cobas°

cobas[®] Babesia

For in vitro diagnostic use

cobas [®] Babesia – 480	P/N: 09040692190
cobas [®] Babesia Control Kit	P/N: 09040706190
cobas [®] NHP Negative Control Kit	P/N: 09051554190
cobas [®] omni MGP Reagent	P/N: 06997546190
cobas [®] omni Specimen Diluent	P/N: 06997511190
cobas [®] omni Lysis Reagent	P/N: 06997538190
cobas [®] omni Wash Reagent	P/N: 06997503190

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Intended use

The **cobas**[®] Babesia test for use on the **cobas**[®] 5800/6800/8800 systems is a qualitative in vitro nucleic acid screening test for the direct detection of *Babesia* (*B. microti, B, duncani, B. divergens, and B. venatorum*) DNA and RNA in whole blood samples from individual human donors, including donors of whole blood and blood components, and other living donors. This test is also intended for use to screen organ and tissue donors when donor samples are obtained while the donor's heart is still beating. Whole blood samples from all donors may be screened as individual samples or in pools comprised of aliquots of individual samples.

This test may also be used as an aid in diagnosis of *Babesia* in samples collected from individuals suspected of Babesiosis by their healthcare provider.

When used as an aid in diagnosis, whole blood samples should only be tested individually.

This test is not intended for use on samples of cord blood.

This test is not intended for use on cadaveric blood specimens.

Summary and explanation of the test

Background

Babesia is a protozoan parasite that infects red blood cells (RBCs) and may cause a disease known as babesiosis. Babesiosis may be treated with antibiotics and anti-parasitics. No vaccine is available.¹

Most cases of babesiosis are asymptomatic, and symptoms, if they occur may include flu-like symptoms (fever, chills, sweats, headache, myalgia, arthralgia) and hemolytic anemia or thrombocytopenia. Babesiosis is potentially life threatening in patients with asplenia, weakened immune systems (e.g., due to cancer, lymphoma, or Acquired Immunodeficiency Syndrome [AIDS]), comorbidities, such as liver or kidney disease, or who are over the age of 50. In these immunocompromised patients, babesiosis can lead to multi-organ dysfunction, disseminated intravascular coagulation, and death can occur.¹

More than a hundred species of *Babesia* have been identified. Four *Babesia* species are known to cause human disease: *B. microti, B. duncani, B. divergens, and B. venatorum.* The bite of a tick (*Ixodes* spp.) is the usual means through which *Babesia* is transmitted, but *Babesia* may also be transmitted by transfusion or from mother to child during pregnancy or delivery. The *Ixodes* spp. ticks that carry *Babesia* have a global distribution.² The vast majority of transfusion-associated cases, as well as clinical cases, in the United States (US) are due to *Babesia microti*, and approximately 2% of reported cases are due to *Babesia duncani*.³ *Ixodes ricinus* is the predominant species in Europe, while *I. persulcataus* and *I. ovatus* are the predominant *Ixodes* tick species in Asia.² To date, transfusion-transmitted babesiosis cases are exclusive to the United States and Canada.⁴ *Babesia* is one of the most-commonly-transmitted transfusion-associated infection in the US.^{5,6} Human Babesia infections have been reported in Australia,¹ Austria,⁷ Belgium,⁸ Bolivia,⁹ China,¹⁰⁻¹² Czech Republic,¹ Egypt,¹ Equitorial Guinea,¹ Finland,¹ France,¹³ Germany, ¹ Italy,¹ Mexico,¹⁴ Montenegro,¹ Norway,¹⁵ Poland,¹ Portugal,¹ South Africa,¹ Spain,¹⁶ and Switzerland.¹

Babesiosis can be transmitted in areas that are not considered at high risk for transmission of the parasite because blood donors may travel to endemic areas. Blood donors may be unaware that they carry the parasite, may have asymptomatic parasitemia, and may remain infectious for a year or more. Further, the parasite is viable in blood products. The majority of transfusion-associated cases are associated with erythrocytes (including leukoreduced or irradiated units), with a

handful of cases due to whole blood-derived platelet transfusion. Prospective testing of 89,153 blood donations in endemic areas of the US yielded a 0.38% positive rate for *Babesia*.¹⁷

Rationale for NAT testing

Babesia is usually tick-borne but is also transmissible by transfusion.¹⁷ Clinicians may miss the diagnosis of transfusion-associated babesiosis since the clinical presentation is non-specific, and the wide distribution of blood products means that cases can occur outside of areas of high *Babesia* prevalence and outside of the peak summer months of tick-borne disease.

Like other infectious diseases for which blood donations are screened, blood donations must be screened with a sensitive assay to detect *Babesia* so that infected units may be interdicted and discarded. **cobas**[®] Babesia provides a sensitive and specific method to detect *Babesia* and thereby provide heightened protection from transfusion-transmitted *Babesia* infection for recipients of donated blood components or products and will further improve the safety of the blood supply.

Explanation of the test

cobas[°] Babesia is a qualitative PCR test for the detection of *Babesia* DNA and RNA that is run on the **cobas**[°] 5800/6800/8800 system. The **cobas**[°] Babesia test detects four species of Babesia; *Babesia microti* (most prevalent in the US), *Babesia duncani*, *Babesia divergens* (most prevalent in Europe) and *Babesia venatorum* in a single test of an individual or pooled donation. An individual sample may be tested as an aid in diagnosis.

Principles of the procedure

cobas[®] Babesia is based on fully automated sample preparation (nucleic acid extraction and purification) followed by PCR amplification and detection.

The **cobas**[°] 5800 system consists of a single integrated instrument. The **cobas**[°] 6800/8800 systems consist of the sample supply module, the transfer module, the processing module, and the analytic module. Automated data management is performed by the **cobas**[°] 5800 or 6800/8800 software which assigns test results for all tests as non-reactive, reactive, or invalid. When using the **cobas**[°] 5800/6800/8800 systems, results can be reviewed directly on the system screen, and printed as a report.

For donor screening, samples should be tested as individual samples or, optionally, can be tested in pools comprised of aliquots of individual samples. The **cobas**^{*} **Synergy** software with the Hamilton MICROLAB^{*} STAR/STARlet IVD may optionally be used in a pre-analytical step if pooling is to be performed.

Whole blood may be collected in the designated Roche Whole Blood Collection Tube. Alternatively, whole blood collected in EDTA may be transferred manually to the Roche Whole Blood Collection Tube. The whole blood collection tube includes a proprietary additive to lyse cells within the whole blood, releasing and preserving nucleic acids. The tube containing the lysed whole blood is the primary tube on the analyzer, on which the universal sample preparation steps will be performed by the **cobas**^{*} 5800/6800/8800 systems.

Armored RNA internal control (IC) molecules are added during universal sample preparation and serve as a full process control from sample preparation through amplification/detection. The IC monitors for interference that could cause false negative results. Potentially affected samples are invalidated.

The test also utilizes two external controls: a positive and a negative control. In addition to the sample lysis and release of nucleic acid which occurs in the primary tube, nucleic acids are also released by addition of proteinase and lysis reagent to the sample and controls. The released nucleic acids bind to the silica surface of the magnetic glass particles, which are

added to the sample. Unbound substances and impurities, such as denatured proteins, cellular debris, and potential PCR inhibitors (such as hemoglobin) are removed with subsequent wash reagent steps and purified nucleic acids are eluted from the glass particles with elution buffer at elevated temperature.

Selective amplification of target nucleic acid from the donor sample is achieved by the use of specific forward and reverse primers which are selected from highly conserved regions of the target nucleic acid. A thermostable DNA polymerase enzyme is used for both reverse-transcription and amplification. The master mix includes deoxyuridine triphosphate (dUTP), instead of deoxythimidine triphosphate (dTTP), which is incorporated into the newly synthesized DNA (amplicon).¹⁸⁻²⁰ Any contaminating amplicons from previous PCR runs are destroyed by the AmpErase enzyme [uracil-N-glycosylase], which is included in the PCR mix, when heated in the first thermal cycling step. However, newly formed amplicons are not destroyed since the AmpErase enzyme is inactivated once exposed to temperatures above 55°C.

The **cobas**[•] Babesia master mix contains detection probes which are specific for *Babesia* and IC nucleic acid. The specific *Babesia* and IC detection probes are each labeled with one of two unique fluorescent dyes which acts as a reporter. Each probe also has a second dye which acts as a quencher. The two reporter dyes are measured at defined wavelengths, thus permitting detection and discrimination of the amplified *Babesia* target and the IC.^{21,22} When not bound to the target sequence, the fluorescent signal of the intact probes is suppressed by the quencher dye. During the PCR amplification step, hybridization of the probes to the specific single-stranded DNA template results in cleavage by the 5' to 3' nuclease activity of the DNA polymerase resulting in separation of the reporter and quencher dyes and the generation of a fluorescent signal. With each PCR cycle, increasing amounts of cleaved probes are generated and the cumulative signal of the reporter dye is concomitantly increased. Since the two specific reporter dyes are measured at defined wavelengths, simultaneous detection and discrimination of the amplified *Babesia* target and the IC are possible.

Reagents and materials

cobas[®] Babesia reagents and controls

All unopened reagents and controls shall be stored as recommended in Table 1 to Table 4.

Table 1 cobas[®] Babesia test

Store at 2-8°C 480 test cassette (P/N 09040692190)

Kit components	Reagent ingredients	Quantity per kit
Proteinase Solution (PASE)	Tris buffer, < 0.05% EDTA, calcium chloride, calcium acetate, 8% (w/v) proteinase, glycerol	38 mL
	EUH208: Contains Subtilisin from Bacillus subtilis. May produce an allergic reaction.	
Internal Control (IC)	Tris buffer, < 0.05% EDTA, < 0.001% internal control armored RNA construct (non-infectious RNA encapsulated in MS2 bacteriophage), < 0.002% Poly rA RNA (synthetic), < 0.1% sodium azide	38 mL
Elution Buffer (EB)	Tris buffer, 0.2% methyl-4 hydroxybenzoate	38 mL
Master Mix Reagent 1 (MMX-R1)	Manganese acetate, potassium hydroxide, < 0.1% sodium azide	14.5 mL
Babesia Master Mix Reagent 2 (MMX-R2)	Tricine buffer, potassium acetate, glycerol, 18% dimethyl sulfoxide, < 0.1% Tween 20, EDTA, < 0.14% dATP, dGTP, dCTP, dUTPs, < 0.01% upstream and downstream <i>Babesia</i> and internal control primers, < 0.01% Fluorescent-labeled <i>Babesia</i> probes, < 0.01% fluorescent-labeled internal control probe, < 0.01% oligonucleotide aptamer, < 0.01% Z05D DNA polymerase, < 0.01% AmpErase (uracil-N-glycosylase) enzyme (microbial), < 0.1% sodium azide	17.5 mL

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Table 2 cobas[®] Babesia Control Kit

Store at 2-8°C (P/N 09040706190)

Kit components	Reagent ingredients	Quantity per kit	Safety symbol and warning*
Babesia Positive Control (Babesia (+) C)	< 0.001% Synthetic (armored) <i>Babesia</i> RNA encapsulated in MS2 bacteriophage coat protein, Normal human plasma, <i>Babesia</i> DNA and RNA not detectable by PCR methods. 0.1% ProClin [®] 300 preservative**	10.4 mL (16 x 0.65 mL)	 WARNING H317: May cause an allergic skin reaction. H412: Harmful to aquatic life with long lasting effects. P261: Avoid breathing dust/fume/gas/mist/vapours/spray. P273: Avoid release to the environment. P280: Wear protective gloves. P333 + P313: If skin irritation or rash occurs: Get medical advice/attention. P362 + P364: Take off contaminated clothing and wash it before reuse. P501: Dispose of contents/ container to an approved waste disposal plant. 55965-84-9 reaction mass of 5-chloro-2-methyl-2H-isothiazol-3-one and 2-methyl-2H-isothiazol-3-one (3:1)

* Product safety labeling primarily follows EU GHS guidance

**Hazardous substance

Table 3 cobas[®] NHP Negative Control Kit

Store at 2-8°C (P/N 0<u>9051554190)</u>

Kit components	Reagent ingredients	Quantity per kit	Safety symbol and warning*
Normal Human Plasma Negative Control (NHP-NC)	Normal human plasma, <i>Babesia</i> DNA and RNA not detectable by PCR methods. < 0.1% ProClin [®] 300 preservative**	16 mL (16 x 1mL)	WARNING H317: May cause an allergic skin reaction. P261: Avoid breathing dust/fume/gas/mist/ vapours/spray. P272: Contaminated work clothing should not be allowed out of the workplace. P280: Wear protective gloves. P333 + P313: If skin irritation or rash occurs: Get medical advice/attention. P362 + P364: Take off contaminated clothing before reuse. P501: Dispose of contents/ container to an approved waste disposal plant. 55965-84-9 reaction mass of 5-chloro-2- methyl-2H-isothiazol-3-one and 2-

* Product safety labeling primarily follows EU GHS guidance

**Hazardous substance

cobas[®] omni reagents for sample preparation

 Table 4 cobas[®] omni reagents for sample preparation*

Reagents	Reagent ingredients	Quantity per kit	Safety symbol and warning**
cobas[®] omni MGP Reagent (MGP) Store at 2–8°C (P/N 06997546190)	Magnetic glass particles, Tris buffer, 0.1% methyl-4 hydroxybenzoate, < 0.1% sodium azide	480 tests	Not applicable
cobas[®] omni Specimen Diluent (SPEC DIL) Store at 2–8°C (P/N 06997511190)	Tris buffer, 0.1% methyl-4 hydroxybenzoate, < 0.1% sodium azide	4 x 875 mL	Not applicable
cobas [®] omni Lysis Reagent (LYS) Store at 2–8°C (P/N 06997538190)	42.56% (w/w) guanidine thiocyanate***, 5% (w/v) polydocanol***, 2% (w/v) dithiothreitol***, dihydro sodium citrate	4 x 875 mL	 DANGER H302 + H332: Harmful if swallowed or if inhaled. H314: Causes severe skin burns and eye damage. H411: Toxic to aquatic life with long lasting effects. EUH032: Contact with acids liberates very toxic gas. P273: Avoid release to the environment. P280: Wear protective gloves/protective clothing/eye protection/face protection. P303 + P361 + P353: IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water. P304 + P340 + P310: IF INHALED: Remove person to fresh air and keep comfortable for breathing. Call a POISON CENTER/doctor. P305 + P351 + P338 + P310: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/doctor. P391: Collect spillage. S93-84-0 guanidinium thiocyanate 9002-92-0 Polidocanol 3483-12-3 (R*,R*)-1.4-dimercaptobutane-2.3-diol
cobas [®] omni Wash Reagent (WASH) Store at 15–30°C (P/N 06997503190)	Sodium citrate dihydrate, 0.1% methyl-4 hydroxybenzoate	4.2 L	Not applicable

* These reagents are not included in the **cobas*** Babesia test kit. See listing of additional materials required (Table 8 and Table 9).

** Product safety labeling primarily follows EU GHS guidance.

***Hazardous substance

Reagent storage and handling requirements

Opened reagents shall be stored and will be handled as specified in Table 5, Table 6, and Table 7.

When reagents are not loaded on the **cobas**[®] 5800/6800/8800 systems, store them at the corresponding temperature specified in Table 5.

Reagent	Storage temperature
cobas [®] Babesia - 480	2-8°C
cobas[®] Babesia Control Kit	2-8°C
cobas [®] NHP Negative Control Kit	2-8°C
cobas [®] omni Lysis Reagent	2-8°C
cobas [®] omni MGP Reagent	2-8°C
cobas [®] omni Specimen Diluent	2-8°C
cobas [®] omni Wash Reagent	15–30°C

 Table 5
 Reagent storage (when reagent is not on the system)

Reagent handling requirements for the cobas® 5800 system

Reagents loaded onto the **cobas**[®] 5800 system are stored at appropriate temperatures and their expiration is monitored by the system. The system allows reagents to be used only if all of the conditions shown in Table 6 are met. The system automatically prevents use of expired reagents. Table 6 allows the user to understand the reagent handling conditions enforced by the **cobas**[®] 5800 system.

Reagent	Kit expiration date	Open-kit stability	Number of runs for which this kit can be used	On-board stability (cumulative time on board outside refrigerator)
cobas [®] Babesia – 480	Date not passed	60 days from first usage	Max 40 runs	Max 36 days**
cobas[®] Babesia Control Kit	Date not passed	Not applicable ^a	Not applicable	Max 36 days**
cobas [®] NHP Negative Control Kit	Date not passed	Not applicable ^a	Not applicable	Max 36 days**
cobas [®] omni Lysis Reagent	Date not passed	30 days since loading*	Not applicable	Not applicable
cobas [®] omni MGP Reagent	Date not passed	30 days since loading*	Not applicable	Not applicable
cobas [®] omni Specimen Diluent	Date not passed	30 days since loading*	Not applicable	Not applicable
cobas [®] omni Wash Reagent	Date not passed	30 days since loading*	Not applicable	Not applicable

 Table 6
 Reagent expiry conditions enforced by the cobas[®] 5800 system

^a Single use reagents

* Time is measured from the first time that reagent is loaded onto the **cobas*** 6800/8800 Systems.

Reagent handling requirements for the cobas[®] 6800/8800 systems

Reagents loaded onto the **cobas**[®] 6800/8800 systems are stored at appropriate temperatures and their expiration is monitored by the system. The system allows reagents to be used only if all of the conditions shown in Table 7 are met. The system automatically prevents use of expired reagents. Table 7 allows the user to understand the reagent handling conditions enforced by the **cobas**[®] 6800/8800 systems.

Reagent	Kit expiration date	Open-kit stability	Number of runs for which this kit can be used	On-board stability (cumulative time on board outside refrigerator)
cobas [®] Babesia – 480	Date not passed	60 days from first usage	Max 20 runs	Max 20 hours
cobas [®] Babesia Control Kit	Date not passed	Not applicable ^a	Not applicable	Max 10 hours
cobas [®] NHP Negative Control Kit	Date not passed	Not applicable ^a	Not applicable	Max 10 hours
cobas [®] omni Lysis Reagent	Date not passed	30 days since loading*	Not applicable	Not applicable
cobas [®] omni MGP Reagent	Date not passed	30 days since loading*	Not applicable	Not applicable
cobas [®] omni Specimen Diluent	Date not passed	30 days since loading*	Not applicable	Not applicable
cobas [®] omni Wash Reagent	Date not passed	30 days since loading*	Not applicable	Not applicable

^a Single use reagents

* Time is measured from the first time that reagent is loaded onto the **cobas*** 6800/8800 systems.

Additional materials required for the cobas[®] 5800 system

 Table 8
 Material and consumables for use on cobas[®] 5800 system

Material	P/N
Roche Whole Blood Collection Tube	08827907001
cobas [®] omni Processing Plate 24	08413975001
cobas [®] omni Amplification Plate 24	08499853001
cobas [®] omni Liquid Waste Plate 24	08413983001
CORE Tips with Filter, 1 mL	04639642001
CORE Tips with Filter, 300 µL	07345607001
cobas [®] omni Liquid Waste Container	07094388001
cobas [®] omni Lysis Reagent	06997538190
cobas [®] omni MGP Reagent	06997546190
cobas [®] omni Specimen Diluent	06997511190
cobas [®] omni Wash Reagent	06997503190
Solid Waste Bag	07435967001
or	or
Solid Waste Bag with Insert	08030073001

Additional materials required for the cobas[®] 6800/8800 systems

Table 9Material and consumables for use on **cobas**[®] 6800/8800 systems

Material	P/N
Roche Whole Blood Collection Tube	08827907001
cobas [®] omni Processing Plate	05534917001
cobas [®] omni Amplification Plate	05534941001
cobas [®] omni Pipette Tips	05534925001
cobas [®] omni Liquid Waste Container	07094388001
cobas [®] omni Lysis Reagent	06997538190
cobas® omni MGP Reagent	06997546190
cobas [®] omni Specimen Diluent	06997511190
cobas® omni Wash Reagent	06997503190
Solid Waste Bag	07435967001
or	or
Solid Waste Bag With Insert	08030073001
Solid Waste Container	07094361001
or	or
Solid Waste Bag with Insert	08030073001
09355944001-02EN	

Instrumentation and software required

The **cobas**[®] Babesia analysis package for the **cobas**[®] 5800 system shall be installed on the **cobas**[®] 5800 system. The x800 Data Manager software for the **cobas**[®] 5800 system will be provided with the system. The **cobas**[®] **Synergy** software shall be installed, if applicable.

The **cobas**[®] 6800/8800 software and **cobas**[®] Babesia analysis package shall be installed on the instrument(s). The Instrument Gateway (IG) server will be provided with the system. The **cobas**[®] **Synergy** software shall be installed, if applicable.

Table 10 Instrumentation

Equipment	P/N
cobas [®] 5800 system	08707464001
cobas [®] 6800 system (Option Moveable)	05524245001 and 06379672001
cobas [®] 6800 system (Fix)	05524245001 and 06379664001
cobas [®] 8800 system	05412722001
Sample Supply Module	06301037001
Option for pipetting and pooling	P/N
cobas[®] Synergy Software electronic license (cobas [®] 5800 system only) (Optional)	09311246001
cobas [®] Synergy Software electronic license (cobas [®] 6800/8800 systems) (Optional)	09311238001
Hamilton MICROLAB® STAR IVD	04640535001
Hamilton MICROLAB [®] STAR/let IVD	04872649001

Refer to the **cobas**^{*} 5800 system User Assistance or the **cobas**^{*} 6800/8800 systems User Assistance for additional information. Refer to the **cobas**^{*} Synergy software User Assistance, for additional information for primary and secondary sample tubes accepted on the instruments.

Note: Contact your local Roche representative for a detailed order list for sample racks, racks for clotted tips and rack trays accepted on the instruments.

Precautions and handling requirements

Warnings and precautions

As with any test procedure, good laboratory practice is essential to the proper performance of this assay. Due to the high sensitivity of this test, care should be taken to keep reagents and amplification mixtures free of contamination.

- For in vitro diagnostic use only.
- All samples should be handled as if infectious, using good laboratory procedures as outlined in Biosafety in Microbiological and Biomedical Laboratories and in the CLSI Document M29-A4.^{23,24} Only personnel proficient in handling infectious materials and the use of **cobas**^{*} Babesia and **cobas**^{*} 5800/6800/8800 systems and (optionally) the Hamilton Microlab^{*} STAR/STARlet IVD with the **cobas**^{*} **Synergy** software should perform this procedure.
- All human-sourced materials should be considered potentially infectious and should be handled with universal precautions. If spillage occurs, immediately disinfect with a freshly prepared solution of 0.6% sodium hypochlorite in distilled or deionized water or follow appropriate site procedures.
- **cobas**[®] Babesia Control Kit and **cobas**[®] NHP Negative Control Kit contain plasma derived from human blood. Testing of normal human plasma by PCR methods also showed no detectable *Babesia* DNA and RNA. No known test method can offer complete assurance that products derived from human blood will not transmit infectious agents.
- The additive in the Roche Whole Blood Collection Tube contains guanidine hydrochloride. Do not allow direct contact between guanidine hydrochloride and sodium hypochlorite (bleach) or other highly reactive reagents such as acids or bases. These mixtures can release a noxious gas. If additive containing guanidine hydrochloride is spilled, clean with suitable laboratory detergent and water. If the spilled additive contains potentially infectious agents, FIRST clean the affected area with laboratory detergent and water, and then with 0.6% sodium hypochlorite.
- The use of sterile disposable pipettes and nuclease-free pipette tips is recommended. Use only supplied or specified required consumables to ensure optimal test performance.
- Closely follow procedures and guidelines provided to ensure that the test is performed correctly. Any deviation from the procedures and guidelines may affect optimal test performance.
- False positive results may occur if carryover of samples is not adequately controlled during sample handling and processing.
- Inform your local competent authority and manufacturer about any serious incidents which may occur when using this assay.

Reagent handling

- Handle all reagents, controls, and samples according to good laboratory practice in order to prevent carryover of samples or controls.
- Before use, visually inspect each reagent cassette, diluent, lysis reagent, and wash reagent to ensure that there are no signs of leakage. If there is any evidence of leakage, do not use that material for testing.
- **cobas**[®] **omni** Lysis Reagent contains guanidine thiocyanate, a potentially hazardous chemical. Avoid contact of reagents with the skin, eyes, or mucous membranes. If contact does occur, immediately wash with generous amounts of water; otherwise, burns can occur.
- The additive in the Roche Whole Blood Collection Tube contains guanidine hydrochloride, a potentially hazardous chemical. Avoid contact of this additive with the skin, eyes, or mucous membranes. If contact does occur, immediately wash with generous amounts of water; otherwise, burns can occur.
- **cobas**[®] Babesia kits, **cobas**[®] **omni** MGP Reagent, and **cobas**[®] **omni** Specimen Diluent contain sodium azide as a preservative. Avoid contact of reagents with the skin, eyes, or mucous membranes. If contact does occur, immediately wash with generous amounts of water; otherwise, burns can occur. If these reagents are spilled, dilute with water before wiping dry.
- Do not allow **cobas**[®] **omni** Lysis Reagent, which contains guanidine thiocyanate, to contact sodium hypochlorite (bleach) solution. This mixture can produce a highly toxic gas.
- Safety Data Sheets (SDS) are available on request from your local Roche representative.
- Dispose of all materials that have come in contact with samples and reagents in accordance with country, state, and local regulations.

Good laboratory practice

- Do not pipette by mouth.
- Do not eat, drink, or smoke in designated work areas.
- Wear laboratory gloves, laboratory coats, and eye protection when handling samples and reagents. Gloves must be changed between handling samples and **cobas**[®] Babesia kits and **cobas**[®] **omni** reagents to prevent contamination. Avoid contaminating gloves when handling samples and controls. Change gloves if contaminated by sample, control, or reagents.
- Wash hands thoroughly after handling samples and kit reagents, and after removing the gloves.
- Thoroughly clean and disinfect all laboratory work surfaces with a freshly prepared solution of 0.6% sodium hypochlorite in distilled or deionized water. Follow by wiping the surface with 70% ethanol.
- If spills occur on the **cobas**[®] 6800/8800 instruments, follow the instructions in the **cobas**[®] 6800/8800 systems User Assistance to properly clean and decontaminate the surface of instrument(s).
- If spills occur on the **cobas**[®] 5800 instrument, follow the instructions in the **cobas**[®] 5800 system User Assistance to properly clean and decontaminate the surfaces of the instrument(s).

Sample collection, transport and storage and pooling

Note: Handle all samples and controls as if they are capable of transmitting infectious agents. Store all donor samples at specified temperatures. Sample stability is affected by elevated temperatures.

Centrifuge samples at 1000 rcf (relative centrifugal force) for 2 minutes.

Living donor and diagnostic samples

- Whole blood collected in the Roche Whole Blood Collection Tube may be used with **cobas**[®] Babesia. Follow the sample collection tube manufacturer instructions for handling and centrifugation.
- Whole blood collected in the Roche Whole Blood Collection Tube may be stored for up to 60 days with the following conditions:
 - For storage above 8°C, samples may be stored for 72 hours at up to 25°C, and up to 30°C for 24 hours during the 72 hours.

Other than noted above, samples are stored at 2-8°C. In addition the Roche Whole Blood Collection Tube may be stored within the first 12 days after collection for up to 12 months at -20°C (\pm 5°C) with three freeze/thaw cycles. Refer to Figure 1.

Figure 1 Sample storage conditions for samples collected in the Roche Whole Blood Collection Tube



- If the Roche Whole Blood Collection Tube of a sample is not available for testing (e.g., if the tube is damaged or if whole blood was not collected using the Roche Whole Blood Collection Tube), whole blood collected in EDTA may be used with **cobas**[®] Babesia.
- Before testing with **cobas**[®] Babesia 1.1 mL of EDTA whole blood must be **manually transferred** to the Roche Whole Blood Collection Tube.
- Whole blood collected in EDTA may be stored for up to 12 days prior to dilution in the Roche Whole Blood Collection Tube with the following conditions:
 - For storage above 8°C, samples may be stored for 72 hours at up to 25°C, and up to 30°C for 24 hours during the 72 hours.
 - Other than noted above, samples are stored at 2-8°C. Refer to Figure 2.
- After dilution in the whole blood collection tube the tube may be stored for up to 36 hours at 2-25°C.

Figure 2 Sample storage conditions for samples collected in EDTA



• If samples are to be shipped, they should be packaged and labeled in compliance with applicable country and/or international regulations covering the transport of samples and etiologic agents.

Instructions for use

Automated sample pipetting and pooling (optional)

cobas[®] **Synergy** software with the Hamilton MICROLAB[®] STAR/STARlet can be used as an optional component of the **cobas**[®] 5800/6800/8800 systems for automated pipetting and pooling of aliquots of multiple primary samples into one pooled sample. Refer to the **cobas**[®] **Synergy** software User Assistance for more information.

Procedural notes

- Do not use **cobas**[®] Babesia reagents, **cobas**[®] Babesia Control Kit, **cobas**[®] NHP Negative Control Kit or **cobas**[®] **omni** reagents after their expiry dates.
- Do not reuse consumables. They are for one-time use only.
- Refer to the **cobas**^{*} 5800 system User Assistance for proper maintenance of instruments.
- Refer to the **cobas**[®] 6800/8800 systems User Assistance or to the **cobas**[®] **Synergy** software User Assistance as applicable for details on optional pooling procedures.
- Invalid results may be influenced by a number of contributing factors including, but not limited to, sample characteristics, interfering substances and pre-analytical workflows.

Running cobas[®] Babesia on the cobas[®] 5800 system

The test procedure is described in detail in the **cobas**[®] 5800 system User Assistance or refer to the **cobas**[®] **Synergy** software User Assistance as applicable for details on optional pooling procedures.

Figure 3 cobas[®] Babesia test procedure

1	Pipetting and pooling
2	Loading sample racks onto the systemLoad sample racks onto the systemOrder tests manually if no LIS orders are available
3	Refill reagent and consumables as prompted by the system Load test specific reagent cassette(s) Load control mini racks Load processing tips Load elution tips Load processing plates Load liquid waste plates Load amplification plates Load MGP cassette Refill specimen diluent Refill yash reagent
4	Start the run by choosing the Start button manually on the user interface. All subsequent runs will start automatically if not manually postponed.
5	Review results
6	Remove any sample tubes Clean up the instrument • Empty reagent cassettes • Empty Control mini racks • Empty amplification plate drawer • Empty liquid waste • Empty solid waste

Running cobas[®] Babesia on the cobas[®] 6800/8800 systems

The test procedure is described in detail in the **cobas**[®] 6800/8800 **s**ystems. User Assistance or refer to the **cobas**[®] **Synergy** software User Assistance as applicable for details on optional pooling procedures.

Figure 4 below summarizes the procedure.

Figure 4 cobas® Babesia test procedure



Results

The **cobas**[®] 5800 and **cobas**[®] 6800/8800 systems automatically detect *Babesia* nucleic acid simultaneously for the samples and controls.

Quality control and validity of results on the cobas® 5800 system

The **cobas**[®] 5800 system will be delivered with the default setting of controls (positive and negative) scheduled with every run, but can be configured to a less frequent control schedule, by a Roche service engineer or by contacting Roche customer technical support, based on laboratory procedures and/or local regulations.

- In the **cobas**[®] 5800 software and/or report, check for flags and their associated results to ensure control validity.
- The associated samples are valid if no flags appear for all controls.

Invalidation of results is performed automatically by the **cobas**[®] 5800 system based on negative and positive control failures.

Control results on the cobas[®] 5800 system

The results of the controls are shown in the **cobas**[•] 5800 software in the "Controls" app.

- Controls are marked with "Valid" in the column "Control result" if all Targets of the control are reported valid. Controls are marked with 'Invalid' in the column "Control result" if all or one Target of the control are reported invalid.
- Controls marked with 'Invalid' show a flag in the "Flags" column. More information on why the control is reported invalid including flag information will be shown in the detail view.

If the positive control is invalid, repeat testing of the positive controls and all associated samples. If the negative control is invalid, repeat testing of all controls and all associated samples.

Negative Control	Flag	Result	Interpretation
(-) C	A flag is shown	Invalid	The entire batch is assigned invalid if the result for the (-) C is invalid.
Positive Control	Flag	Result	Interpretation
Babesia (+) C	A flag is shown	Invalid	The entire batch is assigned invalid if the result for the Babesia (+) C is invalid.

 Table 11 Control flags for negative and positive controls on the cobas[®] 5800 system

If one of the controls is invalid, repeat testing of the respective control(s) and all associated samples.

Quality control and validity of results on the cobas[®] 6800/8800 systems

- One negative control [(–) C] and one positive control [Babesia (+) C] are processed with each batch.
- In the **cobas**^{*} 6800/8800 software and/or report, check for flags and their associated results to ensure the batch validity.
- The batch is valid if no flags appear for both controls.

Invalidation of results is performed automatically by the **cobas**[®] 6800/8800 software based on negative and positive control failures.

Control results on the cobas[®] 6800/8800 systems

Negative Control	Flag	Result	Interpretation
(–) C	Q02	Invalid	The entire batch is assigned invalid if the result for the (-) C is invalid.
Positive Control	Flag	Result	Interpretation
Babesia (+) C	Q02	Invalid	The entire batch is assigned invalid if the result for the Babesia (+) C is invalid.

Table 12 Control flags for negative and positive controls

If the batch is invalid, repeat testing of the entire batch including samples and controls.

Interpretation of results

For a valid batch, check each individual sample for flags in the **cobas**[®] 5800/6800/8800 software and/or report. The result interpretation should be as follows:

- A valid batch may include both valid and invalid donor sample results dependent on flags obtained for the individual samples.
- Sample results are valid only if the respective positive control and the negative control of the corresponding batch are valid.

Two parameters are measured simultaneously for each sample: one for *Babesia* and the internal control. Final sample results for **cobas**[®] Babesia are reported by the software. In addition to the overall results (**cobas**[®] 6800/8800 only), individual target result will be displayed in the **cobas**[®] 5800/6800/8800 software and should be interpreted as follows:

Table 13	Target results for	or individual targe	t result interpretation
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Target results	Interpretation
Babesia Non-Reactive	No target signal detected for Babesia and IC signal detected.
Babesia Reactive	Target signal detected for Babesia and IC signal may be or may not be detected.
Invalid	Target and/or internal control are not meeting validity criteria.

If using the **cobas**[®] **Synergy** software, review of the final result calculation should be performed through the **cobas**[®] **Synergy** software.

Additional information for interpretation of results on the cobas® 5800 system

The results of the samples are shown in the **cobas**[°] 5800 system. It is recommended to review results in in the **cobas**[°] **Synergy** software.

- Samples associated with a valid control batch (as defined by your system control configuration) are shown as 'Valid' in the "Control result" column. Samples associated with a failed control batch are shown as 'Invalid' in the "Control result" column.
- If the associated controls of a sample result are invalid, a specific flag will be added to the sample result as follows:
 - Q05D: Result validation failure because of an invalid positive control
 - Q06D: Result validation failure because of an invalid negative control
- The values in "Results" column for individual sample target result should be interpreted as shown in Table 13 above.
 - The **cobas**[®] 5800 system will display individual target results. The overall result will be shown only in the result view of the **cobas**[®] **Synergy** software.
 - For more detailed information on sample results and flags refer to the **cobas**[®] 5800 system User Assistance.

Interpretation of results on the cobas[®] 6800/8800 systems

For a valid batch, check each individual sample for flags in the **cobas**[®] 6800/8800 systems software and/or report. The result interpretation should be as follows:

- Samples are marked with "Yes" in the column 'Valid' if all requested Target Results reported valid results. Samples marked with "No" in the column 'Valid' may require additional interpretation and action.
- The values for individual sample target result should be interpreted as shown in Table 13 above
- For more detailed information on sample results and flags refer to the **cobas**[®] 6800/8800 system User Assistance.

Repeat testing of individual sample(s)

Sample tubes with a final result of Invalid for the target require repeat testing.

Procedural limitations

- cobas[®] Babesia has been evaluated only for use in combination with the cobas[®] Babesia Control Kit, cobas[®] NHP Negative Control Kit, cobas[®] omni MGP Reagent, cobas[®] omni Lysis Reagent, cobas[®] omni Specimen Diluent, and cobas[®] omni Wash Reagent for use on the cobas[®] 6800/8800 systems.
- Reliable results depend on proper sample collection, storage and handling procedures.
- Detection of *Babesia* DNA and RNA is dependent on the number of *Babesia* infected red blood cells present in the sample and may be affected by sample collection, storage and handling, patient factors (i.e., age, presence of symptoms), and/or stage of infection and pool size.
- Rare mutations within the highly conserved regions of a *Babesia* genome covered by **cobas**[•] Babesia, may affect primers and/or probe binding resulting in the failure to detect presence of the *Babesia* organism.
- Due to inherent differences between technologies, it is recommended that, prior to switching from one technology to the next, users perform method correlation studies in their laboratory to qualify technology differences. Users should follow their own specific policies/procedures.
- Performance has not been established for cadaveric blood specimens.

System equivalency/system comparison

System equivalency of the **cobas**[°] 5800 system with the **cobas**[°] 6800/8800 systems was demonstrated via equivalency studies. The results presented in these Instructions for Use are based on equivalent performance for all systems.

Non-clinical performance evaluation

Key performance characteristics

Limit of Detection (LoD)

The limit of detection (LoD) of **cobas**[®] Babesia was determined using the following *Babesia* infected red blood cells (iRBC) diluted in human whole blood.

- The *B. microti* infected RBC were obtained from hamster infected with *B. microti* (ATCC, *Babesia* microti Gray, Strain 30221).
- The *B. duncani* infected RBC were obtained from hamster infected with *B. duncani* (ATCC, Strain PRA 302)
- The *B. divergens* infected RBC were obtained from fresh infected sheep blood with *B. divergens* (Oniris, Strain B128)
- The *B. venatorum* infected RBC were obtained from fresh infected sheep blood with *B. venatorum* (Oniris, Strain C201)

The stock titer was provided by the vendor and it was assigned as percentage parasitemia (*Babesia* infected red blood cells per mL, Giemsa stain).

For each of the infected red blood cells stocks, 3 independent dilution series were prepared in human whole blood. Before testing with **cobas**[®] Babesia each panel member was diluted in the Roche Whole Blood Collection Tube containing a pre-analytic chaotropic reagent, a guanidine based additive used to lyse the cells within the whole blood, releasing and preserving nucleic acids.

Each dilution series was tested using three different lots of **cobas**[•] Babesia kits with approximately 42 replicates per lot, for a total of approximately 126 replicates per concentration. For each *Babesia* species, PROBIT analysis on the data combined across dilution series and reagent lots was used to estimate the LoD, along with the lower and upper limit of 95% confidence interval (Table 14). The reactivity rates observed in the LoD studies for *Babesia* are summarized in Table 15 to Table 18.

Analyte	Measuring units	LoD	Lower 95% confidence limit	Upper 95% confidence limit
Babesia microti	iRBC/mL	6.1	5.0	7.9
Babesia duncani	iRBC/mL	50.2	44.2	58.8
Babesia divergens	iRBC/mL	26.1	22.3	31.8
Babesia venatorum	iRBC/mL	40.0	34.1	48.7

Table 14 Results of PROBIT analysis on LoD data collected with Babesia infected red blood cells in human whole blood

Table 15 Reactivity rates summary for Babesia microti

<i>Babesia</i> concentration (iRBC/mL)	Number reactive	Number of valid replicates	% Reactive	95% Lower confidence bound (one-sided)
11.8	126	126	100.0%	97.7%
5.9	119	126	94.4%	89.8%
3.0	103	126	81.7%	75.1%
1.5	68	126	54.0%	46.3%
0.6	33	125	26.4%	20.0%

 Table 16
 Reactivity rates summary for Babesia duncani

<i>Babesia</i> concentration (iRBC/mL)	Number reactive	Number of valid replicates	% Reactive	95% Lower confidence bound (one-sided)
80.0	126	126	100.0%	97.7%
40.0	115	126	91.3%	86.0%
20.0	47	126	37.3%	30.1%
10.0	8	126	6.3%	3.2%
5.0	2	126	1.6%	0.3%

 Table 17
 Reactivity rates summary for Babesia divergens

Babesia concentration (iRBC/mL)	Number reactive	Number of valid replicates	% Reactive	95% Lower confidence bound (one-sided)
40.0	126	126	100.0%	97.7%
20.0	119	126	94.4%	89.8%
10.0	63	125	50.4%	42.7%
5.0	26	126	20.6%	14.9%
2.5	12	126	9.5%	5.6%

<i>Babesia</i> concentration (iRBC/mL)	Number reactive	Number of valid replicates	% Reactive	95% Lower confidence bound (one-sided)
40.0	124	126	98.4%	95.1%
20.0	90	126	71.4%	64.1%
10.0	38	126	30.2%	23.4%
5.0	9	126	7.1%	3.8%
2.5	4	126	3.2%	1.1%

Table 18 Reactivity rates summary for Babesia venatorum

Genotype verification

The performance of **cobas**[®] Babesia to detect 4 species of *Babesia* was determined by testing a total of 10 unique clinical samples for *Babesia* microti and 3 *Babesia* cultured isolates. All clinical samples were quantified traceable to the *Babesia microti* Roche Secondary Standard. All clinical samples were tested neat and after dilution with *Babesia* negative human whole blood to 4 x LoD of **cobas**[®] Babesia. All 3 *Babesia* cultures were tested after dilution with *Babesia* negative human whole blood to 4 x LoD of **cobas**[®] Babesia. All clinical samples and cultures were detected neat and/or at 4 x LoD.

Analytical specificity

The analytical specificity of **cobas**[®] Babesia was evaluated for cross-reactivity with15 microorganisms at 10⁵ - 10⁶ copies, CFU or IU/mL, which included 5 viral isolates, 1 parasite, 8 bacterial strains and 1 yeast isolate (Table 19). The microorganisms were added to Babesia-negative human whole blood and tested with and without *Babesia* added to a concentration of approximately 3 x LoD of **cobas**[®] Babesia. The tested microorganisms do not cross-react or interfere with **cobas**[®] Babesia.

Bacteria	Viruses	Parasites	Yeast
Anaplasma phagocytophilum	Hepatitis B Virus	Plasmodium falciparum	Candida albicans
Propionibacterium acnes	Hepatitis C Virus	-	-
Staphylococcus aureus	Human Immunodeficiency Virus	-	-
Staphylococcus epidermidis	Parvovirus B19	-	-
Borrelia burgdorferi	West Nile Virus	-	-
Borrelia hermsii	-	-	-
Borrelia parkeri	-	-	-
Borrelia recurrentis	-	-	-

Table 19 Microorganisms tested for analytical specificity

Analytical specificity – interfering substances

Endogenous interference substances

Whole blood samples with abnormally high levels of triglycerides (33 g/L), hemoglobin (\geq 20 g/dL), unconjugated bilirubin (0.2 g/L), albumin (60 g/L), and human DNA (0.002 g/L) were tested with and without *Babesia* added to a concentration of 3 x LoD of **cobas**^{\circ} Babesia. Samples containing these endogenous substances did not interfere with the sensitivity or specificity of **cobas**^{\circ} Babesia.

Exogenous interference substances

Babesia-negative human whole blood samples containing abnormally high concentrations of drugs (Table 20) were tested with and without *Babesia* added to a concentration of 3 x LoD of **cobas**[®] Babesia. These exogenous substances did not interfere with the sensitivity or specificity of **cobas**[®] Babesia.

Name of drug tested	Concentration
Acetaminophen	1324 µmol/L
Acetylsalicylic Acid	3620 µmol/L
Ascorbic Acid	342 µmol/L
Atorvastatin	600 µg Eq/L
Atovaquone	1227 µmol/L
Azithromycin	15.3 μmol/L
Fluoxetine	11.2 μmol/L
Ibuprofen	2425 µmol/L
Loratadine	0.78 μmol/L
Nadolol	3.88 µmol/L
Naproxen	2170 µmol/L
Paroxetine	3.04 µmol/L
Phenylephrine HCL	491 µmol/L
Sertraline	1.96 µmol/L

Table 20 Concentrations of the drugs added into whole blood

Cross contamination

The cross-contamination rate for **cobas**[®] Babesia was determined by testing 237 replicates of *Babesia* negative human whole blood and 230 replicates of a high titer *Babesia* sample at 1.00E+07 particles/mL. The study was performed using the **cobas**[®] 6800 system. In total, 5 runs were performed with positive and negative samples in a checkerboard configuration.

All 237 replicates of the negative sample were non-reactive, resulting in a cross-contamination rate of 0%. The two-sided 95% exact confidence interval was 0% for the lower bound and 1.54% for the upper bound [0%: 1.54%].

Whole system failure

The whole system failure rate of **cobas**[°] Babesia was determined by testing 180 replicates of whole blood spiked with *Babesia microti* at a target concentration of approximately 3 x LoD. Before testing with **cobas**[°] Babesia each panel member was diluted in the Roche Whole Blood Collection Tube containing a pre-analytic chaotropic reagent. The study was performed using the **cobas**[°] 6800 system.

The results of this study determined that all replicates were reactive, resulting in a whole system failure rate of 0%. The two-sided 95% exact confidence interval was 0% for the lower bound and 2.03% for the upper bound [0%: 2.03%].

Clinical performance evaluation

Clinical sensitivity

The clinical sensitivity of **cobas**[®] Babesia was evaluated using 203 individual samples (131 clinical samples (*B. microti*) and 72 contrived samples (*B. microti*, *B. duncani*, *B. venatorum*, *and B. divergens*)) that were known to be *Babesia*-positive based on NAT testing. The samples were characterized with a validated in-house NAT for *Babesia*, which used different primers and probes than those used in **cobas**[®] Babesia. The study was conducted at three testing laboratories, with each site testing all 203 samples, both neat and diluted 1:6 (to simulate pools of 6), using three different lots of **cobas**[®] Babesia.

The clinical sensitivity of **cobas**[°] Babesia with neat samples in this study was 100% (95% two-sided Confidence Interval (CI): 98.2% to 100%) and with samples diluted 1:6 was 100% (95% CI: 98.2% to 100%) (Table 21).

-	Number of	Number of	Number of		Sensitivity	(95% CI*)
	Samples Tested	Samples Reactive	Samples Non-Reactive	Sensitivity (%)	Lower Limit	Upper Limit
Neat	203	203	0	100.0%	98.2%	100.0%
1:6	203	203	0	100.0%	98.2%	100.0%

Table 21 Clinical sensitivity of known Babesia-positive samples

*Clopper-Pearson Exact method

Clinical specificity

The clinical specificity of **cobas**[°] Babesia was evaluated testing blood donations collected at five external laboratory sites. Samples were collected in US states classified as high-endemic, low-endemic, or non-endemic for *Babesia*. Six different **cobas**[°] Babesia reagent lots were used in this study. Clinical specificity of **cobas**[°] Babesia was calculated as the percentage (95% two-sided CI) of *Babesia* donor status-negative donors who had **cobas**[°] Babesia non-reactive results. A total of 168,981 evaluable donations were tested as individual samples. The majority of evaluable donations (143,939) were collected in high-endemic US states.

Individual testing results

Table 22 shows the calculation of the clinical specificity of **cobas**[®] Babesia for overall 168,972 evaluable status-negative donations from individual testing, as well as for high-, low-, and non-endemic US states. The clinical specificity of **cobas**[®] Babesia overall—across all endemicity categories for donations tested individually—was 99.999% (168,970/168,972; 95% CI: 99.996% to 100%) (Table 22). Specificity results were similar—99.999% to 100%—across the 3 endemicity categories (non-, low- and high-endemic). An invalid rate of 0.49% due to internal control failures, instrument failures, protocol deviations, or other incidents was observed for the individual samples.

	-		cobas® Ba	abesia Result	-	
-	Parameter	Total Number of Status-Negative Donations'	Reactive	Non-Reactive	Estimate in Percent (95% Exact CI)	
Overall	Clinical Specificity	168,972	2	168,970	99.999 (99.996, 100.000)	
Non Endemic	Endemic Clinical Specificity 10,824		0	10,824	100.000 (99.966, 100.000)	
Low Endemic	Endemic Clinical Specificity 14,217		0	14,217	100.000 (99.974, 100.000)	
High Endemic	Clinical Specificity	143,931	2	143,929	99.999 (99.995, 100.000)	

 Table 22 Clinical specificity of cobas[®] Babesia – Overall and per Babesia endemicity level

Note: Only evaluable donations are included in this summary table. CI = two-sided exact binomial confidence interval.

Table 23 shows the comparison of **cobas**^{*} Babesia results and donation status for 168,981 evaluable donations, overall and for the three different endemicity levels. Nine (of 11) **cobas**^{*} Babesia-reactive donations were confirmed positive for *Babesia*, including 8 donations collected in US states determined to be high endemic for *Babesia*.

		Donation Stat	us*	Total
-	cobas® Babesia Result	Positive n (%)	Negative n (%)	N
	Reactive	9 (100.000)	2 (0.001)	11
Overall	Non-Reactive	0 (0.000)	168,970 (99.999)	168,970
	Total	9	168,972	168,981
Non Endemic	Reactive	1 (100.000)	0 (0.000)	1
	Non-Reactive	0 (0.000)	10,824 (100.000)	10,824
	Total	1	10,824	10,825
	Reactive	0 (0.000)	0 (0.000)	0
Low Endemic	Non-Reactive	0 (0.000)	14,217 (100.000)	14,217
	Total	0	14,217	14,217
High Endemic	Reactive	8 (100.000)	2 (0.001)	10
	Non-Reactive	0 (0.000)	143,929 (99.999)	143,929
	Total	8	143,931	143,939

Note: Only evaluable donations are included in this summary table.

* Donation Status was assigned based on the testing reactivity pattern observed on the index donation (initial and additional index testing) and/or based on follow-up study results.

Pools of 6 testing results

The clinical specificity for **cobas**[®] Babesia for donations tested in pools of six (PP6) overall across all endemicity categories was 100% (27,606/27,606; 95% CI: 99.987% to 100%) (Table 24). Specificity results were the same across the 3 endemicity categories (non-, low-, and high-endemic).

Endemicity	Parameter	Total Number of Status-Negative Donations	cobas [®] Babesia Reactive	cobas® Babesia Non-Reactive	Estimate in Percent (95% Exact CI)
Non Endemic	Clinical Specificity	cificity 6,485 0 6,485		100.000 (99.943, 100.000)	
Low Endemic	Clinical Specificity	5,834	0 5,834		100.000 (99.937, 100.000)
High Endemic	h Endemic Clinical 15,287 0		15,287	100.000 (99.976, 100.000)	
Overall	Clinical Specificity	27,606	0	27,606	100.000 (99.987, 100.000)

Table 24 Clinical specificity of cobas® Babesia – donations tested in pools of 6 only (donation level)

Note: Only evaluable donations are included in this summary table. CI = two-sided exact binomial confidence interval.

Table 25 shows the comparison of **cobas**[•] Babesia results and donation status for 27,729 evaluable donations from which whole blood samples were tested in PP6.

Table 25 Comparison of cobas	[®] Babesia results with donation	on status by endemicity	- pools of 6 (donation level)
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cobas [®] Babesia Result	Donation Status Positive n (%)	Donation Status Negative n (%)	Total N
Overall, Reactive	7 (100.000)	0 (0.000)	7
Overall, Non-Reactive	0 (0.000)	27,722 (100.000)	27,722
Overall, Total	7	27,722	27,729
Non-Endemic, Reactive	0 (0.000)	0 (0.000)	0
Non-Endemic, Non-Reactive	0 (0.000)	6,590 (100.000)	6,590
Non-Endemic, Total	0	6,590	6,590
Low Endemic, Reactive	0 (0.000)	0 (0.000)	0
Low Endemic, Non-Reactive	0 (0.000)	5,845 (100.000)	5,845
Low Endemic, Total	0	5,845	5,845
High Endemic, Reactive	7 (100.000)	0 (0.000)	7
High Endemic, Non-Reactive	0 (0.000)	15,287 (100.000)	15,287
High Endemic, Total	7	15,287	15,294

Note: Only evaluable donations are included in this summary table. A total of 116/27,729 (0.42%) donations were tested individually (not in pools of 6) in the above table.

Donation Status was assigned based on the testing reactivity pattern observed on the index donation (initial and additional index testing) and/or based on follow-up study results.

Table 26 summarizes the pool reactivity for the 4,610 qualifying PP6. Out of 4,610 PP6, 4,603 (99.85%) pools were non-reactive and 7 (0.15%) were reactive on **cobas**[®] Babesia. Out of 7 reactive pools, 7 contained a status-positive donation, and 0 were donation-status negative (false reactive). The overall pool specificity of **cobas**[®] Babesia was 100% (4,603/4,603 pools; 95% CI: 99.920 to 100%).

Table 26 Pool reactivity in volunteer blood donors

Category	Number of Pools	Percentage of Pools Tested
Total pools tested ^a	4610	100
Non-reactive pools ^b	4603	99.8
Non-reactive pools with all donations status-negative	4603	100
Non-reactive pools with at least one status-positive donation	0	0
Reactive pools ^b	7	0.2
Reactive pools with at least one status-positive donation	7	100
Reactive pools with donations status negative (false-reactive pools)	0	0

^a Note: 37/4610 pools had < 6 donations.

^b Donation Status was assigned based on the testing reactivity pattern observed on the index donation (initial and additional index testing) and/or based on follow-up study results.

For whole blood samples that were tested in PP6, 260 (99.2%) valid cobas® Babesia batches yielded 4,748 (99.00%) valid results.

Reproducibility

The reproducibility of **cobas**[•] Babesia was established by testing a 13-member panel composed of one negative panel member and twelve samples positive for one of each of four *Babesia* species (*B. microti, B. duncani, B. divergens,* and *B. venatorum*) at three different concentrations (approximately 0.5 x, 1-2 x, and approximately 3 x the LoD **cobas**[•] Babesia for each of the four species).

Operators at each of three sites performed five days of testing with each of three lots of **cobas**^{*} Babesia reagents and two valid panel runs (i.e., two batches, each batch composed of one panel and two independent controls) per day were completed to yield up to 270 tests per panel member of *Babesia* species at each of the three concentrations.

All valid batches and test results were analyzed by calculating the percentage of reactive test results for each panel member [Table 27 (*B. microti*), Table 28 (*B. duncani*), Table 29 (*B. divergens*), and Table 30 (*B. venatorum*)]. This study demonstrated that **cobas**[°] Babesia for use on the **cobas**[°] 6800/8800 systems shows reproducible performance across the variables assessed (lot, site, day, batch, and within batch) for detecting *Babesia*.

	Site			Lot		Day		Batch	
<i>Babesia microti</i> Concentration	ID	% Reactive Results	ID	% Reactive Results	ID	% Reactive Results	ID	% Reactive Results	
	1	93.3% (84/90)	1	87.8% (79/90)	1	96.3% (52/54)	1	94.8% (128/135)	
	2	96.7% (87/90)	2	100% (90/90)	2	94.4% (51/54)	2	96.3% (130/135)	
~0.5 x LoD	3	96.7% (87/90)	3	98.9% (89/90)	3	90.7% (49/54)	-	-	
	-	-	-	-	4	96.3% (52/54)	-	-	
	-	-	-	-	5	100.0% (54/54)	-	-	
	1	100.0% (90/90)	1	100.0% (89/89)	1	100.0% (54/54)	1	100.0% (135/135)	
	2	100.0% (90/90)	2	100.0% (90/90)	2	100.0% (54/54)	2	100.0% (134/134)	
1-2 x LoD	3	100.0% (89/89)	3	100.0% (90/90)	3	100.0% (54/54)	-	-	
	-	-	-	-	4	100.0% (53/53)	-	-	
	-	-	-	-	5	100.0% (54/54)	-	-	
	1	100.0% (90/90)	1	100.0% (90/90)	1	100.0% (54/54)	1	100.0% (135/135)	
~3 x LoD	2	100.0% (90/90)	2	100.0% (90/90)	2	100.0% (54/54)	2	100.0% (135/135)	
	3	100.0% (90/90)	3	100.0% (90/90)	3	100.0% (54/54)	-	-	
	-	-	-	_	4	100.0% (54/54)	-	-	
	-	-	-	-	5	100.0% (54/54)	-	-	

Table 27 Test results summarized by site, lot, day, and batch (positive panel members) - Babesia microti

		Site	Lot		Day		Batch	
<i>Babesia duncani</i> Concentration	ID	% Reactive Results	ID	% Reactive Results	ID	% Reactive Results	ID	% Reactive Results
	1	46.7% (42/90)	1	62.2% (56/90)	1	66.7% (36/54)	1	65.2% (88/135)
	2	68.9% (62/90)	2	54.4% (49/90)	2	63.0% (34/54)	2	61.5% (83/135)
~0.5 x LoD	3	74.4% (67/90)	3	73.3% (66/90)	3	57.4% (31/54)	-	-
	-	-	-	-	4	64.8% (35/54)	-	-
	-	-	-	-	5	64.8% (35/54)	-	-
	1	100.0% (90/90)	1	100.0% (90/90)	1	100.0% (53/53)	1	100.0% (134/134)
	2	100.0% (90/90)	2	100.0% (89/89)	2	100.0% (54/54)	2	100.0% (135/135)
1-2 x LoD	3	100.0% (89/89)	3	100.0% (90/90)	3	100.0% (54/54)	-	-
	-	-	-	-	4	100.0% (54/54)	-	-
	-	-	-	-	5	100.0% (54/54)	-	-
	1	100.0% (90/90)	1	100.0% (89/89)	1	100.0% (54/54)	1	100.0% (134/134)
~3 x LoD	2	100.0% (89/89)	2	100.0% (90/90)	2	100.0% (54/54)	2	100.0% (134/134)
	3	100.0% (89/89)	3	100.0% (89/89)	3	100.0% (53/53)	-	-
	-	-	-	-	4	100.0% (54/54)	-	-
	-	-	-	-	5	100.0% (53/53)	-	-

Table 28 Test results summarized by site, lot, day, and batch (positive panel members) - Babesia duncani

	Site		Lot		Day		Batch	
<i>Babesia</i> <i>divergens</i> Concentration	ID	% Reactive Results	ID	% Reactive Results	ID	% Reactive Results	ID	% Reactive Results
~0.5 x LoD	1	35.6% (32/90)	1	60.0% (54/90)	1	55.6% (30/54)	1	52.6% (71/135)
	2	54.4% (49/90)	2	28.9% (26/90)	2	57.4% (31/54)	2	52.6% (71/135)
	3	67.8% (61/90)	3	68.9% (62/90)	3	46.3% (25/54)	-	-
	-	-	-	-	4	51.9% (28/54)	-	-
	-	-	-	-	5	51.9% (28/54)	-	-
1-2 x LoD	1	100.0% (90/90)	1	100.0% (90/90)	1	100.0% (54/54)	1	100.0% (135/135)
	2	100.0% (90/90)	2	100.0% (90/90)	2	100.0% (54/54)	2	100.0% (135/135)
	3	100.0% (90/90)	3	100.0% (90/90)	3	100.0% (54/54)	-	-
	-	-	-	-	4	100.0% (54/54)	-	-
	-	-	-	-	5	100.0% (54/54)	-	-
~3 x LoD	1	100.0% (90/90)	1	100.0% (90/90)	1	100.0% (54/54)	1	100.0% (135/135)
	2	100.0% (90/90)	2	100.0% (90/90)	2	100.0% (54/54)	2	100.0% (135/135)
	3	100.0% (90/90)	3	100.0% (90/90)	3	100.0% (54/54)	-	-
	-	-	-	-	4	100.0% (54/54)	-	-
	-	-	-	-	5	100.0% (54/54)	-	-

Table 29 Test results summarized by site, lot, day, and batch (positive panel members) - Babesia divergens

	Site		Lot		Day		Batch	
<i>Babesia</i> <i>venatorum</i> Concentration	ID	% Reactive Results	ID	% Reactive Results	ID	% Reactive Results	ID	% Reactive Results
~0.5 x LoD	1	95.6% (86/90)	1	100.0% (90/90)	1	100.0% (54/54)	1	100.0% (135/135)
	2	100.0% (90/90)	2	95.6% (86/90)	2	98.1% (53/54)	2	97.0% (131/135)
	3	100.0% (90/90)	3	100.0% (90/90)	3	100.0% (54/54)	-	-
	-	-	-	-	4	96.3% (52/54)	-	-
	-	-	-	-	5	98.1% (53/54)	-	-
1-2 x LoD	1	100.0% (90/90)	1	100.0% (90/90)	1	100.0% (54/54)	1	100.0% (135/135)
	2	100.0% (90/90)	2	100.0% (90/90)	2	100.0% (54/54)	2	100.0% (135/135)
	3	100.0% (90/90)	3	100.0% (90/90)	3	100.0% (54/54)	-	-
	-	-	-	-	4	100.0% (54/54)	-	-
	-	-	-	-	5	100.0% (54/54)	-	-
~3 x LoD	1	100.0% (90/90)	1	100.0% (90/90)	1	100.0% (54/54)	1	100.0% (135/135)
	2	100.0% (90/90)	2	100.0% (90/90)	2	100.0% (54/54)	2	100.0% (135/135)
	3	100.0% (90/90)	3	100.0% (90/90)	3	100.0% (54/54)	-	-
	-	-	-	-	4	100.0% (54/54)	-	-
	-	-	-	-	5	100.0% (54/54)	-	-

Table 30 Test results summarized by site, lot, day, and batch (positive panel members) - Babesia venatorum

Additional information

Key test features

Sample type	Whole blood in Roche Whole Blood Collection Tube
Amount of sample required	850 μL*
Amount of sample processed	500 μL*

* Tubes used for testing may have different dead volumes and require more or less minimum volume. Contact your local Roche service representative for further information.

Symbols

The following symbols are used in labeling for Roche PCR diagnostic products.



Table 31 Symbols used in labeling for Roche PCR diagnostics products

Technical support

For technical support (assistance) please reach out to your local affiliate: https://www.roche.com/about/business/roche_worldwide.htm

Manufacturer and importer



Roche Molecular Systems, Inc. 1080 US Highway 202 South Branchburg, NJ 08876, USA www.roche.com

Made in USA



Roche Diagnostics GmbH Sandhofer Strasse 116 68305 Mannheim, Germany

Trademarks and patents

See https://diagnostics.roche.com/us/en/about-us/patents

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Roche Diagnostics GmbH Sandhofer Str. 116 68305 Mannheim Germany



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Document revision

Document Revision Information				
Doc Rev. 2.0	Updated intended use section to include the assay can be used as an aid in diagnosis.			
03/2025	Updated the use of living donor and donor terminology to sample where relevant.			
	Addition of cobas [®] 5800 instrument throughout.			
	Updated branding and registration information throughout.			
	Updated the harmonized symbol page.			
	Updated Trademarks and patents section, including the link.			
	Updated Principles of the procedure section.			
	Added Reagent handling requirements for cobas [®] 5800 system section.			
	Added Additional materials required for the cobas [®] 5800 section.			
	Updated Instrumentation and software required section.			
	Updated Precautions and handling requirements section.			
	Updated Instructions for use section.			
	Updated Results section and added System equivalency/system comparison section.			
	Please contact your local Roche Representative if you have any questions.			

The summary of safety and performance report can be found using the following link: https://ec.europa.eu/tools/eudamed