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

In Vitro Diagnostics
Marketing Notification No. 13A2X00197220004

**Revised: January 2017 (3rd edition)
*Revised: February 2012 (2nd edition)

This package insert must be read carefully prior to use.

Digoxin assay kit
(Classification No.: 30386000)

Nanopia TDM Digoxin

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. 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.
4. 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.
5. 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.
6. Perform a quality control test prior to assay to ensure accuracy.

Description (Kit Components)

Component: Ingredients
DIG Antibody Solution 1: Anti-digoxin mouse monoclonal antibody
DIG Latex Reagent 2: Digoxin-coated latex

Intended Use

Measurement of digoxin in serum or plasma

Digoxin is a digitalis product that enhances myocardial contractility.[1)] It is most commonly used for treatment of congestive cardiac failure and arrhythmias such as atrial fibrillation. The therapeutic range of digoxin is narrow and individual variation occurs with respect to the absorption, distribution, metabolism, and excretion of this drug. In addition, the blood level relative to dosage is altered by concomitant medications or changes of the underlying disease. Monitoring the blood level of digoxin is effective for designing a regimens that achieves appropriate efficacy while avoiding symptoms of toxicity.[2), 3)]

Assay Principle

1. Assay Principle

When a certain amount of anti-digoxin antibody is added and reacted with a sample, consumption of the antibody depends on its content in the sample. When digoxin-coated latex is added, residual anti-digoxin antibody reacts with the latex and forms aggregates. Since the extent of aggregation depends on the digoxin concentration in the sample, the digoxin concentration can be determined by measuring aggregation as the change of absorbance.

Sample (digoxin) + Anti-digoxin antibody ⟶ Antigen-antibody reaction

Unreacted anti-digoxin antibody + Digoxin-coated latex ⟶ Aggregation by antigen-antibody reaction

2. Features

1) Because a highly specific monoclonal antibody is used, this product shows excellent sensitivity and accuracy.
2) Liquid reagents, ready-to-use.
3) Applicable to various automated analyzers.

Procedural Precautions ** *

1. Properties of Samples and Sampling Methods

1) Samples
Serum and plasma (heparin plasma, EDTA plasma and citrated plasma) may be used. Do not use whole blood.
2) Storage of samples[2)]
If serum or plasma samples cannot be measured on the day of separation, store them as follows. Avoid repetition of freezing and thawing.
2–8°C: for tests within 1 week
≤ -20°C: for tests within 6 months
Bring samples to room temperature (15–30°C) before use.
3) Caution must be exercised, because a separating agent, etc. in the blood collection tube may affect assay values.[9)]
4) Sampling should be performed after removing insoluble matter from the sample.
5) It has been reported that blood samples should be collected at 12 hours after administration to accurately evaluate the blood level of digoxin.[3)]

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 500 mg/dL), ascorbic acid (up to 50 mg/dL), or rheumatoid factors (up to 500 U/L). If samples contain chyle, artifactual elevation of the digoxin level may occur.
2) Because mouse antibody is used in the assay, artifactual elevation of results may occur if the sample contains human anti-mouse antibody. In this case, perform re-measurement by another method.
3) The following drugs and compounds show no cross-reactivity with this assay system at the following concentrations.

Substance	Concentration (μg/mL)
Acetaminophen	1000
Cortisone	10
Estriol	10
Phenytoin	100
Prednisone	10
Progesterone	10
Secobarbital	100
Testosterone	5
17-α-OH-progesterone	10
Quinidine	100
Hydrochlorothiazide	100
Cortisol	10
Dehydroisoandrosterone	10
Lidocaine	100
Prednisolone	10
Propranolol	100
Spironolactone	10
Phenobarbital	100
Procainamide	100
11-OH-progesterone	10
Ouabain octahydrate	0.15
Furosemide	50

4) Cross-reactivity with the following cardiac glycosides and their metabolites is as follows.

Substance	Concen-tration (μg/mL)	Cross-reactivity (%)
Digoxigenin	50	3.6
Digoxigenin-bis-digitoxoside	5	108.0
Digoxigenin-mono-digitoxoside	5	82.0
Digitoxin	50	4.4
Digitoxigenin	500	0.7
D-(+)-digitoxose	10000	0
Gitoxin	150	0.5

3. Others

1) Use the calibrator designated by SEKISUI MEDICAL as the calibration material.
2) Precautions for assay range
If the digoxin concentration in the sample exceeds the measurement range, dilute the sample with the Negative Calibrator designated by SEKISUI MEDICAL and perform re-measurement.
Do not use any other solution for dilution.

Dosage/Administration (Assay Procedure) **

1. Preparation of reagents

Reagent (1): DIG Antibody Solution 1 is ready to use.
Reagent (2): DIG Latex Reagent 2 is ready to use.
Before using this product, gently invert the DIG Latex Reagent 2 bottle to mix it thoroughly, and check that there are no bubbles.

2. Assay Procedure

This product is compatible with various types of automated analyzer. An example of the assay procedure is indicated below.

Sample 10 μL + Reagent (1) 210 μL → 37°C 5 min → Reagent (2) 70 μL → 37°C 36 sec → Measurement (Absorbance I※) → 37°C 4 min 24 sec → Measurement (Absorbance II※) → Calculation of concentration

※Absorbance I and II: Absorbance at 700 nm
Calibration material: Calibrator designated by SEKISUI MEDICAL (manufacture's assigned value)

Assessment of Assay Results **

1. Therapeutic range

The therapeutic range of digoxin is reported to be (0.5)–1.5 ng/mL taking safety into consideration.[10] At concentrations ≥ 1.5 ng/mL, extracardiac symptoms of digitalis intoxication may occur.[10]

2. Interpretation of results

The blood level of digoxin is affected by the sampling time; dosage; dosage form; method of administration; concomitant medications; and the absorption, distribution, metabolism, and elimination of individual drugs. Therefore, assay results should be interpreted carefully by taking the influence of these factors into consideration.
The correlation between the blood concentration and the clinical response also vary with age, renal function, thyroid function, type and severity of heart disease, and concomitant medications.
The therapeutic range is only a general guide. Assay results and data should be interpreted carefully while taking the symptoms of each patient into consideration.

3. 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) The difference in absorbance between standard solution (0.5 ng/mL) and another standard solution (0 ng/mL) is ≥ 0.03.
2) The difference in absorbance between standard solution (5 ng/mL) and another standard solution (0.5 ng/mL) is ≥ 0.15.

2. Accuracy: 85–115 % of the expected assay value

3. Within-run Reproducibility:

Coefficient of variation ≤ 15 %

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

4. Measurement Range[11]: (On Hitachi 7170S automated analyzer)

0.2–5 ng /mL

5. Correlation[11]

1) Serum N=40 r=0.991 y=0.98x–0.01

Control method: Approved in vitro diagnostic (enzyme immunoassay)

2) Plasma N=40 r=0.997 y=1.02x+0.03
Control method: Approved in vitro diagnostic (enzyme immunoassay)

6. Standard Material
Digoxin (U.S. Pharmacopoeia)

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) Each of the constituent reagents contains sodium azide as an antiseptic agent. Therefore, if the reagent comes in accidentally contact with eyes, mouth or skin, rinse immediately with ample water as first aid, and consult the doctor if required.

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 mix materials from different kit lot numbers.
5) 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.
5) Each of the constituent reagents contains sodium azide as an antiseptic agent. It can react with lead or copper pipes to produce the highly explosive metal azide. Therefore, the reagent should be flushed with large amounts of water during disposal.

4. Other precautions
Do not use the containers for other purposes.

Storage and Shelf Life **

1. Storage temperature: 2–8°C
2. Shelf life: 2 years from the date of manufacture
(The expiration date is printed on the outer package.)

Packaging

Name		Package
Nanopia TDM Digoxin	DIG Antibody Solution 1	1 × 42 mL
	DIG Latex Reagent 2	1 × 14 mL

Constituent reagents are available in other configurations. For further details please contact SEKISUI MEDICAL CO., LTD.

References * *

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