

# CMVscan™

## PASSIVE LATEX AGGLUTINATION TEST FOR THE DETECTION OF ANTIBODIES TO CYTOMEGALOVIRUS (CMV)

### I. INTENDED USE

The **CMVscan™** Card Test is a passive agglutination test for the detection of antibodies to cytomegalovirus in human serum and plasma. The test can be performed qualitatively with an undiluted serum to determine the presence of antibodies to CMV and quantitatively using serial two-fold dilutions to determine the CMV antibody titer.

The **CMVscan™** Card Test performed as a qualitative test on a single specimen is designed to detect the presence of CMV antibodies. The **CMVscan™** Card Test can be used as a diagnostic tool or to screen donor specimens. It will perform satisfactorily with acute phase or convalescent phase antibodies. Antibody present in a single specimen should only be taken as evidence of prior exposure to the virus.

The quantitative test can be used to determine the amount of antibody in serum or plasma. When using properly paired specimens (at least two weeks apart), demonstration of seroconversion or four-fold or greater rise in antibody titer may serve as evidence of recent infection. Both specimens should be tested simultaneously. The absence of a four-fold titer rise does not necessarily rule out the possibility of exposure and infection (see "Summary and Explanation").

### II. SUMMARY AND EXPLANATION

Cytomegalovirus (CMV) is a ubiquitous human viral pathogen belonging to the family of herpes viruses. CMV infection is usually asymptomatic and can persist in the host as a chronic or latent infection.<sup>1</sup>

Certain individuals are at a greater risk in developing more severe forms of CMV infection. Congenitally infected newborns, especially those who acquire CMV during a maternal primary infection, are more prone to develop severe cytomegalic inclusion disease (CID).<sup>2</sup> The severe form of CID may be fatal or can cause permanent neurological sequelae, such as mental retardation, deafness, microcephaly and motor dysfunction. Transfusion of CMV-infected blood products or transplantation of CMV-infected donor organs can result in a mononucleosis-type syndrome in an immunocompromised recipient. Low birth weight neonates are also at high risk to CMV mononucleosis through transfusion of CMV-infected blood products.<sup>3</sup>

Selection of CMV seronegative blood donors or organ donors by screening with a serological test for antibody has been reported to be effective in reducing the occurrence of CMV infection in CMV seronegative recipients.<sup>3</sup>

Virus excretion is common during both primary and recurrent CMV infection and can persist sporadically for months or years.<sup>4</sup> Seroconversion, or a significant rise in titer, may indicate recent infection, but cannot differentiate between primary or recurrent antibody response. Also, conversion from seronegativity to positivity or four-fold or greater change in antibody titer between paired sera may occasionally be caused by Influenza A or *Mycoplasma pneumoniae* infections, suggesting stress reactivation of CMV antibody.<sup>5</sup>

The timing of antibody response during a primary infection may differ slightly according to the antibody test methodology. With this technology, the pattern of antibody response during a primary CMV infection has not been demonstrated.

### III. PRINCIPLES OF THE PROCEDURE

Passive latex agglutination provides a simple and rapid means for routinely detecting antibodies to specific viral or bacterial antigens. The detection of antibodies to specific antigens can be used to determine either immune status or evidence of prior exposure to the suspected pathogen. Early in primary infection, antibodies may not be detectable.

The **CMVscan™** Card Test is based upon the principle of passive latex agglutination. Latex particles, which have previously been sensitized with CMV viral antigens, will agglutinate in the presence of antibody to CMV. After a suitable reaction time, the agglutinated particles will be visible to the naked eye. In the absence of specific antibody or in the presence of low concentrations of antibody, the latex particles will not agglutinate and will appear smooth and evenly dispersed. The **CMVscan™** Card Test will detect IgM and IgG antibodies. Detection of IgA and IgE antibodies, while likely, has not yet been demonstrated.

CMV antibody positive serum and CMV antibody negative serum controls are provided with the kit to demonstrate the difference between agglutination and non-agglutination.

### IV. REAGENTS

Reagent A, **CMVscan™** Latex Antigen, CMV (strain AD169) antigen-coated latex particles with 0.02% gentamicin and 0.02% sodium azide (preservatives).

Reagent B,	<b>CMVscan™</b> Card Dilution Buffer, phosphate buffered saline solution, pH 7.4, containing bovine serum albumin, with 0.02% sodium azide (preservative).
Control ++,	<b>CMVscan™</b> High Reactive Control (human serum), with 0.1% sodium azide (preservative).
Control +,	<b>CMVscan™</b> Low Reactive Control (human serum), with 0.1% sodium azide (preservative).
Control -,	<b>CMVscan™</b> Nonreactive Control (human serum), with 0.1% sodium azide (preservative).

V. **PRECAUTIONS:** For *in vitro* Diagnostic Use.

After review by the U. S. Centers for Disease Control and Prevention (CDC) and the U. S. Food and Drug Administration (FDA) under CLIA '88, this product has been identified as moderate complexity.

Reagents: Do not use beyond the expiration date. Upon removal from refrigeration, allow reagents to warm to room temperature (23 to 29°C) before use. **DO NOT** mix reagents from different kit lot numbers. Avoid microbial contamination of reagents.

**CMVscan™** Latex Antigen (Reagent A) should be vortexed at the beginning of testing each batch of specimens. To assure proper drop delivery when dispensing **CMVscan™** Latex Antigen (Reagent A), the dispensing bottle must be inverted vertically.

The latex antigen has been prepared from disrupted CMV that has been determined to have been inactivated by bioassay procedures.

The serum controls are derived from human blood tested by an FDA-approved method for the presence of the antibody to HIV (human immunodeficiency virus) to and HBsAg (hepatitis B surface antigen) and found to be nonreactive.

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**WARNING:** Because no test method can offer complete assurance that HIV, hepatitis B virus, or other infectious agents are absent, SPECIMENS AND THESE REAGENTS SHOULD BE HANDLED AS THOUGH CAPABLE OF TRANSMITTING AN INFECTIOUS DISEASE. The FDA recommends such material be handled at a Biosafety Level 2. BSL2 is referenced in the CDC/National Institutes of Health (NIH) manual, *Biosafety in Microbiological and Biomedical Laboratories*.

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Warning: Reagents contain sodium azide. Very toxic by inhalation, in contact with skin, and if swallowed. Contact with acids liberates very toxic gas. After contact with skin, wash immediately with plenty of water. Sodium azides may react with lead and copper plumbing to form highly explosive metal azides. On disposal, flush with a large volume of water to prevent azide build-up.

Test Cards: Cards must be flat for proper reactions. If necessary, flatten cards by bowing back in a direction opposite to that of the curl. Care should be taken not to finger-mark the test areas, since this may result in an oily deposit and improper test results. Use each card once and discard. Store cards in the original package in a dry area at room temperature.

Reading of Test Results: To help differentiate weak agglutination from no agglutination, a brief hand rotation of the card must be made following mechanical rotation. Results should be read promptly under a high intensity incandescent lamp. Fluorescent lighting is generally insufficient to distinguish minimally reactive results. The use of magnification in reading test results is not recommended. Failure to add sample results in inability to spread sample to fill circle, as required in the procedure.

Rotation: The recommended rotation speed is  $100 \pm 2$  rpm, but rotation between 95 and 110 rpm does not significantly affect the results obtained. The rotator should circumscribe a circle approximately two centimeters in diameter in the horizontal plane. A moistened humidifying cover should be used to prevent drying of test specimens during rotation.

Storage of Reagents: Refrigerate at 2 to 8°C. **DO NOT FREEZE.** Reagents should be recapped and returned to refrigeration when not in use.

## VI. SPECIMEN COLLECTION AND PREPARATION

Whole blood is collected and the serum is separated. Specimens may be stored up to one week at 2 to 8°C to retard bacterial contamination, or frozen at minus 18°C or lower if longer storage is required. Serum specimens with obvious microbial contamination or icterus should not be tested with this method.

The presence of mild lipemia or hemolysis does not affect the test.

No special preparation of the patient is required prior to specimen collection.

Plasma specimens containing heparin as an anticoagulant can be used for qualitative or quantitative testing using the same procedures as for serum samples. Plasma specimens containing CPDA-1, EDTA, CPD and CP<sub>2</sub>D as an anticoagulant can also be used for qualitative or quantitative testing after a 1:2 dilution is made with the Card Dilution Buffer. For an explanation of a 1:2 dilution, see "Quantitative Testing," step 3.d. Testing of CPDA-1 plasma samples from

platelet units stored at 22°C for five days and from red cell units stored at 2 to 6°C for 14 days has been successful. Other various anticoagulants and storage conditions can be used after appropriate testing has demonstrated equivalence to fresh serum or plasma specimens. Heating the samples at 56°C for 30 minutes has no effect on the qualitative performance of the test.

**VII. PROCEDURES:**

Review “Precautions” and “Specimen Collection and Preparation” prior to performing procedures. The testing area, reagents, test specimens and test components should be at room temperature (23 to 29°C) when used.

Materials provided:	No. 255126 (30 Tests)	No. 255001 (100 Tests)	No. 255205 (500 Tests)
Reagent A, <b>CMVscan™</b> Latex Antigen	0.5 mL	1.6 mL	5 x 1.6 mL
Reagent B, <b>CMVscan™</b> Card Dilution Buffer	5.0 mL	20.0 mL	20.0 mL
Control ++, <b>CMVscan™</b> High Reactive Control (human serum)	1.0 mL	1.0 mL	3 x 1.0 mL
Control +, <b>CMVscan™</b> Low Reactive Control (human serum)	1.0 mL	1.0 mL	3 x 1.0 mL
Control -, <b>CMVscan™</b> Nonreactive Control (human serum)	1.0 mL	1.0 mL	2 x 1.0 mL
Test Cards	4	5	20
Plastic stirrers	33	120	600

Materials Required But Not Provided: Rotator with humidifying cover, micropipettor, 50 µL delivery, centrifuge, high intensity incandescent lamp and vortex mixer.

Also required are the necessary equipment and labware used for preparation, storage and handling of serologic specimens.

**Performance of CMV Antibody Testing:**

1. Vortex Reagent A for 5 to 10 seconds (use highest speed setting for variable speed mixers). Vortexing is necessary at the beginning of testing each batch of specimens even if more than one batch is tested per day.

2. Mark the card to identify the controls and all samples being tested.

3. Qualitative Testing

With a micropipettor, place 50  $\mu$ L each of Control ++ and Control - and patient samples onto the appropriate circles using a new tip each time.

3. Quantitative Testing

Dilution of Controls and Samples:

a. With a micropipettor, add 50  $\mu$ L of Control - onto circle 1 in row marked "Nonreactive Control." No serial dilutions of this control are needed.

b. Move to a new row. With a micropipettor, place 50  $\mu$ L of Reagent B in circles 2-7, leaving circle 1 empty.

c. With a micropipettor, place 50  $\mu$ L of Control ++ onto circle 1.

d. Using the same micropipettor and tip, add an additional 50  $\mu$ L of Control ++ directly into buffer in circle 2, and mix by drawing up and down with micropipettor 7 times. The serum in circle 2 is now a 1:2 dilution.

e. Using the same micropipettor and tip, transfer 50  $\mu$ L of 1:2 dilution directly into the buffer in circle 3, mix as before, and continue this preparation of serial two-fold dilutions through circle 7. Withdraw 50  $\mu$ L from circle 7 and discard. The dilution in circle 7 is now 1:64.

Qualitative Testing, con't

Quantitative Testing, con't

(If further dilutions are required, continue procedures described in steps "a" through "e" through next row of circles. Rather than discarding excess 50  $\mu$ L of diluted specimen in circle 7, discard from whatever circle is last in next row.)

- f. Repeat steps "b" through "e" for Control + and each sample being tested.
4. Using a new plastic stirrer for each circle, spread the serum to fill the entire circle.
4. Using a new plastic stirrer for each control and test sample, start at last circle and spread serum dilution to fill the entire circle. Proceed to next low dilution until each circle of sample row is spread.
5. Gently invert the Reagent A bottle several times to thoroughly mix the latex reagent. Before uncapping, gently tap the base on a counter top to assure no latex reagent remains in the tip.
6. Holding the bottle in an inverted, vertical position, dispense one free-falling drop of Reagent A (approximately 15  $\mu$ L) onto each circle containing the serum.
7. Hand rotate the card three or four times back-and-forth to distribute the latex antigen throughout each circle. Avoid cross contamination of test areas in adjacent circles.
8. Place the card on a rotator and rotate for eight minutes under a moistened humidifying cover.
9. Immediately following mechanical rotation, read the card macroscopically in the wet state under a high intensity incandescent lamp. Gently tilt the card (three or four back-and-forth motions) to help differentiate weak agglutination from no agglutination.

### VIII. INTERPRETATION OF TEST RESULTS

1. Qualitative Test: The Reactive Controls should show agglutination, while the Nonreactive Control should show no agglutination.

Report as Positive:

Reactive: Showing any agglutination of the **CMVscan™** Latex Antigen (Reagent A).

Report as Negative:

Nonreactive: Suspension remains evenly dispersed, showing no agglutination of the **CMVscan™** Latex Antigen (Reagent A).

The presence of CMV antibodies is an indication of previous exposure to the virus but does not indicate immunity to subsequent re-infection. Recurrent infections can occur; however, the clinical severity may be less than seen in primary infection.<sup>2</sup> The absence of CMV antibodies is an indication that there has been no exposure to the virus.

2. Quantitative Test: Report reactivity in terms of the highest dilution showing any agglutination of the **CMVscan™** Latex Antigen (Reagent A). Specimens showing no agglutination at any dilution are reported as nonreactive.

Demonstration of seroconversion or a four-fold or greater rise in antibody titer on properly collected paired specimens may serve as evidence of recent infection.<sup>6</sup>

3. Controls: The reactive controls are formulated to produce definite agglutination within the labeled dilutions. Do not report control endpoints as "Reactive" unless definite agglutination is observed, assuring that the antigen antibody system is performing properly within the test environment. The nonreactive control should show no agglutination. If controls do not produce appropriate response, test is invalid.

Refer to the following example.	1:1 Undiluted	1:2	1:4	1:8	1:16	1:32	1:64
High Reactive Control ++	R	R	R	R	R	R	R
Low Reactive Control +	R	R	R	R	N	N	N
Nonreactive Control -	N						
Sample No. 1	R	R	R	N	N	N	N
Sample No. 2	R	R	R	R	R	R	N

R = Reactive

N = Nonreactive

Report as: High Reactive Control: Reactive,  $\geq$  1:64 dilution

Low Reactive Control: Reactive, 1:8 dilution

Nonreactive Control: Nonreactive

Sample No.1: Reactive, 1:4 dilution

Sample No.2: Reactive, 1:32 dilution

**Quality Control:**

**Diagnostic Testing:** The **CMVscan™** Test Control + and Control - should be tested each day of use for quality control of the qualitative procedure. When using the quantitative procedure. Control ++ and Control + should be titered with each batch of patient samples. <sup>1,2</sup>

**Donor Screening (using qualitative procedure):** The **CMVscan™** Test Control - and a 1:4 dilution of the Control + should be tested with each batch of patient samples. Refer to the following procedures to make a 1:4 dilution:

Option 1: (For use when testing one batch per day)

1. With a micropipettor, place 50 µL of Reagent B on circles A1 and A2.
2. Using the same tip, add 50 µL of Control + to circle A1, and mix by drawing up and down with micropipettor 7 times.
3. Using the same micropipettor and tip, transfer 50 µL from circle A1 to circle A2, and mix as before. Withdraw 50 µL from circle A2 and discard.
4. The dilution in the circle is now a 1:4 dilution of the Control + and should be tested immediately using the qualitative test procedure.

Option 2: (For use when testing more than one batch per day)

1. With a micropipettor, place 150 µL of Reagent B into a clean, dry test tube.
2. With a micropipettor, add 50 µL of Control + to the test tube.
3. Mix thoroughly by vortexing or shaking.
4. The dilution in the tube now is a 1:4 dilution of the Control + and may be used for up to 24 hours to perform quality control using the qualitative procedure.

## IX. LIMITATIONS OF PROCEDURES

The use of components or procedures other than recommended in this package insert may lead to incorrect results.

As with any serologic test, patients with acute infection may not have detectable antibody.

In addition, test results from neonates should be interpreted with caution, since the presence of CMV antibody is usually the result of passive transfer from the mother to the fetus. A negative test may be useful in excluding possible infection, but a diagnosis of active CMV infection may require viral culture.

Samples with abnormally high antibody levels to infectious agents other than CMV have not been tested.

## X. EXPECTED VALUES

The incidence of CMV infection is dependent upon geographical, socioeconomic, and age factors. Serological studies indicate that 25-50% of the American population have CMV antibodies present by the age of 15.<sup>7</sup> In adult populations, the incidence of antibodies to CMV has been reported between 15% and 70%.<sup>8</sup>

From four clinical centers, a total of 1095 random specimens were evaluated by **CMVscan™**. The samples were prospectively collected from mainly an adult population. In two centers, the specimens were entirely from blood bank donors. The other two sites represented a mixture of blood donors, organ transplant donors/recipients and miscellaneous cases where CMV antibody titers were routinely being requested. The sites were in the mid-Atlantic and southeastern United States. In the patient and blood donor populations, 53% and 34% of specimens, respectively, were positive for antibody to CMV.

## XI. PERFORMANCE CHARACTERISTICS

**Qualitative Performance:** The qualitative performance of the **CMVscan™** Card Test was determined with prospectively collected sera at two clinical centers and two blood banks.

At each clinical site, the specimens were tested by three methods. **CMVscan™** Card Test and a commercially available indirect hemagglutination assay (IHA) were used at both sites. The third method at site 1 was a commercially available solid phase fluorescence immunoassay (FIA). The third method at site 2 was a commercially available enzyme-linked immunosorbent assay (ELISA). A consensus result of reactive or non-reactive for antibodies to CMV was assigned to each serum specimen based on agreement of any two or more of the three test methods. The results are given in Table 1 and 2 and summarized in Table 3.

TABLE 1

**CMVscan™ Card Test Performance**  
With a Patient Population; Site 1

		Consensus Result <sup>a</sup>		
		+	-	
CMVscan™ Card Test Result	+	182	4	Sensitivity = 100% (182/182) (95% C.I. = 98.0 - 100.0)
	-	0	96	
TOTAL		182	100	

TABLE 2

**CMVscan™ Card Test Performance**  
With a Patient Population; Site 2

		Consensus Result <sup>a</sup>		
		+	-	
CMVscan™ Card Test Result	+	119	4	Sensitivity = 98% (119/121) (95% C.I. = 94.2 - 99.8)
	-	2	165	
TOTAL		121	169	

TABLE 3

**CMVscan™ Card Test Performance**  
With a Patient Population;  
Combined Sites

		Consensus Result <sup>a</sup>		
		+	-	
CMVscan™ Card Test Result	+	301	8	Sensitivity = 99% (301/303) (95% C.I. = 97.6 - 99.9)
	-	2	261	
TOTAL		303	269	

<sup>a</sup>Consensus of two of the three assays

Blood bank 1 tested specimens with **CMVscan™** Card Test, a commercially available IHA and an in-house ELISA. Blood bank 2 tested specimens with **CMVscan™** Card Test, a commercially available IHA, a commercially available solid phase FIA, two commercially available ELISA, and a commercially available indirect fluorescent assay. A consensus result of reactive or nonreactive for antibodies to CMV was assigned to each serum specimen based on agreement of the majority of test methods. The results are given in Tables 4 and 5 and summarized in Table 6.

TABLE 4

**CMVscan™** Card Test Performance  
With a Blood Donor Population;  
Site 3

		Consensus Result <sup>a</sup>		
		+	-	
CMVscan™ Card Test Result	+	117	5	Sensitivity = 97% (117/121) (95% C.I. = 94.2 - 99.8)
	-	4	188	
TOTAL		121	193	Specificity = 97% (188/193) (95% C.I. = 94.1 - 99.2)

TABLE 5

**CMVscan™** Card Test Performance  
With a Blood Donor Population; Site 4<sup>9</sup>

		Consensus Result <sup>b</sup>		
		+	-	
CMVscan™ Card Test Result	+	58	2	Sensitivity = 100% (58/58) (95% C.I. = 93.8 - 100.0)
	-	0	149	
TOTAL		58	151	Specificity = 99% (149/151) (95% C.I. = 95.3 - 99.8)

TABLE 6

**CMVscan™ Card Test Performance**  
 With a Blood Donor Population;  
 Combined Sites

		Consensus Result <sup>a</sup>		
		+	-	
<b>CMVscan™</b> Card Test Result	+	175	7	Sensitivity = 98% (175/179) (95% C.I. = 94.4 - 99.4)
	-	4	337	Specificity = 98% (337/344) (95% C.I. = 95.9 - 99.2)
TOTAL		179	344	

<sup>a</sup>Consensus of two of the three assays

<sup>b</sup>Consensus of four of the six assays

No prozoning was seen in the clinical trials or in-house studies. Specimen titers of 1:1024 or below were evaluated with the **CMVscan™** Card Test Kit.

Reproducibility: The ability of the **CMVscan™** Latex Agglutination Test to reproducibly quantitate serum antibody to CMV was demonstrated by testing a coded panel of 50 serum pairs. Reproducibility, as defined by the ability to give agreement to within one two-fold dilution on duplicates, was determined to be 98%.

Summary of Results		
Agreement of Duplicates	<b>CMVscan™</b> Latex	
	No.	%
Both of Same Titer	32	64
One Dilution Difference	17	34
Two Dilution Difference	1	2
Total No. of Pairs	50	
Reproducibility	49/50 = 98 %	

Interferences: To test the possible interference of antibodies to other agents with the performance of the **CMVscan™** latex reagent, a special group of sera were analyzed for CMV antibody by latex agglutination and indirect hemagglutination assay. Multiple samples positive for rheumatoid factor, rubella, herpes simplex, Epstein-Barr, varicella

zoster and/or *Toxoplasma gondii* and anti-nuclear antibodies were found nonreactive for CMV antibody suggesting lack of cross reactivity or interference.

## XII. AVAILABILITY

Cat. No.	Description
<b>255126</b>	<b>CMVscan™</b> 30 Test Kit (Qualitative)
<b>255001</b>	<b>CMVscan™</b> 100 Test Kit (Qualitative)
<b>255205</b>	<b>CMVscan™</b> 500 Test Kit (Qualitative).
<b>278051</b>	<b>Macro-Vue™ Card Test Rotator</b> (with humidifying cover), 100 ±2 rpm, automatic timer, friction drive, Model 51-II (110 V).
<b>277979</b>	<b>Macro-Vue™ Card Test Rotator</b> Accessories Package, containing one 15" x 7" extension top and two humidifying covers.

## XIII. REFERENCES

1. Ho, M.: Characteristics of Cytomegalovirus. In "Cytomegalovirus—Biology and Infection," Plenum Medical Book Co., New York, 9-32, 1982.
2. Stagno, S., Pass, R.F., Dworsky, M.E., Henderson, R.E., Moore, E.G., Walton, P.D. and Alford, C.A., Congenital Cytomegalovirus Infection, N. Eng. J. Med., 306:945, 1982.
3. Adler, S.P.: Transfusion-associated Cytomegalovirus Infections. Rev. Inf. Dis. 5:977-993, 1983.
4. Hanshaw, J.V.: Cytomegalovirus. In "Infectious Diseases of the Fetus and Newborn Infant" by Remington, J.S. and Klein, J.O., W.B. Saunders Co., Philadelphia, PA, 104-142, 1983.
5. Chernesky, M.A., Ray, C.G., Smith, T.F.: Laboratory Diagnosis of Viral Infections, *Cumitech*, 15:9-11, May 1982.
6. Prince, A.M., Szmunes, W., Millian, S.J. and Davis, D.S.: A Serologic Study of Cytomegalovirus Infections Associated with Blood Transfusions, N. Eng. J. Med., 284:1125, 1971.
7. Sullivan, J.L. and Hanshaw, J.B.: Human Cytomegalovirus Infections. In "Human Herpesvirus Infections - Clinical Aspects" ed. by Glaser, R. and Gottleib-Stematsky, T. Marcel Dekker, Inc., New York, 57-83, 1982.
8. Betts, R.F.: The Relationship of Epidemiology and Treatment Factors to Infection and Allograft Survival in Renal Transplantation. In "CMV: Pathogenesis and Prevention of Human Infection," ed. by Plotkin, S.A., Michelson, S., Pagano, J., and Rapp, F., Alan R. Liss, Inc., New York, 87-99, 1984.

9. Beckwith, D.G., Halstead, D.C., Alpaugh, K., A., Blount-Fronefield, D.A., and Toth, K. Comparison of a Latex Test with Five Other Methods for Determining the Presence of Antibody Against Cytomegalovirus. J. Clin. Microbiol. 21:328-331, 1985.

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