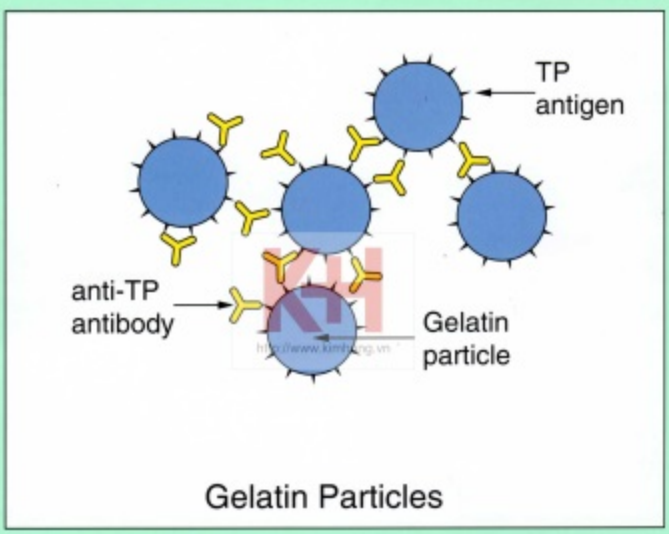
SERODIA®-TP•PA

PASSIVE PARTICLE AGGLUTINATION TEST FOR DETECTION OF ANTIBODIES TO T. PALLIDUM AT THE VARIOUS STAGES OF SYPHILIS.



Gelatin Particles

1. INTENDED TO USE

SERODIA-TP•PA is an in vitro Passive Particle Agglutination Assay for the detection of antibodies to Treponema Pallidum both in serum or plasma specimens.

2. FEATURES

(1) SIMPLE TEST PROCEDURES
(2) PLASMA AND SERUM APPLICABLE
(3) HIGH SPECIFICITY AND SENSITIVITY

FUJIREBIO INC.

SERODIA-TP·PA

PASSIVE PARTICLE AGGLUTINATION TEST FOR DETECTION OF ANTIBODIES TO T. PALLIDUM AT THE VARIOUS STAGES OF SYPHILIS.

1.Stability

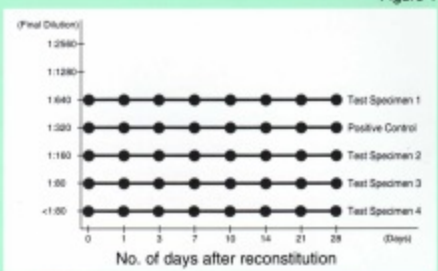
Using kits from lot number of K-40301 at Fujirebio's Hachioji Laboratories, stability after reconstitution was examined at the following different dates respectively from its manufacturing.

Up to 28th day after reconstitution, no fluctuation in the respective titers was observed with all the panels tested.

No further extension than the 28th day after reconstitution was investigated in this study.*

* In light of matter of Quality Control, however, the stability after reconstitution is set 7 days under proper storage conditions at 2~10℃ on the Package Insert.

Figure 1



No. of days after reconstitution

2.Influence of 3 different kinds of Anticoagulants

11 plasma and serum panels were investigated in the Comparative Study to check whether there would be any discrepancies in its test results between serum and plasma specimens of the same blood.

Anticoagulants used in this study were citrate, EDTA and heparin.

As detailed in the diagram, the discrepancies in its test results between the respective two different specimens (serum/plasma) were kept in all the cases within plus/minus 1 doubling dilution. This Comparative Study showed that no significant influence was recognized from the Anticoagulants.
(Department of Venereology, Nihon University, School of Medicine)

Table 1

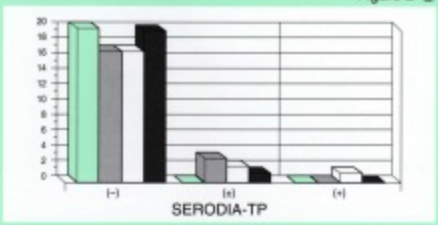
Test specimen	Serum specimen	Plasma specimen		
		Sodium citrate	EDTA	Heparin
1	1: 160	1: 160	1: 160	1: 160
2	1: 5120	1: 2560	1: 5120	1: 5120
3	1: 1280	1: 1280	1: 1280	1: 1280
4	1: 640	1: 320	1: 640	1: 640
5	1: 5120	1:10240	1:10240	1:10240
6	1: 320	1: 320	1: 320	1: 320
7	1:40960	1:20480	1:20480	1:20480
8	1: 2560	1: 1280	1: 1280	1: 2560
9	1: 640	1: 640	1: 640	1: 640
10	1: 2560	1: 1280	1: 2560	1: 2560
11	1: 640	1: 640	1: 640	1: 640

3.High Specificity

The three products (SERODIA-TP•PA/SERODIA-TP/TPHA) were tested to check the occurrence rate of Non-Specific Agglutinations.

Non-Specific Agglutination could not find with SERODIA-TP•PA while SERODIA-TP/TPHA showed Non-Specific Agglutinations.

Figure 2-②



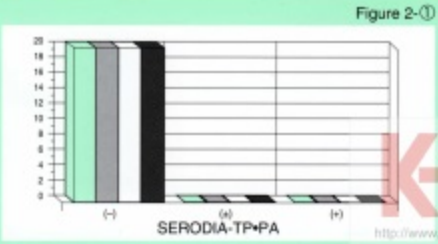
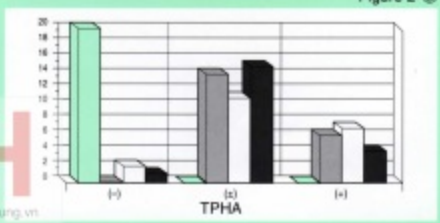


Figure 2-①

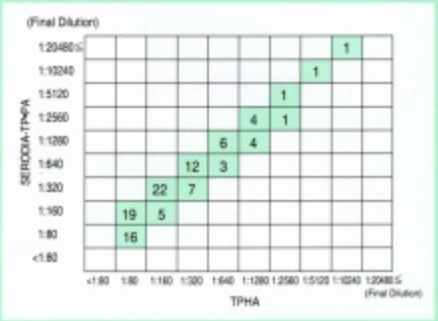
Figure 2-③



4.Correlation-1

Correlation studies were performed by comparing SERODIA-TP•PA and TPHA on 102 specimens. As shown in Figure 3, the correlation within plus minus 1 doubling dilution was 100%.

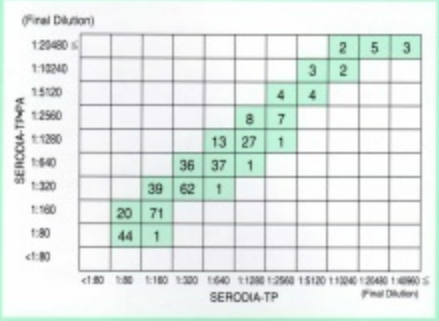
Figure 3



5.Correlation - 2

391 positive samples (serum/plasma) were assayed comparatively to study a correlation between SERODIA-TP and SERODIA-TP•PA.
As shown in Figure 4, all the results between the two different products corresponded 100% within plus/minus 1 doubling dilution.

Figure 4



6.Correlation - 3

A Comparative Study was performed using various kinds of serum samples against SERODIA-TP•PA and SERODIA-TP
(1,586 from healthy adults/279 from pregnant women/180 suffering from Rheumatoid Arthritis).

The correlation ration between the two products was 99.8% (2,040/2,045).

Table 2

		SERODIA-TP			
		+	±	−	Total
SERODIA-TP•PA	+	30	2 *1	0	32
	±	0	0	1*2	1
	−	0	2 *3	2010	2012
	Total	30	4	2011	2045

Number of specimen N=2,045
1,586 from healthy adults
279 from pregnant women
180 suffering from
Rheumatoid Arthritis

*1 FTA-ABS(+)
*2 FTA-ABS(±)
*3 FTA-ABS(−)

Outline of Syphilis

Syphilis is an acute and chronic infectious disease caused by Treponema pallidum (Spirochaeta pallida) which is a genus of motile bacteria, 5-15 μ in length and 0.2 μ in width, containing about 10 flexible, undulating, spiral shaped rods.

As the T. pallidum cannot grow in artificial culture media, diagnostic tests utilizing T. Pallidum antigens have been slow in coming.

Syphilis designated as a venereal disease, or VD, along with Gonorrhea, Chancroid and Lymphogranuloma venereum is transmitted by direct contact, usually through sexual intercourse. After an incubation period of 12 to 30 days, the first symptom to appear are chancres, soon followed by syphilitic ulcers which then spontaneously disappear in a few weeks. During this first stage (Primary syphilis), the T. pallidum propagates in related lymph nodes to be distributed to the whole body through the blood stream.Eventually serological tests turn positive 4-6 weeks after infection.

The second stage constitutes symptomatic syphilis which develops the secondary syphilid, a skin eruption of various appearances with mucous patches and the latent syphilis without any symptoms.

The third stage is marked by the formation of gumma, or syphiloma, and cardiovascular lesions.

At the final stage, parasyphilis, lesions reach to the central nervous system.

Though the above clinical courses is typical of acquired syphilis, patients with parasyphilis are quite rare. On the other hand, congenital syphilis is caused by T. pallidum transmitted through the placenta where it infects the fetus. Treatment with antibiotics such as penicillins and macrolides at the earliest disease stage and prophylactic measures are ways to prevent epidemics. For this purpose, antenatal and donor blood screenings are mandatory in most of countries around the world.

Disease stage	Primary	Secondary	Tertiary	Quaternary
Period	3weeks	3months	3years	10years
Serological test	Negative	Positive		
Progress	Infection Chancre	Syphilitic roseola Papular syphilid Mucous plaque Condyloma latum Syphilitic leukoderma Alopecia syphilitica	Gumma Nodular syphilis	Cardiovascular syphilis Neurosyphilis

Clinical Significance in Serodiagnosis of Syphilis

Darkfield Examination is a means for diagnosing syphilis in the primary stages by demonstrating motile treponemes in a chancre, while serological tests are often not positive for 14-21 days after contact.

However, there is difficulty in detecting treponemes from dry eruption or blood with this technique. Thus serological tests are recognized as important indicators in syphilis diagnosis.

Currently performed serological tests are classified into two groups by the kinds of antigens utilized: One is a Serologic Test for Syphilis, STS, utilizing lipoidal antigens. This includes the Rapid Plasma Reagin (RPR) test, Venereal Disease Research Lab (VDRL) test and modified Wasserman test, and the other ranges from TP Hemagglutination, or TPHA to Fluorescent Treponemal Antibody Absorption (FTA-ABS) and Enzyme immunoassay (EIA) utilizing treponemal antigens. In practice, for a rapid screening, combined STS and TPHA tests are performed and, if necessary, confirmed by FTA-ABS. TPHA and FTA-ABS are especially recommended as diagnostic aids for patients with reactive RPR who have atypical signs of primary or secondary syphilis, or who have no signs of syphilis. To diagnose syphilis and monitor its treatment, quantitative assays such as antibody titer measurements have become widely used. Furthermore, IgM detection before seroconversion to IgG at early or latent syphilis contributes a great deal to the early diagnosis of both congenital and acquired syphilis and to effective therapy monitoring.

Progression in Antibody Production at the Primary Stage of Syphilis

When infected with T. pallidum, the body's immune system is stimulated to fend it off. One of a series of defenses is humoral immunity whereby the B cells begin producing. T. pallidum-specific antibodies. IgM is the first to be produced upon infection early in primary syphilis. Then gradually IgG production, peaking and then decreasing. While IgM disappears when active infection ceases, IgG remains positive at certain degrees, though in lower levels, in patients' blood streams long after the disease has been cured.

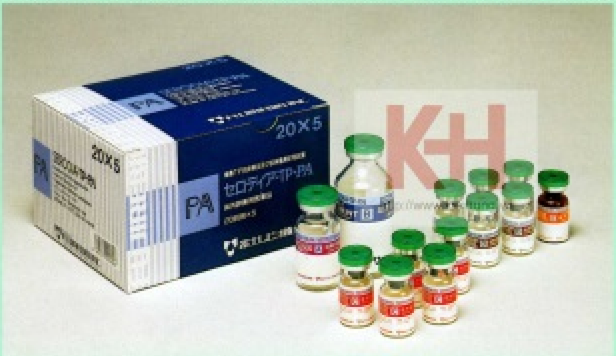
KIT COMPONENTS

The kit contains sufficient reagents to perform 100, 220, 550, and 600 qualitative tests.
Each kit contains the following reagents and accessories:

	REAGENTS				
Maximum Assays	Reconstituting Solution (Liquid)	Sample Diluent (Liquid)	Sensitized Particles (Lyophilized)	Unsensitized Particles (Lyophilized)	Positive Control (Liquid)
Screening:100(20x5)	1 vialx8ml	1 vial x 29ml	5 vialsx0.6ml*	5 vialsx0.6ml*	1 vialx0.5ml
Screening:220(55x4)	1 vialx18ml	1 bottlex60ml	4 vialsx1.5ml*	4 vialsx1.5ml*	1 vialx0.5ml
Screening:550(110x5)	2 vialsx18ml	2 bottlesx60ml	5 vialsx3ml*	5 vialsx3ml*	1 vialx0.5ml
Screening:600(300x2)	2 vialsx18ml	2 bottlesx60ml	2 vialsx8ml*	2 vialsx8ml*	1 vialx0.5ml

*After reconstitution.

Accessories : Droppers(25 μ l/drop) : 2 droppers(20x5,55x4,110x5) : 4 droppers(300x2)



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