DRG® Myoglobin/CKMB Troponin I Combo (Cassette) (RAP-4829)

As of 4 April 2008 **RUO in the USA**

For professional in vitro use only.

INTENDED USE

The **Cardiac Combo Rapid Test** is a rapid chromatographic immunoassay for the qualitative detection of human Myoglobin, CK-MB and cardiac Troponin I in whole blood, serum or plasma as an aid in the determination of myocardial infarction (MI).

SUMMARY

Myoglobin (MYO), Creatine Kinase MB (CK-MB) and cardiac Troponin I (cTnI) are proteins released into the bloodstream after cardiac injury. Myoglobin is a heme-protein normally found in skeletal and cardiac muscle with a molecular weight of 17.8 kDa. It constitutes about 2 percent of total muscle protein and is responsible for transporting oxygen within muscle cells.[1] When muscle cells are damaged, Myoglobin is released into the blood rapidly due to its relatively small size. The level of Myoglobin increases measurably above baseline within 2-4 hours post-infarct, peaking at 9-12 hours, and returning to baseline within 24-36 hours.[2,3] CK-MB is an enzyme also present in the cardiac muscle, with a molecular weight of 87.0 kDa.[4] Creatine Kinase is a dimeric molecule formed from two subunits designated as "M" and "B", which combine to form three different isoenzymes, CK-MM, CK-BB and CK-MB. CK-MB is the isoenzyme of Creatine Kinase most involved in the metabolism of cardiac muscle tissue.[5] The release of CK-MB into the blood following an MI can be detected within 3-8 hours after the onset of symptoms. It peaks within 9 to 30 hours, and returns to baseline levels within 48 to 72 hours.[6] Cardiac Troponin I is a protein found in cardiac muscle, with a molecular weight of 22.5 kDa.[7] Troponin I is part of a three subunit complex comprised of Troponin T and Troponin C. Along with tropomyosin, this structural complex forms the main component that regulates the calcium sensitive ATPase activity of actomyosin in striated skeletal and cardiac muscle.[8] After cardiac injury occurs, Troponin I is released into the blood 4-6 hours after the onset of pain. The release pattern of Troponin I is similar to CK-MB, but while CK-MB levels return to normal after 72 hours, Troponin I remains elevated for 6-10 days, thus providing for a longer window of detection for cardiac injury.

The **Cardiac Combo Rapid Test** utilizes a combination of antibody coated particles and capture reagents to qualitatively detect Myoglobin, CK-MB and Troponin I in whole blood, serum or plasma.

The minimum detection level is 50 ng/mL Myoglobin, 5 ng/mL CK-MB and 0.5 ng/mL Troponin I.

PRINCIPLE

The **Cardiac Combo Rapid Test** is a qualitative, membrane based immunoassay for the detection of Myoglobin, CK-MB and Troponin I in whole blood, serum or plasma. The membrane is pre-coated with specific capture antibodies in each of the test line regions of the test. During testing, the whole blood, serum or plasma specimen reacts with the particle coated with specific antibodies. The mixture migrates upward on the membrane chromatographically by capillary action to react with the specific capture antibodies on the membrane and generates a colored line. The presence of this colored line in the specific test line region indicates a positive result, while its absence indicates a negative result. To serve as a procedural control, a colored line will always appear in the control line region indicating that proper volume of specimen has been added and membrane wicking has occurred.

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REAGENTS

The test contains anti-Myoglobin antibody coated particles, anti-CK-MB antibody coated particles, anti-Troponin I antibody coated particles, and capture antibodies coated on the membrane.

PRECAUTIONS

- For in vitro use only.
- Do not use after the expiration date.
- The test device should remain in the sealed pouch until use.
- Do not use if pouch is damaged.
- Do not eat, drink or smoke in the area where the specimens or kits are handled.
- Humidity and temperature can adversely affect results.
- Handle all specimens as if they contain infectious agents. Observe established precautions against microbiological hazards throughout the procedure and follow the standard procedures for proper disposal of specimens.
- Wear protective clothing such as laboratory coats, disposable gloves or eye protection when specimens are being tested.

STORAGE AND STABILITY

The kit can be stored at room temperature or refrigerated (2-30°C). The test strip is stable through the expiration date printed on the sealed pouch. The test strip must remain in the sealed pouch until use.

- Do not freeze.
- Do not use beyond the expiration date.

MATERIALS

MATERIALS PROVIDED

- 20 Test devices
- Disposable specimen droppers
- Package insert

MATERIALS REQUIRED BUT NOT PROVIDED

- Specimen collection container
- Centrifuge
- Lancets (for fingerstick whole blood only)
- Heparinized capillary tubes and dispensing bulb (for fingerstick whole blood only)
- Timer

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SPECIMEN COLLECTION AND PREPARATION

- The **Cardiac Combo Rapid Test** can be performed using whole blood (from venipuncture or fingerstick), serum or plasma.
- To collect **Fingerstick Whole Blood specimens**:
  - Wash the patient's hand with soap and warm water or clean with an alcohol swab. Allow to dry.
  - Massage the hand without touching the puncture site by rubbing down the hand towards the fingertip of the middle or ring finger.
  - Puncture the skin with a sterile lancet. Wipe away the first sign of blood.
  - Gently rub the hand from wrist to palm to finger to form a rounded drop of blood over the puncture site.
  - Add the Fingerstick Whole Blood specimen to the test device by using a capillary tube:
  - Touch the end of the capillary tube to the blood until filled to approximately 100 µL. Avoid air bubbles.
  - Place the bulb onto the top end of the capillary tube, then squeeze the bulb to dispense the whole blood into the specimen well (S) of the test device
- Add the Fingerstick Whole Blood specimen to the test device by using **hanging drops**:
  - Position the patient's finger so that the drop of blood is just above the specimen well (S) of the test device.
  - Allow 4 hanging drops of fingerstick whole blood to fall into the specimen well (S) of the test device, or move the patient's finger so that the hanging drop touches the specimen well (S). Avoid touching the finger directly to the specimen well (S).
- Separate serum or plasma from blood as soon as possible to avoid hemolysis. Use only clear, non-hemolyzed specimens.
- Testing should be performed immediately after specimen collection. Do not leave the specimens at room temperature for prolonged periods. Serum and plasma specimens may be stored at 2-8°C for up to 3 days. For long-term storage, specimens should be kept below -20°C. Whole blood collected by venipuncture should be stored at 2-8°C if the test is to be run within 2 days of collection. Do not freeze whole blood specimens. Whole blood collected by fingerstick should be tested immediately.
- Bring specimens to room temperature prior to testing. Frozen specimens must be completely thawed and mixed well prior to testing. Specimens should not be frozen and thawed repeatedly.
- If specimens are to be shipped, they should be packed in compliance with local regulations covering the transportation of etiologic agents.

DIRECTIONS FOR USE

1. Allow the test device, specimen and/or controls to equilibrate to room temperature (15-30°C) prior to testing.
2. Remove the test device from the sealed pouch and use it as soon as possible. Best results will be obtained if the test is performed immediately after opening the foil pouch.
3. Place the test device on a clean and level surface.

4 a. For **Serum or Plasma** specimens:
Hold the dropper vertically and **transfer 2 drops of serum or plasma** (approximately 50 µL) to the specimen well (S) of the test device, then start the timer. See illustration below.

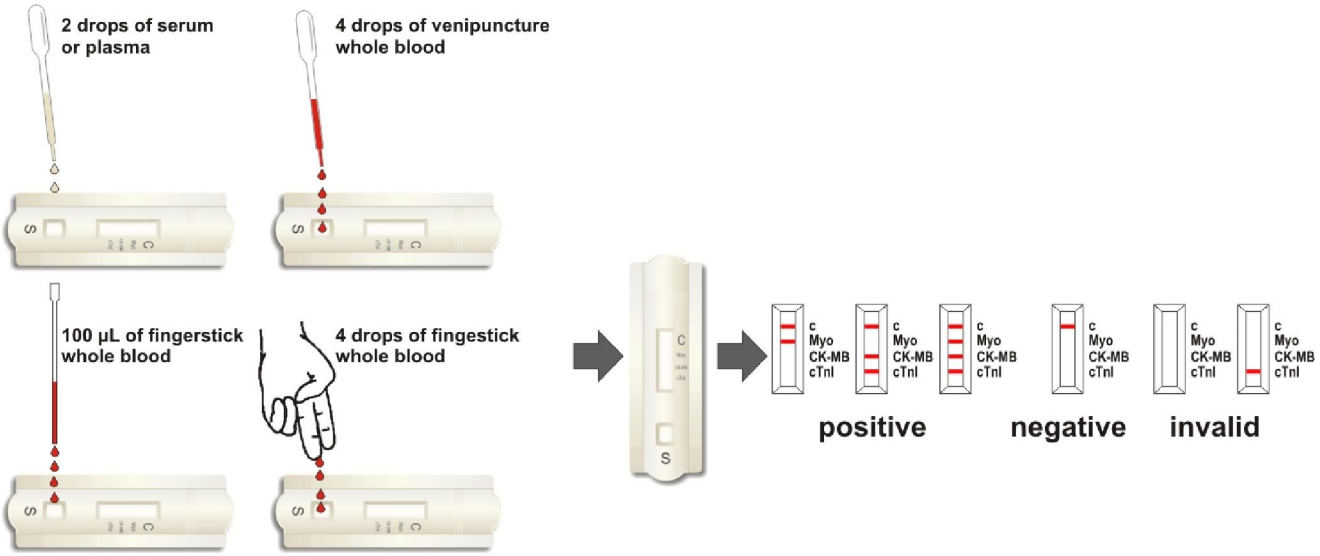
4 b. For **Venipuncture Whole Blood** specimens:
Hold the dropper vertically and **transfer 4 drops of venipuncture whole blood** (approximately 100 µL) to the specimen well (S) of the test device, then start the timer. See illustration below.

4 c. For **Fingerstick Whole Blood** specimens:

To use a capillary tube: Fill the capillary tube and **transfer approximately 100 µL of fingerstick whole blood** specimen to the specimen well (S) of the test device, then start the timer. See illustration below.

To use hanging drops: Allow **4 hanging drops of fingerstick whole blood specimen** (approximately 100 µL) to fall into the center of the specimen well (S) on the test device, then start the timer. See illustration below.

5. Wait for the coloured line(s) to appear. **Read results at 10 minutes.** Do not interpret results after more than 20 minutes.



INTERPRETATION OF RESULTS

Negative: **One colored line appears in the control line region (C).** No apparent colored lines appear in any of the test line region(s). This indicates that the concentration of Myoglobin, CK-MB and Troponin I are below the minimum detection levels.

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Positive:* **A colored line in the control line region (C) and the presence of one or more colored lines in the test line regions indicates a positive result**. This indicates that the concentration of Myoglobin, CK-MB and/or Troponin I is above the minimum detection level.

Invalid: **Control line (C) fails to appear.** Insufficient specimen volume or incorrect procedural techniques are the most likely reasons for control line failure. Review the procedure and repeat the test with a new test card. If the problem persists, discontinue using the test kit immediately and contact your local distributor.

***NOTE:** The intensity of the color in the test line region(s) will vary depending on the concentration of Myoglobin, CK-MB and/or Troponin I present in the specimen. Therefore, any shade of color in the test line regions should be considered positive.*

QUALITY CONTROL

An internal procedural control is included in the test. A colored line appearing in the control line region (C) is an internal procedural control. It confirms sufficient specimen volume, adequate membrane wicking and correct procedural technique.
Control standards are not supplied with this kit; however it is recommended that positive and negative controls be tested as a good laboratory practice to confirm the test procedure and to verify proper test performance.

LIMITATIONS

1. The Cardiac Combo Rapid Test is for *in vitro* use only. This test should be used for the detection of Myoglobin, CK-MB, and Troponin I in whole blood, serum or plasma specimens only. Neither the quantitative value nor the rate of increase in Myoglobin, CK-MB and Troponin I can be determined by this qualitative test.
2. The Cardiac Combo Rapid Test will only indicate the qualitative level of Myoglobin, CK-MB and Troponin I in the specimen and should not be used as the sole criteria for the diagnosis of myocardial infarction.
3. The Cardiac Combo Rapid Test cannot detect less than 50 ng/mL Myoglobin, 5 ng/mL CK-MB and 0.5 ng/mL Troponin I in specimens. A negative result at any time does not preclude the possibility of myocardial infarction.
4. As with all diagnostic tests, all results must be interpreted together with other clinical information available to the physician.
5. Unusually high titers of heterophile antibodies or rheumatoid factor (RF) may affect the results. Even if test results are positive, further clinical evaluation should be considered with other clinical information available to the physician.

EXPECTED VALUES

The **Cardiac Combo Rapid Test** has been compared with a leading commercial Myoglobin/CK-MB/T EIA test, demonstrating an overall accuracy of 98.0% with Myoglobin, 99.8% with CK-MB, and 98.5% with Troponin I.

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PERFORMANCE CHARACTERISTICS

Sensitivity and Specificity

The **Cardiac Combo Rapid Test Card** has been evaluated with a leading commercial Myoglobin/CK-MB/Troponin I EIA test using clinical specimens. The results show that relative to leading EIA tests, the **Cardiac Combo Rapid Test** exhibits 100% sensitivity and 97.7% specificity for Myoglobin, 100% sensitivity and 99.8% specificity for CK-MB, and 98.7% sensitivity and 98.4% specificity for Troponin I.

Myoglobin Test vs. EIA

Method		EIA		Total Results
MYO Test	Results	Positive	Negative	
	Positive	60	9	69
	Negative	0	374	374
Total Results		60	383	443

Relative Sensitivity: 100% (94.0%-100%)*
Relative Specificity: 97.7% (95.6%-98.9%)*
Accuracy: 98.0% (96.2%-99.1%)* (* 95% Confidence Interval)

CK-MB Test vs. EIA

Method		EIA		Total Results
CK-MB Test	Results	Positive	Negative	
	Positive	54	1	55
	Negative	0	422	422
Total Results		54	423	477

Relative Sensitivity: 100% (93.4%-100.0%) *
Relative Specificity: 99.8% (98.7%-99.9%)*
Accuracy: 99.8% (98.8% to 99.9%)* (* 95% Confidence Interval)

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Troponin I Test vs. EIA

Method		EIA		Total Results
cTnI Test	Results	Positive	Negative	
	Positive	225	8	233
	Negative	3	505	508
Total Results		228	513	741

Relative Sensitivity: 98.7% (96.2%- 99.7%)*
Relative Specificity: 98.4% (97.0%-99.3%)*
Accuracy: 98.5% (97.4%-99.3%)* (* 95% Confidence Interval)

Precision

Intra-Assay

Within-run precision has been determined by using replicates of 10 tests for each of three lots using
Myoglobin specimen levels at 0 ng/mL, 50 ng/mL, 100 ng/mL, 200 ng/mL and 400 ng/mL,
CK-MB specimen levels at 0 ng/mL, 5 ng/mL, 10 ng/mL, 20 ng/mL and 40 ng/mL and
Troponin I specimen levels at 0 ng/mL, 2 ng/mL, 5 ng/mL, 10 ng/mL and 20 ng/mL.
The specimens were correctly identified > 99% of the time.

Inter-Assay

Between-run precision has been determined by 3 independent assays on the same fifteen specimens:
0 ng/mL, 50 ng/mL, 100 ng/mL, 200 ng/mL and 400 ng/mL of Myoglobin,
0 ng/mL, 5 ng/mL, 10 ng/mL, 20 ng/mL, and 40 ng/mL of CK-MB and
0 ng/mL, 2 ng/mL, 5 ng/mL, 10 ng/mL and 20 ng/mL of Troponin I.
Three different lots of the Myoglobin/CK-MB/ Troponin I Combi Test Card have been tested using these specimens. The specimens were correctly identified > 99% of the time.

Cross-Reactivity

Sera containing known amounts of antibodies to Myoglobin, CK-MB and Troponin I have been tested with 10,000 ng/mL Skeletal Troponin I,
2,000 ng/mL Troponin T,
1,390 ng/mL CK-MM,
1,000 ng/mL CK-BB and
20,000 ng/mL Cardiac Myosin.
No cross-reactivity was observed, indicating that the Cardiac Combo Rapid Test has a high degree of specificity for Myoglobin, CK-MB and Troponin I.

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Interfering Substances

The **Cardiac Combo Rapid Test** has been tested and no interference was observed in specimens containing 110 mg/mL human albumin, 6 mg/mL bilirubin, 10 mg/mL hemoglobin, 5 mg/mL cholesterol and 15 mg/mL triglycerides.
The following compounds have also been tested using the Cardiac Combo Rapid Test and no interference was observed.

Acetaminophen	Chloramphanicol	Flunarizine Hydrochloride	Nifedipine
Acetoacetic Acid	Chlordiazepoxide	Furosemide	Oxalic Acid
Acetylsalicylic acid	Cilazapril	Gentisic Acid	Oxazepam
Anisodamine	Creatine	Hydrochlorothiazide	Pentoxifyline
Ascorbic Acid	Diclofenac	Isosorbide Mononitrate	Phenobarbital
Atenolol	Digoxin	Labetalol	Quinine
Atorvastatin Calcium	DL-Tyrosine	Metoprolol Tartrate	Ramipril
Caffeine	Ethanol	Moracizine Hydrochloride	Verapamil
Captopril	Felodipine		

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Symbols used with DRG Assays

Symbol	English	Deutsch	Français	Español	Italiano
	Consult instructions for use	Gebrauchsanweisung beachten	Consulter les instructions d'utilisation	Consulte las instrucciones de uso	Consultare le istruzioni per l'uso
CE	European Conformity	CE-Konfirmitäts-kennzeichnung	Conformité aux normes européennes	Conformidad europea	Conformità europea
IVD	In vitro diagnostic device	In-vitro-Diagnostikum	Uage Diagnostic in vitro	Para uso Diagnóstico in vitro	Per uso Diagnostica in vitro
RUO	For research use only	Nur für Forschungszwecke	Seulement dans le cadre de recherches	Sólo para uso en investigación	Solo a scopo di ricerca
REF	Catalogue number	Katalog-Nr.	Numéro de catalogue	Número de catálogo	Numero di Catalogo
LOT	Lot. No. / Batch code	Chargen-Nr.	Numéro de lot	Número de lote	Numero di lotto
Σ	Contains sufficient for <n> tests/	Ausreichend für "n" Ansätze	Contenu suffisant pour "n" tests	Contenido suficiente para <n> ensayos	Contenuto sufficiente per "n" saggi
	Storage Temperature	Lagerungstemperatur	Température de conservation	Temperatura de conservación	Temperatura di conservazione
	Expiration Date	Mindesthaltbarkeits-datum	Date limite d'utilisation	Fecha de caducidad	Data di scadenza
	Legal Manufacturer	Hersteller	Fabricant	Fabricante	Fabbricante
Distributed by	Distributor	Vertreiber	Distributeur	Distribuidor	Distributore
Content	Content	Inhalt	Conditionnement	Contenido	Contenuto
Volume/No.	Volume / No.	Volumen/Anzahl	Volume/Quantité	Volumen/Número	Volume/Quantità

Symbol	Portugues	Dansk	Svenska	Ελληνικά
	Consulte as instruções de utilização	Se brugsanvisning	Se bruksanvisningen	Εγχειρίδιο χρήστη
CE	Conformidade com as normas europeias	Europaeisk overensstemmelse	Europeisk överensstämmelse	Ευρωπαϊκή Συμμόρφωση
IVD	Diagnóstico in vitro	In vitro diagnostik	Diagnostik in vitro	in vitro διαγνωστικό
REF	Catálogo n.º	Katalognummer	Katalog nummer	Αριθμός καταλόγου
LOT	No do lote	Lot nummer	Batch-nummer	Αριθμός Παρτίδος
Σ		Indeholder tilsttrækkeligt til "n" test	Innehåller tillräckligt till "n" tester	Περιεχόμενο επαρκές για «n» εξετάσεις
	Temperatura de conservação	Opbevarings-temperatur	Förvaringstempratur	Θερμοκρασία αποθήκευσης
	Prazo de validade	Udløbsdato	Bäst före datum	Ημερομηνία λήξης
	Fabricante	Producent	Tillverkare	Κατασκευαστής
Content	Conteúdo	Indhold	Innehåll	Περιεχόμενο
Volume/No.	Volume/Número	Volumen/antal	Volym/antal	Όγκος/αριθ..