



Neonatal TSH Test System  
Total Reaction Time = 3hr  
Product Code: 3425-300

## 1.0 INTRODUCTION

**Intended Use: The Quantitative Determination of Thyrotropin Concentration in Human Whole Blood by a Microplate Enzyme Immunoassay, Colorimetric**

## 2.0 SUMMARY AND EXPLANATION OF THE TEST

Determination of hypothyroidism within the first few days of birth has been recognized as the single most important diagnostic test in neonates by the American Thyroid Association. The need for its early detection and treatment has resulted in the establishment of screening centers by federal and state health departments. A program of early screening of neonates for congenital hypothyroidism was started in Quebec, Canada in the early seventies. They used dry blood spots on filter paper as the sampling device. Very soon the program was followed by other major public health institutions in Canada and the US. By 1978, almost one million infants had been screened and an incidence rate of congenital hypothyroidism was established to be approximately 1 in 7000 births.

Congenital hypothyroidism is probably the single most common preventable cause of mental retardation. Diagnosis and treatment of congenital hypothyroidism within the first 1-2 months after birth appears to be necessary in order to prevent severe mental retardation.

Measurement of the serum concentration of thyrotropin (TSH), a glycoprotein with a molecular weight of 28,000 daltons and secreted from the anterior pituitary, is generally regarded as the most sensitive indicator available for the diagnosis of primary and secondary (pituitary) hypothyroidism.<sup>1,2</sup> Increase in serum concentrations of TSH, which is primarily responsible for the synthesis and release of thyroid hormones, is an early and sensitive indicator of decrease thyroid reserve and in conjunction with decreased thyroxine (T4) concentrations is diagnostic of primary hypothyroidism. The expected increase in TSH concentrations demonstrates the classical negative feedback system between the pituitary and thyroid glands. That is, primary thyroid gland failure reduces secretion of the thyroid hormones, which in turn stimulates the release of TSH from the pituitary.

In this method, TSH dried whole blood calibrator, patient specimen or control is first added to a streptavidin coated well. Elution buffer containing biotinylated monoclonal antibodies are added and the reactants mixed. Reaction between the biotinylated x-TSH and the TSH in the dried blood spot forms a complex that binds with the streptavidin coated to the well.

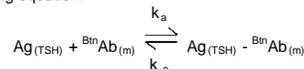
After the completion of the first elution/incubation period, the enzyme conjugate is added to the Ag-Ab complex deposited on the plastic surface. The enzyme labeled x-TSH antibody binds to the TSH making a sandwich complex with two antibodies bound to the antigen during a second incubation. The microplate is washed to remove unreacted enzyme. Finally, the activity of the enzyme present on the surface of the well is quantitated by reaction with a suitable substrate to produce color.

## 3.0 PRINCIPLE

### Sequential immunoenzymometric assay Type 4:

The essential reagents required for a sequential immunoenzymometric assay include high affinity and specificity antibodies (enzyme conjugated and immobilized), with different and distinct epitope recognition, **in excess**, and native antigen. In this procedure, the immobilization takes place during the assay at the surface of a microplate well through the interaction of streptavidin coated on the well and exogenously added biotinylated monoclonal anti-TSH antibody.

Upon mixing elution buffer with monoclonal biotinylated antibody added, and a dried blood spot containing the native antigen, reaction results between the eluted antigen and the antibody to form an antigen-antibody complex. The interaction is illustrated by the following equation:



$\text{B}^{\text{m}}\text{Ab}_{(\text{m})}$  = Biotinylated Monoclonal Antibody (Excess Quantity)

$\text{Ag}_{(\text{TSH})}$  = Native Antigen (Variable Quantity)

$\text{Ag}_{(\text{TSH})} - \text{B}^{\text{m}}\text{Ab}_{(\text{m})}$  = Antigen-Antibody complex (Variable Quant.)

$k_a$  = Rate Constant of Association

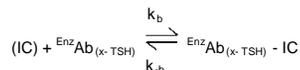
$k_{-a}$  = Rate Constant of Dissociation

$\text{Ag}_{(\text{TSH})} - \text{B}^{\text{m}}\text{Ab}_{(\text{m})} + \text{Streptavidin}_{\text{CW}} \Rightarrow \text{immobilized complex (IC)}$

$\text{Streptavidin}_{\text{CW}}$  = Streptavidin immobilized on well

Immobilized complex (IC) = Ag-Ab bound to the well

After a suitable incubation period, the antibody-antigen bound fraction is separated by decantation or aspiration. Another antibody (directed at a different epitope) labeled with an enzyme is added. Another interaction occurs to form an enzyme labeled antibody-antigen-biotinylated-antibody complex on the surface of the wells.



$\text{EnzAb}_{(\text{x-TSH})}$  = Enzyme labeled Antibody (Excess Quantity)

$\text{EnzAb}_{(\text{x-TSH})} - \text{IC}$  = Antigen-Antibodies Complex

$k_b$  = Rate Constant of Association

$k_{-b}$  = Rate Constant of Dissociation

Excess enzyme is washed off via a wash step. A suitable substrate is added to produce color measurable with the use of a microplate spectrophotometer. The enzyme activity on the well is directly proportional to the TSH concentration in the dried blood spot. By utilizing several different dried spots of known antigen concentration, a dose response curve can be generated from which the antigen concentration of an unknown can be ascertained.

## 4.0 REAGENTS

### Materials Provided:

#### A. N-TSH Calibrators – Dried Blood Spots (Two rows by six dots levels - 2 x 6)

Six (6) levels of TSH Antigen in dried blood spots at approximate concentrations of 0(A), 7 (B), 18(C), 45(D), 110(E) and 250(F)  $\mu\text{IU/ml}$  placed on S&S type 903 filter paper. Store at 2-8°C. A preservative has been added.

**Note 1:** The **Lot Specific** calibrators, whole human blood based, were calibrated using a reference preparation, which was assayed against the WHO 2<sup>nd</sup> IRP 80/558.

**Note 2:** The exact values are printed on the outside of the aluminum pouch.

#### B. N-TSH Controls – Dried Blood Spots (Two rows by three dots - 2 x 3)

Three (3) levels of whole human blood controls with different concentrations of TSH antigen placed on S&S type 903 filter paper. Store at 2-8°C. A preservative has been added.

**Note 1:** The controls, whole human blood based, were manufactured to fall within significant clinical ranges using the same WHO reference preparation as the calibrators (see above).

**Note 2:** The exact values are printed on the outside of the aluminum pouch.

#### C. N-TSH Enzyme Reagent – 13ml/vial - $\text{E}$

One (1) vial containing enzyme labeled affinity purified polyclonal goat x-TSH IgG in buffer, and preservative. Store at 2-8°C.

#### D. N-TSH Biotin Reagent – 13ml vial - $\nabla$

Anti-TSH monoclonal IgG labeled with biotin in buffer, green dye and preservative. Store at 2-8°C.

#### E. Streptavidin Coated Plate – 96 wells – Icon $\downarrow$

One 96-well microplate coated with streptavidin and packaged in an aluminum bag with a drying agent. Store at 2-8°C.

#### F. Wash Solution Concentrate – 20 ml/vial - Icon $\blacktriangledown$

One (1) vial containing a surfactant in buffered saline. A preservative has been added. Store at 2-8°C.

#### G. Substrate Solution – 12ml/vial - Icon $\text{S}^{\text{A}}$

One (1) vial containing tetramethylbenzidine (TMB) and hydrogen peroxide ( $\text{H}_2\text{O}_2$ ) in buffer. Store at 2-8°C.

#### H. Stop Solution – 8ml/vial - Icon $\text{E}^{\text{m}}$

One (1) vial containing a strong acid (1N  $\text{H}_2\text{SO}_4$ ). Store at 2-8°C.

## I. Product Instructions.

**Note 1:** Do not use reagents beyond the kit expiration date.

**Note 2:** Avoid extended exposure to heat and light. **Opened reagents are stable for sixty (60) days when stored at 2-8°C. Kit and component stability are identified on the label.**

**Note 3:** Above reagents are for a single 96-well microplate.

### 4.1 Required But Not Provided:

- Laboratory Shaker capable of 150rpm rotation.
- Dispenser(s) for repetitive deliveries of 0.050ml (50 $\mu\text{l}$ ), 0.100ml (100 $\mu\text{l}$ ) and 0.350ml (350 $\mu\text{l}$ ) volumes with a precision of better than 1.5% (optional).
- Microplate washer or a squeeze bottle (optional).
- Microplate Reader with 450nm and 620nm wavelength absorbance capability
- 1/8" Paper punch for dispensing dried blood spots.
- Absorbent Paper for blotting the microplate wells.
- Plastic wrap or microplate cover for incubation steps.
- Vacuum aspirator (optional) for wash steps.
- Timer.
- Storage container for storage of wash buffer.
- Distilled or deionized water.
- Quality Control Materials.

## 5.0 PRECAUTIONS

**For In Vitro Diagnostic Use  
Not for Internal or External Use in Humans or Animals**

All products that contain human serum have been found to be non-reactive for Hepatitis B Surface Antigen, HIV 1&2 and HCV Antibodies by FDA licensed reagents. Since no known test can offer complete assurance that infectious agents are absent, all human serum products should be handled as potentially hazardous and capable of transmitting disease. Good laboratory procedures for handling blood products can be found in the Center for Disease Control / National Institute of Health, "Biosafety in Microbiological and Biomedical Laboratories," 2nd Edition, 1988, HHS Publication No. (CDC) 88-8395.

**Safe Disposal of kit components must be according to local regulatory and statutory requirement.**

## 6.0 SPECIMEN COLLECTION AND PREPARATION

The sampling from neonates is performed by lancing the heels of the infants and then spotting enough whole blood on S&S filter paper card (Type# 903) to fill the marked circle. Allow the filter paper to dry at room temperature overnight away from heat and moisture. Enclose the dry blood specimen (DBS) in a moisture barrier plastic bag with desiccant and send to the laboratory.

The specimen should be collected 3-7 days post partum, Physical data including age and weight of the infant, whether a multiple birth, or a premature birth etc should accompany the sample. It is important for the clinician to know these facts in order to properly assess the thyroid status of the infant. The dried blood samples are stable at 2-8°C for 2-3 weeks if stored in zip-lock, moisture resistant bags with desiccants. Cord blood can be used upon validation of the process by the individual laboratory.

**In patients receiving therapy with high biotin doses (i.e. >5mg/day), no sample should be taken until at least 8 hours after the last biotin administration, preferably overnight to ensure fasting sample.**

## 7.0 QUALITY CONTROL

Each laboratory should assay controls at levels in the hypothyroid, euthyroid and hyperthyroid range for monitoring assay performance. These controls should be treated as unknowns and values determined in every test procedure performed. Quality control charts should be maintained to follow the performance of the supplied reagents. Pertinent statistical methods should be employed to ascertain trends. The individual laboratory should set acceptable assay performance limits. Significant deviation from established performance can indicate unnoticed change in experimental conditions or degradation of kit reagents. Fresh reagents should be used to determine the reason for the variations.

## 8.0 REAGENT PREPARATION

### 1. Wash Buffer

Dilute contents of wash solution to 1000ml with distilled or deionized water in a suitable storage container. Store at room temperature 2-30°C for up to 60 days.

**Note 1: Do not use reagents that are contaminated or have bacteria growth.**

## 9.0 TEST PROCEDURE

*Before proceeding with the assay, bring all reagents and patient samples to room temperature (20 - 27°C).*

**\*\*Test Procedure should be performed by a skilled individual or trained professional\*\***

- Obtain the required number of microwells for each calibrator, control and patient sample to be assayed in duplicate. **Replace any unused microwell strips back into the aluminum bag, seal and store at 2-8°C.**
- Punch out a 1/8" blood dot out of each calibrator, control and specimens into the assigned wells. **(NOTE: Do not punch blood dots from areas that are printed or that are near the edge of the blood spot.)**
- Add 0.100 ml (100 $\mu\text{l}$ ) of N-TSH Biotin Reagent to all the wells.
- Shake the microplate gently for 20-30 seconds to mix. **(NOTE: Make sure that all blood dots are fully submerged in the liquid and not stuck to the walls of the microwells.)**
- Cover with a microplate cover and rotate for 90 minutes at ambient temperature using a laboratory rotator set @ 150rpm. **(Note: see alternative overnight incubation).**
- Discard the contents of the microplate by decantation or aspiration. If decanting, blot the plate dry with absorbent paper. **(NOTE: Make sure all the blood dots are removed at this point. There should be no dots left in the microwells.)**
- Add 0.350ml (350 $\mu\text{l}$ ) of wash buffer (see Reagent Preparation Section), decant (tap and blot) or aspirate. Repeat four (4) additional times for a total of five (5) washes. **An automatic or manual plate washer can be used. Follow the manufacturer's instruction for proper usage. If a squeeze bottle is employed, fill each well by depressing the container (avoiding air bubbles) to dispense the wash. Decant the wash and repeat four (4) additional times.**
- Add 100  $\mu\text{l}$  of N-TSH Enzyme Reagent to each well.
- Cover the microplate and rotate for 45 minutes at ambient temperature using a laboratory rotator set @ 150rpm. **(Note: see alternative overnight incubation).**
- Repeat wash step #7.
- Add 0.100 ml (100 $\mu\text{l}$ ) of substrate solution to each well.
- Cover the microplate and rotate for 45 minutes at ambient temperature using a laboratory rotator set @ 150rpm. **(Note: see alternative overnight incubation).**
- Add 0.050ml (50 $\mu\text{l}$ ) of stop solution to each well and gently mix for 15-20 seconds. **NOTE: Always add reagents in the same order to minimize reaction time differences between wells.**
- Read the absorbance in each well at 450nm (using a reference wavelength of 620-630nm to minimize well imperfections) in a microplate reader. **The results should be read within fifteen (15) minutes of adding the stop solution.**

### 9.1 Alternate overnight procedure:

1. Substitute overnight incubation (12-16hrs) for the 90 minutes with rotation (Step 5). No rotator is required. Seal the plate(s) with plastic wrap.
2. All other steps remain the same.

### 10.0 CALCULATION OF RESULTS

A dose response curve is used to ascertain the concentration of thyrotropin in unknown specimens.

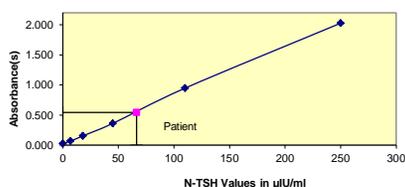
1. Record the absorbance obtained from the printout of the microplate reader as outlined in Example 1.
2. Plot the absorbance for each duplicate serum reference versus the corresponding TSH concentration in  $\mu\text{IU/ml}$  on linear graph paper (do not average the duplicates of the serum references before plotting).
3. Draw the best-fit curve through the plotted points.
4. To determine the concentration of TSH for an unknown, locate the average absorbance of the duplicates for each unknown on the vertical axis of the graph, find the intersecting point on the curve, and read the concentration (in  $\mu\text{IU/ml}$ ) from the horizontal axis of the graph. In the following example, the average absorbance (0.543) intersects the dose response curve at 66.3  $\mu\text{IU/ml}$  TSH concentration (See Figure 1).

**Note:** Computer data reductions software designed for ELISA assay may also be used for the data reduction. If such software is utilized, the validation of the software should be ascertained.

EXAMPLE 1

Sample I.D.	Well Number	Abs (A)	Mean Abs (B)	Value ( $\mu\text{IU/ml}$ )
Cal A	A1	0.024	0.027	0
	B1	0.030		
Cal B	C1	0.069	0.068	7
	D1	0.067		
Cal C	E1	0.156	0.153	18
	F1	0.150		
Cal D	G1	0.369	0.361	45
	H1	0.353		
Cal E	A2	0.937	0.947	110
	B2	0.957		
Cal F	C2	2.056	2.027	250
	D2	1.998		
Control	E2	0.220	0.218	26.2
	F2	0.216		
Control	G2	0.776	0.811	95.3
	H2	0.846		
Patient	A3	0.533	0.543	66.3
	B3	0.553		

Figure 1



\*The data presented in Example 1 and Figure 1 is for illustration only and **should not** be used in lieu of a dose response curve prepared with each assay.

### 11.0 Q.C. PARAMETERS

In order for the assay results to be considered valid the following criteria should be met:

1. The absorbance (OD) of calibrator F should be  $\geq 1.2$
2. Four out of six quality control pools should be within the established ranges.

### 12.0 RISK ANALYSIS

The MSDS and Risk Analysis Form for this product is available on request from Monobind Inc.

### 12.1 Assay Performance

1. It is important that the time of reaction in each well is held constant to achieve reproducible results.
2. Pipetting of samples should not extend beyond ten (10) minutes to avoid assay drift.
3. Highly lipemic, hemolyzed or grossly contaminated specimen(s) should not be used.
4. If more than one (1) plate is used, it is recommended to repeat the dose response curve.
5. The addition of substrate solution initiates a kinetic reaction, terminated by the addition of the stop solution. Therefore, the substrate and stop solution should be added in the same sequence to eliminate any time-deviation during reaction.
6. Plate readers measure vertically. Do not touch the bottom of the wells.
7. Failure to remove adhering solution adequately in the aspiration or decantation wash step(s) may result in poor replication and spurious results.
8. Use components from the same lot. No intermixing of reagents from different batches.
9. Accurate and precise pipetting, as well as following the exact time and temperature requirements prescribed are essential. Any deviation from Monobind IFU may yield inaccurate results.
10. All applicable national standards, regulations and laws, including, but not limited to, good laboratory procedures, must be strictly followed to ensure compliance and proper device usage.
11. It is important to calibrate all the equipment e.g. Pipettes, Readers, Washers and/or the automated instruments used with this device, and to perform routine preventative maintenance.
12. Risk Analysis- as required by CE Mark IVD Directive 98/79/EC - for this and other devices, made by Monobind, can be requested via email from [Monobind@monobind.com](mailto:Monobind@monobind.com).

### 12.2 Interpretation

1. **Measurements and interpretation of results must be performed by a skilled individual or trained professional.**
2. Laboratory results alone are only one aspect for determining patient care and should not be the sole basis for therapy, particularly if the results conflict with other determinants.
3. For valid test results, adequate controls and other parameters must be within the listed ranges and assay requirements.
4. If test kits are altered, such as by mixing parts of different kits, which could produce false test results, or if results are incorrectly interpreted, **Monobind shall have no liability.**
5. If computer controlled data reduction is used to interpret the results of the test, it is imperative that the predicted values for the calibrators fall within 10% of the assigned concentrations.
6. TSH concentration, in the circulation, is dependent upon a multiplicity of factors: hypothalamus gland function, thyroid gland function, and the responsiveness of pituitary to TRH. Thus, thyrotropin concentration alone is not sufficient to assess clinical status.
7. TSH values may be elevated by pharmacological intervention. Domperidone, amidazon, iodide, phenobarbital, and phenytoin have been reported to increase TSH levels.
8. A decrease in thyrotropin values has been reported with the administration of propranolol, methimazol, dopamine and d-thyroxine.<sup>4</sup>
9. Genetic variations or degradation of intact TSH into subunits may affect the binding characteristics of the antibodies and influence the final result. Such samples normally exhibit different results among various assay systems due to the reactivity of the antibodies involved.

### 13.0 EXPECTED RANGES OF VALUES

Recommended guidelines for newborn screening for congenital hypothyroidism have been published by the American Academy of Pediatrics (AAP). For infants 2 to 6 days old, these recommendations categorize TSH concentrations as "normal," "elevated," or "only slightly elevated" relative to values of 20 and 40  $\mu\text{IU/mL}$  (i.e. per milliliter of serum). According to the AAP guidelines, "any infant with a low T4 and TSH concentration greater than 40  $\text{mU/L}$  is considered to have primary hypothyroidism until proved otherwise." Furthermore, "in cases in which the screening TSH concentration is only slightly elevated, above 20  $\text{mU/L}$  but less than 40  $\text{mU/L}$ , another filter paper specimen should be obtained for a subsequent test."

In order to determine the applicability of these ranges to the N-

TSH AccuBind® ELISA Test System, a limited study of 142 newborn normal specimens (3-7 d) was done and the following range was observed.

Range	0.7 $\mu\text{IU/ml}$ - 34 $\mu\text{IU/ml}$
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It is important to keep in mind that establishment of a range of values which can be expected to be found by a given method for a population of "normal"-persons is dependent upon a multiplicity of factors: the specificity of the method, the population tested and the precision of the method in the hands of the analyst. For these reasons each laboratory should depend upon the range of expected values established by the Manufacturer only until an in-house range can be determined by the analysts using the method with a population indigenous to the area in which the laboratory is located.

### 14.0 PERFORMANCE CHARACTERISTICS

#### 14.1 Precision

The within and between assay precisions of the N-TSH AccuBind® ELISA test system were determined by analyses on three different levels of pooled whole blood samples. The number, mean value, standard deviation and coefficient of variation for each of these control sera are presented in Tables 2 and 3.

TABLE 2  
Within Assay Precision (Values in  $\mu\text{IU/ml}$ )

Sample	N	X	$\sigma$	C.V.
Pool 1	24	10.60	0.91	8.6%
Pool 2	24	43.30	3.61	8.3%
Pool 3	24	87.10	4.42	5.1%

TABLE 3  
Between Assay Precision\* (Values in  $\mu\text{IU/ml}$ )

Sample	N	X	$\sigma$	C.V.
Pool 1	10	11.05	1.20	10.8%
Pool 2	10	42.22	3.76	8.9%
Pool 3	10	85.10	5.11	6.0%

\*As measured in ten experiments in duplicate over seven days.

#### 14.2 Sensitivity

The sensitivity (detection limit) was ascertained by determining the variability of the 0  $\mu\text{IU/ml}$  serum calibrator and using the  $2\sigma$  (95% certainty) statistic to calculate the minimum dose. A minimum detectable dose of 1.0  $\mu\text{IU/ml}$  was determined.

#### 14.3 Accuracy

This N-TSH AccuBind® ELISA test system was compared with a reference immunochemiluminescence assay. Biological specimens from hypothyroid, euthyroid and hyperthyroid populations were used (The values ranged from 1.0  $\mu\text{IU/ml}$  - 142  $\mu\text{IU/ml}$ ). The total number of such specimens was 156. The least square regression equation and the correlation coefficient were computed for the N-TSH Elisa in comparison with the reference method. The data obtained is displayed in Table 4.

TABLE 4

Method	Mean (x)	Least Square Regression Analysis	Correlation Coefficient
Monobind	17.83	$y = -1.3223x + 0.975$	0.979
Reference	16.50		

Only slight amounts of bias between the N-TSH test system and the reference method are indicated by the closeness of the mean values. The least square regression equation and correlation coefficient indicates excellent method agreement.

#### 14.4 Specificity

The cross-reactivity of the N-TSH AccuBind® ELISA Test System to selected substances was evaluated by adding the interfering substance to a pool blood matrix at various concentrations. The cross-reactivity was calculated by deriving a ratio between dose of interfering substance to dose of thyrotropin needed to produce the same absorbance.

Substance	Cross Reactivity	Concentration
Thyrotropin (hTSH)	1.0000	-
Follitropin (hFSH)	< 0.0001	1000ng/ml
Lutropin Hormone (hLH)	< 0.0001	1000ng/ml
Chorionic Gonadotropin(hCG)	< 0.0001	1000ng/ml

### 15.0 REFERENCES

1. Hopton MR and Harrap JJ, "Immunoradiometric assay of thyrotropin as a first line thyroid function test in the routine laboratory", *Clinical Chemistry*, 32, 691 (1986).
2. Caldwell G, et al, "A new strategy for thyroid function testing", *Lancet*, I, 1117 (1985).
3. Young DS, Pestaner LC and Gilberman U, "Effects of Drugs on Clinical Laboratory Tests", *Clinical Chemistry*, 21, 3660 (1975).
4. Spencer CA, et al, "Interlaboratory/Intermethod differences in Functional Sensitivity of Immunometric Assays of Thyrotropin (TSH) and Impact on Reliability of Measurement of Subnormal Concentrations of TSH", *Clinical Chemistry*, 41, 367 (1995).
5. American Academy of Pediatrics, "Newborn Screening for congenital hypothyroidism: recommended guidelines", *Pediatrics*, 92, 1203-09 (1993).
6. Centers for Disease Control, Proceedings of a conference on a national model for Standardization of Neonatal Hypothyroid Screening Programs (Atlanta 1979).

Revision: 6 Date: 2019-Jul DCO: 1353  
MP3425 Cat #: 3425-300

Size	1 Plate	2 Plate	5 Plate	10 Plate
Item	96 Test	192 Test	480 Test	960 Test
A)	1 Set	1 Set	2 Sets	4 Sets
B)	1 Set	1 Set	2 Sets	4 Sets
C)	1 x 12 ml	2 x 12 ml	1 x 52 ml	2 x 52 ml
D)	1 x 12 ml	2 x 12 ml	1 x 52 ml	2 x 52 ml
E)	1	2	5	10
F)	1 x 20 ml	1 x 20 ml	1 x 60 ml	2 x 60 ml
G)	1 x 12 ml	2 x 12 ml	1 x 60 ml	2 x 60 ml
H)	1 x 8 ml	2 x 8 ml	1 x 30 ml	2 x 30 ml

For Orders and Inquires, please contact

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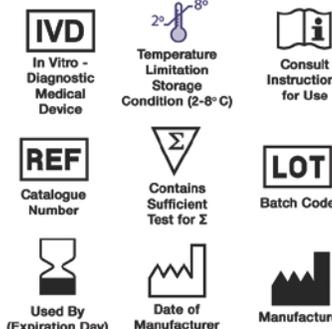
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Glossary of Symbols  
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