This package insert follows the Pharmaceuticals, Medical devices and Other Therapeutic Products Act of Japan.

In Vitro Diagnostics
Marketing Approval No. 21600AMZ00488000

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This package insert must be read carefully prior to use.

Creatinine assay kit
(Classification No.: 30161002)

QUALIGENT CRE

General Precautions **

1. This product is for in vitro diagnostic use, and must not be used for any other purposes.
2. Clinicians should make a comprehensive clinical decision based on assay results in conjunction with clinical symptoms and other examination results.
3. For the effects of an administered drug on the measured value, carefully read the Precautions for Use in the package insert of the drug, especially the section about the effects on laboratory test results. Please also read carefully the "2. Interfering Substances," in the "Procedural Precautions" section, as well as "2. Precautions for Assessment" in the "Assessment of Assay Results" section, of this package insert.
4. This product should be used only as directed in this package insert. Reliability of results cannot be guaranteed if there are any deviations from the instructions in this package insert.
5. If the reagent accidentally comes in contact with eyes and/or mouth, rinse immediately with ample water as first aid, and consult the doctor if required.
6. Carefully read the operating instructions for each type of automated analyzers prior to using this product. Parameters for each type of analyzers are available, and can be requested from SEKISUI MEDICAL CO., LTD. if required.
7. Perform a quality control test prior to assay to ensure accuracy.

Description (Kit Components) *

Component: Ingredients

CRE Enzyme Solution 1:	Creatinase Sarcosine oxidase N-Ethyl-N-sulfobutyl-*m*-toluidine disodium salt
CRE Enzyme Solution 2:	Creatininase 4-Aminoantipyrine

Intended Use

Measurement of creatinine in serum, plasma, or urine

Creatinine is a degradation product of high-energy creatine phosphate that is released into the blood from the muscles and nerves. Creatinine is filtered by the renal glomeruli and is excreted in the urine, mostly without reabsorption.
Because the blood level of creatinine is increased in patients with renal failure, uremia, and heart failure, it plays an important role as an index of kidney function in the diagnosis and evaluation of these diseases.

Assay Principle **

1. Assay Principle

In the first reaction, creatine in samples is degraded into water and oxygen by the action of creatinase, sarcosine oxidase, and catalase.
In the second reaction, creatinine in samples is converted to creatine by the action of creatininase and then sarcosine is produced by the action of creatinase. In the presence of hydrogen peroxide produced by sarcosine oxidase and peroxidase (POD), oxidative condensation of N-ethyl-N-sulfobutyl-*m*-toluidine (ESBmT) and 4-aminoantipyrine is allowed to occur. The concentration of creatinine is determined by measuring the absorbance of the resulting quinone dye (red-purple).

First reaction:

$$\text{Creatine} + H_2O \xrightarrow{\text{Creatinase}} \text{Sarcosine} + \text{Urea}$$

$$\text{Sarcosine} + O_2 + H_2O \xrightarrow{\text{Sarcosine oxidase}} \text{Glycine} + \text{HCHO} + H_2O_2$$

$$2H_2O_2 \xrightarrow{\text{Catalase}} H_2O + O_2$$

Second reaction:

$$\text{Creatinine} + H_2O \xrightarrow{\text{Creatininase}} \text{Creatine}$$

$$\text{Creatine} + H_2O \xrightarrow{\text{Creatinase}} \text{Sarcosine} + \text{Urea}$$

$$\text{Sarcosine} + O_2 + H_2O \xrightarrow{\text{Sarcosine oxidase}} \text{Glycine} + \text{HCHO} + H_2O_2$$

$$H_2O_2 + \text{ESBmT} + \text{4-Aminoantipyrine} \xrightarrow{\text{POD}} \text{Quinone dye (red-purple)}$$

2. Features

1) Liquid reagents, ready-to-use.
2)The enzymatic method is employed.

Procedural Precautions **

1. Properties of Samples and Sampling Methods

1) Samples
Serum, plasma, or urine (primitive or diluted 1:21) may be used.
2) Storage of samples[1)]
If the isolated serum or plasma sample cannot be tested on the same day, specimens should be stored as follows:
2–10°C: for tests within 1 week
≤ -20°C: for tests after more than 1 week
Bring samples to room temperature (15–30°C) before use.
Urine samples should be tested on the same day.

2. Interfering substances

1) Assay results are not affected by free bilirubin (up to 20 mg/dL), conjugated bilirubin (up to

20 mg/dL), hemoglobin (up to 300 mg/dL), ascorbic acid (50 mg/dL), or formazin turbidity (up to 3000 FTU).

2) Turbid samples such as chyle samples may give positive errors to analytical results.

3) In high immunoglobulin samples, turbidity may be produced after adding the first reagent, and negative errors may be given to analytical results.

4) Sodium azide that is added as a preservative for samples may give positive errors to analytical results.

3. Others

1) Always use Serum Multicalibrator (SEKISUI), Seronorm Multicalibrator or Anaserum CRE Standard Solution for calibration.

2) Precautions for assay range
If the concentration of sample exceeds assay range, dilute the sample with saline and repeat the measurement.

Dosage/Administration (Assay Procedure) **

1. Preparation of reagents

Reagent (1): CRE Enzyme Solution 1 is ready to use.

Reagent (2): CRE Enzyme Solution 2 is ready to use.

2. Assay Procedure

This product is compatible with Hitachi 9000 series and LABOSPECT series automated analyzers. Assay procedure is indicated below.

Sample 2.5 μL + Reagent (1) 100 μL → (37°C, 5 min) → Measurement (Absorbance I※)

+ Reagent (2) 50 μL → (37°C, 5 min) → Measurement (Absorbance II※)

→ Calculation of concentration

※ Absorbance I and II: The difference in absorbance between 700 nm and 546 nm

Calibration material: Serum Multicalibrator (SEKISUI), Seronorm Multicalibrator or Anaserum CRE Standard Solution (Manufacture's assigned value)

Reagent blank: Purified water or saline

Assessment of Assay Results **

1. Reference standard range[2)]

Serum: Male, 0.65–1.07 mg/dL
Female, 0.46–0.79 mg/dL

Urine: 0.5–1.5 g/day

2. Precautions for Assessment

There may be reactions or interfering reactions with non-target substances. If assay results appear to be unreliable, repeat the measurement (if necessary, after dilution) or try another analytical methods.

Performance

1. Sensitivity

1) Reagent blank: absorbance being equal to or lower than 0.05

2) Sensitivity: The absorbance is 0.15–0.27 per 10 mg/dL of creatinine.

2. Accuracy: 90–110% of the expected assay value

3. Within-run Reproducibility:

Coefficient of variation ≤ 5%

(Test methods used for 1. –3. are in-house methods.)

4. Measurement Range[10)]: (On a Hitachi 9000 series automated analyzer)

0.1–230 mg/dL

5. Correlatio[10)]

1) Serum N=75 r=0.999 y=1.03x -0.03
Control method: Approved in vitro diagnostic (enzymatic method)

2) Plasma N=50 r=0.999 y=0.98x-0.01
Control method: Approved in vitro diagnostic (enzymatic method)

3) Urine (primitive urine)
N=55 r=0.999 y=0.97 x+1.82
Reference method: Approved in vitro diagnostic (Enzymatic method: urine diluted 1:21)

6. Standard Material

SRM914 (NIST)

Precautions for Use or Handling

1. Precautions for Handling (to Ensure Safety)

1) All samples used in the test should be handled as a material possibly infected with HIV, HBV, HCV, or other viruses. To prevent infection, use disposable gloves and avoid mouth pipetting during the test.

2) Proclin 300, which possesses skin-irritative potential, is added as an antiseptic agent in the CRE Enzyme Solution 2. Therefore, if the reagent comes in contact with skin or clothes, rinse immediately with ample water, and consult the doctor if skin irritation develops.

2. Precautions for use

1) This product should be stored as directed, without freezing. Freezing can deteriorate the reagents, which can produce inaccurate results. Therefore, avoid using the reagents which have been previously frozen.

2) Do not use expired reagents. Use of such reagents cannot guarantee the reliability of measurement values.

3) Do not replenish the reagents.

4) Do not perform the assay under direct sunlight

3. Precautions for Disposal

1) Before disposal, used samples and their containers must be immersed in sodium hypochlorite solution at a concentration of greater than 0.1% for longer than 1 hour or autoclaved at 121ºC for 20 minutes.

2) To prevent infections from spilled samples or solutions containing samples, wipe the spilled area thoroughly with disinfectants such as sodium hypochlorite solution at a concentration of greater than 0.1%.

3) The reagents and treated samples should be discarded as medical waste or industrial waste according to the waste disposal regulations.

4) The reagents should be disposed of in accordance with the Water Pollution Control act or related regulations.

4. Other precautions

1) Do not use the containers for other purposes.
2) Do not take apart the reagent cartridge before use.

Storage and Shelf Life

1. Storage temperature: 2–10°C
2. Shelf life: 13 months from the date of manufacture (The expiration date is printed on the outer package.)

Packaging *

Name	Package		
QUALIGENT CRE	Set (Cassette for Hitachi 9000 series)	CRE Enzyme Solution 1 1 × 15.0 mL CRE Enzyme Solution 2 1 × 7.5 mL	× 2
	L set (Set for Hitachi LABOSPECT series)	CRE Enzyme Solution 1 1 ×40 mL CRE Enzyme Solution 2 1 × 20 mL	× 2

References **

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