NAT, as needed, to determine the true status of the samples. Of the 500 tested samples, 204 were initially reactive with the Procleix Plasmodium Assay (204/500, 40.8%), of which 195 (195/500, 39%) were confirmed positive for *Plasmodium* (Table 4) and 24 (24/195, 12.31%) were non-reactive in serology testing, indicating either a window period case (pre-seroconversion detection) or a false negative in serology testing.

Table 4. Clinical Sensitivity of the Procleix Plasmodium Assay in Samples for Asymptomatic Donors in an Endemic Area

Sample Type	n	True Positive*	False Negative	% Sensitivity	95% CI
Individual Donations	500	195	0	100	98.13-100

n = number of specimens
CI = Clopper-Pearson confidence interval
* 130 were *P. falciparum*, 6 were *P. malariae*, 9 were *P. ovale*, 1 was co-infected *P. falciparum* and *P. ovale* and 49 were unknown

ANALYTICAL PERFORMANCE

WITHIN-LABORATORY PRECISION AND REPEATABILITY

Within laboratory precision and repeatability of the Procleix Plasmodium Assay was evaluated using whole blood lysates with *Plasmodium falciparum (P. falciparum)* at ~0.5xLoD, ~3xLOD, ~10xLOD and ~50xLOD. The positive whole blood panel members were created by spiking *Plasmodium*-negative whole blood with cultured *P. falciparum*. A negative whole blood lysate panel member was also prepared from *Plasmodium*-negative whole blood.

Each panel member was tested twice per run, 2 runs per day, for 20 days. A total of 80 tests were tested for each panel member per assay (20 days x 2 runs per day x 2 tests per run = 80 tests per panel member). Testing was performed using 1 Procleix Plasmodium Assay reagent kit lot on 1 Procleix Panther System by 1 proficient operator. All valid assay results were evaluated for the within laboratory precision and repeatability of the Plasmodium Assay.

Analysis included evaluation of percent agreement and mean S/CO ratios for panel members, and evaluation of standard deviation (SD) and %CV of the S/CO ratios for repeatability and within-laboratory precision. The mean analyte S/CO ratios were analyzed for the positive and negative panel members and the Internal Control S/CO ratios were analyzed for the negative panel members. The percent agreement between the assay results and the true status of each panel member was calculated using the analyte S/CO for all panel members. Percent agreement, mean signal to cutoff ratios (S/CO) with 95% Clopper-Pearson confidence intervals (CI), repeatability and within-laboratory precision for each panel member and the internal control are summarized in Table 5 and Table 6 respectively. The Procleix Plasmodium Assay is repeatable over multiple days across runs with a measured within-laboratory precision of <7% CV.

Table 5. Procleix Plasmodium Assay Repeatability Summary for *Plasmodium* Analyte

P. falciparum parasites/mL	n	% Agreement	Mean Analyte S/CO (95% CI)	Repeatability		Within-Laboratory	
				SD	%CV	SD	%CV
2.31 (~0.5x LOD)	69*	86.25	12.67 (12.47 - 12.87)	0.48	3.81	0.83	6.58
13.86 (~3x LOD)	80	100	13.10 (13.00 - 13.19)	0.30	2.32	0.43	3.31
46.2 (~10x LOD)	80	100	12.59 (12.47 - 12.70)	0.40	3.21	0.48	3.82
231 (~50x LOD)	80	100	12.96 (12.85 - 13.08)	0.29	2.24	0.52	3.98
Negative	80	100	0.00 (0.00008 - 0.003)	0.01	422.77	0.01	459.38

*Analyzed for concordant reactive replicates only out of 80 total replicates tested. LOD= Limit of detection, N= number of reactions, % = Percent, S/CO = Signal to Cutoff Ratio, SD = Standard Deviation, CV = Coefficient of variation, 95% CI = 95% Lower and Upper Confidence Intervals (Score Method)

Table 6. Procleix Plasmodium Assay Repeatability Summary for Internal Control

Panel member	n	% Agreement	Mean IC S/CO (95% CI)	Repeatability		Within-Laboratory	
				SD	%CV	SD	%CV
Negative	80	100	2.07 (2.04 - 2.10)	0.13	6.06	0.13	6.50

N= number of reactions, % = Percent, S/CO = Signal to Cutoff Ratio, SD = Standard Deviation, CV = Coefficient of variation, IC = Internal Control, 95% CI = 95% Lower and Upper Confidence Intervals (Score Method)

ANALYTICAL SENSITIVITY OF THE PROCLEIX PLASMODIUM ASSAY

Assay sensitivity was evaluated with serially diluted *in vitro* transcripts containing the sequences corresponding to the 18S ribosomal RNA of *P. falciparum*, *P. ovale*, *P. malariae*, *P. vivax*, and *P. knowlesi* (GenBank Accession numbers JQ627151, KF018656, AF488000, U93233, and L07560, respectively). Assay sensitivity for the detection of *P. falciparum*, *P. ovale*, *P. malariae*, *P. vivax*, and *P. knowlesi* was also evaluated with infected RBCs grown in culture or from clinical specimens serially diluted in human whole blood, prior to lysis in PTM using 0.9 mL of whole blood in 2.7 mL of PTM.

Two (2) independent reagent kit lots and one (1) blended reagent kit lot (comprising components of the two independent lots) were used to test 20 replicates of each copy level evenly for a total of 60 replicates per level, unless noted. There were 6 invalid reactions due to failure of the Internal Control to amplify and 5 invalid tests due to instrument hardware errors. Additional tests of the samples were repeated to achieve the required valid number of tests. There was 1 false positive in the *P. ovale* 0 copy/mL level of the parasite panel, retested in duplicate giving 100% agreement.

The average analyte S/CO ratio and percent coefficient of variation (%CV) for samples containing positive material were calculated from concordant results only (S/CO > 1.0). The 95% confidence intervals of the reactivity rates were based on the Clopper-Pearson method. Estimations of 50% and 95% limit of detection rates were determined by probit analysis[21].

The detection rates for *Plasmodium in vitro* transcripts are shown in Tables 7 through 11. The detection rates for *Plasmodium* parasites/mL (p/mL) are shown in Tables 12 through 16.

Table 7. Detection of *P. vivax* in *vitro* Transcript

P. vivax in vitro Transcript, copies/mL	Number of Reactive/Tested	% Reactive (95% CI)	Average S/CO	%CV
100	60/60	100 (94.04–100)	12.05	3.13
30	60/60	100 (94.04–100)	11.96	4.84
10	55/60	91.67 (81.61–97.24)	11.33	12.20
3	30/60	50.00 (36.81–63.19)	11.25	10.46
1	12/60	20.00 (10.78–32.33)	10.44	24.54
0	0/120	0 (0–3.03)	0	677.59

CI = Clopper-Pearson Confidence Interval; S/CO = Signal to Cutoff ratio in concordant replicates only; CV = Coefficient of variance

Table 8. Detection of *P. ovale in vitro* Transcript

P. ovale in vitro Transcript, copies/mL	Number of Reactive/Tested	% Reactive (95% CI)	Average S/CO	%CV
100	60/60	100 (94.04–100)	12.17	3.69
30	60/60	100 (94.04–100)	11.94	4.52
10	57/60	95.00 (86.08–98.96)	11.79	5.49
3	32/60	53.33 (40.00–66.33)	10.66	15.19
1	21/60	35.00 (23.13–48.40)	11.35	7.30
0	0/120	0 (0–3.03)	0	677.59

CI = Clopper-Pearson Confidence Interval; S/CO = Signal to Cutoff ratio in concordant replicates only; CV = Coefficient of variance

Table 9. Detection of *P. malariae in vitro* Transcript

P. malariae in vitro Transcript, copies/mL	Number of Reactive/Tested	% Reactive (95% CI)	Average S/CO	%CV
100	60/60	100 (94.04–100)	12.99	2.29
30	60/60	100 (94.04–100)	12.70	4.24
10	58/60	96.67 (88.47–99.59)	12.26	9.81
3	34/60	56.67 (43.24–69.41)	11.84	13.29
1	6/60	10.00 (3.76–20.51)	10.62	28.70
0	0/120	0 (0–3.03)	0	677.59

CI = Clopper-Pearson Confidence Interval; S/CO = Signal to Cutoff ratio in concordant replicates only; CV = Coefficient of variance

Table 10. Detection of *P. knowlesi in vitro* Transcript

P. knowlesi in vitro Transcript, copies/mL	Number of Reactive/Tested	% Reactive (95% CI)	Average S/CO	%CV
100	60/60	100 (94.04–100)	12.47	4.36
30	60/60	100 (94.04–100)	12.35	4.81
10	58/60	96.67 (88.47–99.59)	12.06	6.78
3	30/60	50.00 (36.81–63.19)	11.44	11.67
1	9/60	15.00 (7.10–26.57)	10.82	30.64
0	0/120	0 (0–3.03)	0	677.59

CI = Clopper-Pearson Confidence Interval; S/CO = Signal to Cutoff ratio in concordant replicates only; CV = Coefficient of variance

Table 11. Detection of *P. falciparum in vitro* Transcript

P. falciparum in vitro Transcript, copies/mL	Number of Reactive/Tested	% Reactive (95% CI)	Average S/CO	%CV
100	60/60	100 (94.04–100)	12.62	3.61
30	60/60	100 (94.04–100)	12.40	3.89
10	55/60	91.67 (81.61–97.24)	11.99	7.72
3	29/60	48.33 (35.23–61.61)	11.38	17.36
1	8/60	13.33 (5.94–24.59)	10.76	16.70
0	0/120	0 (0–3.03)	0	677.59

CI = Clopper-Pearson Confidence Interval; S/CO = Signal to Cutoff ratio in concordant replicates only; CV = Coefficient of variance

Table 12. Detection of *P. vivax* parasites

P. vivax p/mL	Number of Reactive/Tested	% Reactive (95% CI)	Average S/CO	%CV
6	60/60	100 (94.04–100)	12.09	4.57
4	57/60	95.00 (86.08–98.96)	12.01	5.24
2	58/60	96.67 (88.47–99.59)	11.48	17.06
1	39/60	65.00 (51.60–76.87)	10.79	11.08
0.5	24/60	40.00 (27.56–53.46)	11.05	10.56
0	0/60	0 (0–5.96)	0.01	212.54

CI = Clopper-Pearson Confidence Interval; S/CO = Signal to Cutoff ratio in concordant replicates only; CV = Coefficient of variance; p = parasites

Table 13. Detection of *P. ovale* parasites

P. ovale p/mL	Number of Reactive/Tested	% Reactive (95% CI)	Average S/CO	%CV
8	60/60	100 (94.04–100)	10.45	18.62
6	52/60	86.67 (75.41–94.06)	10.82	17.13
4	50/60	83.33 (71.48–91.71)	10.92	15.71
2	36/60	60.00 (46.54–72.44)	10.49	17.90
1	22/60	36.67 (24.59–50.10)	10.69	15.08
0.5	9/60	15.00 (7.10–26.57)	9.15	32.54
0	0/80	0 (0–4.51)	0	401.08

CI = Clopper-Pearson Confidence Interval; S/CO = Signal to Cutoff ratio in concordant replicates only; CV = Coefficient of variance; p = parasites

Table 14. Detection of *P. malariae* parasites

P. malariae p/mL	Number of Reactive/Tested	% Reactive (95% CI)	Average S/CO	%CV
6	60/60	100 (94.04–100)	12.44	4.83
4	60/60	100 (94.04–100)	12.04	8.11
2	54/60	90.00 (79.49–96.24)	11.51	11.03
1	45/60	75.00 (62.14–85.28)	11.21	13.56
0.5	37/60	61.67 (48.21–73.93)	10.92	21.95
0	0/60	0 (0–5.96)	0	774.6

CI = Clopper-Pearson Confidence Interval; S/CO = Signal to Cutoff ratio in concordant replicates only; CV = Coefficient of variance; p = parasites

Table 15. Detection of *P. knowlesi* parasites

P. knowlesi p/mL	Number of Reactive/Tested	% Reactive (95% CI)	Average S/CO	%CV
6	60/60	100 (94.04–100)	12.53	6.73
4	60/60	100 (94.04–100)	12.27	6.55
2	56/60	93.33 (83.80–98.15)	12.09	12.72
1	42/60	70.00 (56.79–81.15)	11.83	10.59
0.5	23/60	38.33 (26.07–51.79)	11.18	26.55
0	0/60	0 (0–5.96)	0	543.06

CI = Clopper-Pearson Confidence Interval; S/CO = Signal to Cutoff ratio in concordant replicates only; CV = Coefficient of variance; p = parasites

Table 16. Detection of *P. falciparum* parasites

P. falciparum p/mL	Number of Reactive/Tested	% Reactive (95% CI)	Average S/CO	%CV
8	40/40	100 (91.19–100)	11.70	6.98
6	59/60	98.33 (91.06–99.96)	12.54	5.66
4	59/60	98.33 (91.06–99.96)	11.86	12.83
2	48/60	80.00 (67.67–89.22)	11.32	19.24
1	38/60	63.33 (49.90–75.41)	10.98	22.31
0.5	18/60	30.00 (18.85–43.21)	10.46	24.23
0	0/60	0 (0–5.96)	0	N/A

CI = Clopper-Pearson Confidence Interval; S/CO = Signal to Cutoff ratio in concordant replicates only; CV = Coefficient of variance; p = parasites

Probit Analysis

The 50% and 95% limit of detection probabilities for *Plasmodium in vitro* transcript and *Plasmodium* parasites were determined by probit analysis, using the Gompertz model.[21] For the *Plasmodium in vitro* transcript, the 50% Limit of Detection (LOD) estimates ranged from 2.14 to 3.35 copies/mL and the 95% LOD estimates ranged from 8.47 to 11.89 copies/mL (Table 17). For the *Plasmodium* parasites, the 50% LOD estimates ranged from 0.38 to 1.65 parasites/mL and the 95% LOD estimates ranged from 2.10 to 6.82 parasites/mL (Table 18).

Table 17. Summary of Detection of *Plasmodium* IVT Panels – Gompertz Probit Analysis

***Plasmodium* species**	**Limit of 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)

Table 18. Detection of *Plasmodium* parasites – Gompertz Probit Analysis

***Plasmodium* species**	**Limit of 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)

SPECIFICITY AND SENSITIVITY OF THE PROCLEIX PLASMODIUM ASSAY IN THE PRESENCE OF DONOR AND DONATION FACTORS

When tested with the Procleix Plasmodium Assay, no interference was observed for whole blood specimens containing the following substances: albumin (60,000 mg/L), hemoglobin (5000 mg/L), bilirubin (200 mg/L), gamma globulin (60,000 mg/L), and lipids (30,000 mg/L). Specificity and sensitivity were 100%.

No interference was observed in whole blood specimens from patients with autoimmune or other diseases not caused by *Plasmodium* infection. Multiple whole blood specimens from each group of patients with the following autoimmune or other conditions were evaluated: alcoholic cirrhosis, antinuclear antibody, elevated alanine aminotransferase, multiple myeloma, multiple sclerosis, rheumatoid arthritis, rheumatoid factor, and systemic lupus erythematosus. Specificity and sensitivity were 100%.

No cross-reactivity or interference was observed in whole blood specimens contaminated with bacteria or fungi. Whole blood specimens spiked with the following microorganisms were evaluated: *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Micrococcus luteus*, *Corynebacterium diphtheriae*, *Propionibacterium acnes*, *Candida albicans*, and *Pneumocystis carinii*. Specificity and sensitivity were 100%.

No cross-reactivity or interference was observed in whole blood specimens from subjects infected with other blood-borne pathogens, or those that had received flu, HBV, or SARS-CoV-2 vaccines. Multiple whole blood specimens from each group of the following infections were evaluated: *Babesia microti; Borrelia. burgdorferi*; *Borrelia. hermsii*; *Borrelia. recurrentis;* dengue virus types 1–4, hepatitis A virus (HAV); hepatitis B virus (HBV); hepatitis C virus (HCV); human immunodeficiency virus 1 and 2 (HIV 1/2); parvovirus B-19; West Nile virus (WNV); hepatitis E virus (HEV); chikungunya (CHIKV); cytomegalovirus (CMV); human T-lymphotropic virus 1 and 2 (HTLV-1/2); Epstein-Barr virus (EBV); herpes simplex virus type 1 (HSV-1); rubella virus; Usutu virus; yellow fever virus (YFV); Zika virus; influenza virus H1N1; and influenza, HBV and SARS-CoV-2 vaccinated individuals. Specificity and sensitivity were 100%.

SPECIFICITY AND SENSITIVITY OF THE PROCLEIX PLASMODIUM ASSAY IN THE PRESENCE OF EXOGENOUS SUBSTANCES

No interference was observed in whole blood containing the following substances: acetaminophen (1324 µmol/L), acetylsalicylic acid (3620 µmol/L), ascorbic acid (342 µmol/L), atorvastatin (600 µg Eq/L), ibuprofen (2425 µmol/L), loratadine (0.78 µmol/L), Loratadine metabolite, Desloratadine (also known as Descarboethoxyloratadine) (0.97umol/L), naproxen (2170 µmol/L), and phenylephrine HCl (491 µmol/L). Specificity and sensitivity were 100%.

BIBLIOGRAPHY

1. **Rossati, A., Bargiacchi, O., Kroumova, V., Zaramella, M., Caputo, A., & Garavelli, P.L.** (2016). Climate, environment and transmission of malaria. Infezioni in Medicina, 24(2), 93–104.
2. **Bauserman, M., Conroy, A.L., North, K., Patterson, J., Bose, C., & Meshnick, S.** (2019). An overview of malaria in pregnancy. Seminars in Perinatology, 43(5), 282–290. https://doi.org/10.1053/j.semperi.2019.03.018
3. **Garraud, O.** (2006). Mechanisms of transfusion-linked parasite infection. Transfusion Clinique et Biologique, 13(5), 290–297. https://doi.org/10.1016/j.tracli.2006.11.005
4. **Gowda, D.C., & Wu, X.** (2018). Parasite recognition and signaling mechanisms in innate immune responses to malaria. Frontiers in Immunology, 9, 3006. https://doi.org/10.3389/fimmu.2018.03006
5. **O'Brien, S.F., Ward, S., Gallian, P., Fabra, C., Pillonel, J., Kitchen, A.D., Davison, K., Seed, C.R., Delage, G., Steele, W.R., & Leiby, D.A.** (2019). Malaria blood safety policy in five non-endemic countries: a retrospective comparison through the lens of the ABO risk-based decision-making framework. Blood Transfusion, 17(2), 94–102. https://doi.org/10.2450/2019.0222-18
6. **White, N.J.** (1996). The treatment of malaria. New England Journal of Medicine, 335(11), 800–806. https://doi.org/10.1056/NEJM199609123351107
7. **Milner, D.A. Jr.** (2018). Malaria pathogenesis. Cold Spring Harbor Perspectives in Medicine, 8(1), a025569. https://doi.org/10.1101/cshperspect.a025569
8. **Tatem, A.J., Jia, P., Ordanovich, D., et al.** (2017). The geography of imported malaria to non-endemic countries: a meta-analysis of nationally reported statistics. The Lancet Infectious Diseases, 17(1), 98–107. https://doi.org/10.1016/S1473-3099(16)30326-7
9. **Centers for Disease Control and Prevention.** (2023). Locally acquired cases of malaria in Florida and Texas. CDC. https://www.cdc.gov/malaria/new_info/2023/malaria_florida.html (Accessed September 27, 2023)
10. **Courtney, A.P., Boyanton, B.L. Jr., Strebeck, P.V., et al.** (2024). Locally acquired (autochthonous) mosquito-transmitted Plasmodium vivax malaria — Saline County, Arkansas, September 2023. MMWR Morbidity and Mortality Weekly Report, 73, 946–949. https://doi.org/10.15585/mmwr.mm7342a2
11. **U.S. Food and Drug Administration.** (2025). Recommendations to reduce the risk of transfusion-transmitted malaria: Draft guidance for industry. FDA. Recommendations to Reduce the Risk of Transfusion-Transmitted Malaria; Draft Guidance for Industry (fda.gov)
12. **Verra, F., Angheben, A., Martello, E., Giorli, G., Perandin, F., & Bisoffi, Z.** (2018). A systematic review of transfusion-transmitted malaria in non-endemic areas. Malaria Journal, 17(1), 36. https://doi.org/10.1186/s12936-018-2181-0
13. **Wipasa, J., Suphavilai, C., Okell, L.C., Cook, J., Corran, P.H., Thaikla, K., Liewsaree, W., Riley, E.M., & Hafalla, J.C.R.** (2010). Long-lived antibody and B cell memory responses to the human malaria parasites, Plasmodium falciparum and Plasmodium vivax. PLoS Pathogens, 6(2), e1000770. https://doi.org/10.1371/journal.ppat.1000770
14. **Leiby, D.A., Nguyen, M.L., & Notari, E.P.** (2008). Impact of donor deferrals for malaria on blood availability in the United States. Transfusion, 48(10), 2222–2228. https://doi.org/10.1111/j.1537-2995.2008.01825.x
15. **Kacian, D.L., & Fultz, T.J.** (1995). Nucleic acid sequence amplification methods. U.S. Patent, 5,399,491.
16. **Arnold, L.J., Hammond, P.W., Wiese, W.A., & Nelson, N.C.** (1989). Assay formats involving acridinium-ester-labeled DNA probes. Clinical Chemistry, 35, 1588–1594.
17. **Nelson, N.C., Cheikh, A., Matsuda, E., & Becker, M.** (1996). Simultaneous detection of multiple nucleic acid targets in a homogeneous format. Biochemistry, 35, 8429–8438. https://doi.org/10.1021/bi960085+
18. **Centers for Disease Control and Prevention.** (1987). Recommendations for prevention of HIV transmission in health-care settings. MMWR, 36(Suppl. 2S).
19. **Clinical and Laboratory Standards Institute.** (2011). Clinical Laboratory Waste Management (3rd ed.). CLSI document GP5A3E, Villanova, PA.
20. **U.S. Department of Labor, Occupational Safety and Health Administration.** (n.d.). Bloodborne Pathogens, 29 CFR Part 1910.1030.
21. **Finney, D.J., & Tattersfield, F.** (1947). Probit Analysis: A Statistical Treatment of the Sigmoid Response Curve. The University Press, Cambridge, UK.7.

2026-03

The latest package insert is available at the Grifols Technical Library website: www.techdocs.grifols.com. For a paper copy delivered free of charge please contact Grifols Technical Service.

Manufactured by:
Grifols Diagnostic Solutions Inc.
10808 Willow Court
San Diego, CA 92127 USA
+1 (800) 452-6877

U.S. License No. 2032

Grifols Customer Service

Americas
Telephone (in U.S.): +1 (888) 244-7667
Or: +1 (323) 441-7762
Email: DxSCMCustomer.Service@grifols.com

Grifols Technical Service

For technical support and service assistance, please contact Grifols Technical Service. Contact information for all regions can be obtained by visiting the Grifols Technical Library at www.techdocs.grifols.com and navigating to the **Contact Us** tab.

Package Insert Master Document Revision History

Revision	Date	Description
Revision 001	19May2025	Original Submission to FDA
Revision 002	27Jan2026	Updated Precaution section to align with new SDS including updating GHS health pictograms, H-codes, and P-codes Updated Grifols legal address to 10808 Willow Court, San Diego, CA-92127 USA Updated the copyright year to 2026 FDA feedback has been incorporated in accordance with the Procleix Babesia Assay CBE-30 submission (125673/32) filed on July 2, 2025. Applicable edits to Procleix Plasmodium Assay have been included: • Specimen collection, storage, and Handling section: In points F and G edited for clearer instructions. • Reagent Preparation: In section H – point no “5” removed “and warm the internal control reagent to room temperature” and point no “7” included before mixing step. Specimen Preparation (Manual Lysis Instruction): In section C – point no “1”, edited for clearer instructions.
Revision 003	06Mar2026	FDA recommended edits to the Intended Use • Add Procleix Panther System • Clarify organ and tissue donor samples obtained when donor's heart beating FDA recommended edits to Clinical Reproducibility, Specificity, Sensitivity • Updated % of agreement value in high negative panel member • Clarified Reproducibility performed on 2 independent lots, updated Table 1 • Updated Table 1 "n" number of samples • Add text to provide content to Table 2 Lot-to-Lot Reproducibility Study • Update Table 2 with data from 3 independent lots • Clarify 2 independent lots and 1 combined lot used in testing for Clinical Specificity, Clinical Sensitivity of Known-Positive Samples and Clinical Sensitivity of Unknown Status FDA recommended edits to Analytical Sensitivity • Clarify 2 independent lots and 1 combined lot used in testing • Replace instances of "infected RBCs" with "parasites" • Minor corrections
Revision 004	11Mar2026	FDA recommended edits to align with other Procleix assay package inserts: • Storage and Handling Instructions: Add note to not use expired reagents as Item C. and renumber following steps. • Materials Required But Not Provided: Adjust formatting (line position). Performance Characteristics: Minor correction to title of Table 1.