



# Test Definition: CIFS

Cutaneous Immunofluorescence Antibodies,  
IgG and IgG4, Serum

## Overview

### Useful For

Confirming the presence of IgG and/or IgG4 antibodies to diagnose pemphigoid, pemphigus, epidermolysis bullosa acquisita, or bullous lupus erythematosus

### Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CIFST	CIFS Titer, IgG, S	No	No

### Testing Algorithm

If IgG anti-cell surface or anti-basement membrane zone antibodies are present, then the IgG antibody titer will be reflexed and performed at an additional charge.

For more information see [Autoimmune Blistering Disease Diagnostic Algorithm](#).

### Special Instructions

- [Autoimmune Blistering Disease Diagnostic Algorithm](#)

### Method Name

Indirect Immunofluorescence Assay (IFA)

### NY State Available

Yes

## Specimen

### Specimen Type

Serum

### Specimen Required

**Collection Container/Tube:**

**Supplies:** Sarstedt Aliquot Tube, 5 mL (T914)

**Preferred:** Serum gel

**Acceptable:** Red top

**Submission Container/Tube:** Plastic vial

**Specimen Volume:** 2 mL

**Collection Instructions:** Centrifuge and aliquot serum into a plastic vial.

**Specimen Minimum Volume**

0.5 mL

**Reject Due To**

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

**Specimen Stability Information**

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	14 days	
	Ambient	14 days	
	Frozen	30 days	

**Clinical & Interpretive****Clinical Information**

Immunoglobulin G (IgG) and/or IgG4 anti-basement membrane zone (BMZ) antibodies are produced by patients with pemphigoid, pemphigus, and other rare autoimmune blistering disorders such as epidermolysis bullosa acquisita and bullous lupus erythematosus. In most patients with bullous pemphigoid, serum contains IgG anti-BMZ antibodies, while in cicatricial pemphigoid circulating IgG anti-BMZ antibodies are found in a minority of cases.

Circulating IgG4 is also variably present. Sensitivity of detection of anti-BMZ antibodies is increased when serum is tested using both sodium chloride-split primate skin and primate esophagus as substrates and using both IgG and IgG4 reactants.

**Reference Values**

Negative

**Interpretation**

Results will be negative in individuals without any known autoimmune blistering disease.

Indirect immunofluorescence (IF) testing may aid in the diagnosis of these conditions when correlated with histopathologic, direct immunofluorescence, and clinical information.

Anti-basement membrane zone (BMZ) antibodies correlate with a diagnosis of bullous pemphigoid, cicatricial pemphigoid, epidermolysis bullosa acquisita (EBA), or bullous eruption of lupus erythematosus (LE).

Anti-cell surface antibodies correlate with a diagnosis of pemphigus.

If serum contains anti-BMZ antibodies, the pattern of fluorescence on sodium chloride (NaCl)-split skin substrate helps distinguish pemphigoid from EBA and bullous LE. Staining of the roof (epidermal side) or both epidermal and dermal sides of NaCl-split skin correlates with the diagnosis of pemphigoid, while fluorescence localized only to the dermal side of the split-skin substrate correlates with either EBA or bullous LE.

The report includes presence and titer of circulating antibodies.

If the serum contains BMZ antibodies on the split-skin substrate, patterns will be reported as one of the following:

1. Epidermal pattern, suggestive of pemphigoid
2. Dermal pattern, suggestive of epidermolysis bullosa acquisita, bullous lupus erythematosus, or rare pemphigoid variants
3. Mixed pattern, suggestive of rare pemphigoid variants

If serum contains BMZ antibodies on the primate esophagus substrate, patterns will be reported as one of the following:

- BMZ (linear) pattern, suggestive of a subepidermal autoimmune mucocutaneous blistering disorder
- Intercellular substance (cell-surface) pattern, suggestive of pemphigus

### Cautions

Results should be interpreted in conjunction with clinical information, histopathologic pattern, and results of direct immunofluorescence (DIF) study. In particular, the finding of low titer ( $< \text{or} = 1:80$ ) antibodies should not be used alone (ie, without histopathologic or DIF support) to diagnose these conditions.

### Clinical Reference

1. Beutner EH, Chorzelski TP, Kumar V, eds. *Immunopathology of the Skin*. 3rd ed. Wiley Medical Publication; 1987
2. Gammon WR, Briggaman RA, Inman AO 3rd, Queen LL, Wheeler CE. Differentiating anti-lamina lucida and anti-sublamina densa anti-BMZ antibodies by indirect immunofluorescence on 1.0 M sodium chloride-separated skin. *J Invest Dermatol*. 1984;82(2):139-144
3. Tirumalae R, Kalegowda IY. Role of BIOCHIP indirect immunofluorescence test in cutaneous vesiculobullous diseases. *Am J Dermatopathol*. 2020;42(5):322-328
4. Lehman JS, Aghazadeh Mohandesi N, Agrawal S, et al. Indirect immunofluorescence testing for immunoglobulin G4 and IgG increases test sensitivity over that of IIF testing for IgG alone for pemphigoid and pemphigus diseases: A retrospective study of 278 cases. *J Am Acad Dermatol*. 2024:S0190-9622(24)03372-3

### Performance

#### Method Description

Frozen sections of primate esophagus and sodium chloride-split primate skin are overlaid with dilutions of patient's serum, incubated, covered with fluorescein-conjugated IgG and IgG4 anti-serum, and interpreted using a fluorescence microscope.(Unpublished Mayo method)

#### PDF Report

No

**Day(s) Performed**

Monday through Friday

**Report Available**

2 to 7 days

**Specimen Retention Time**

30 days

**Performing Laboratory Location**

Mayo Clinic Laboratories - Rochester Main Campus

**Fees & Codes****Fees**

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact [Customer Service](#).

**Test Classification**

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

**CPT Code Information**

88346

88350

88350 (if appropriate)

**LOINC® Information**

Test ID	Test Order Name	Order LOINC® Value
CIFS	Cutaneous Immflour. Ab, IgG/IgG4, S	In Process

Result ID	Test Result Name	Result LOINC® Value
21539	Cell Surface Ab IgG	93233-5
21540	Basement Membrane IgG	29994-1
21542	Primate Split Skin IgG	104832-1
21638	Other	48767-8
622319	Cell Surface Ab IgG4	In Process
622320	Basement Membrane IgG4	In Process
622322	Primate Split Skin IgG4	In Process