

## Overview

### Useful For

Aiding in the diagnosis and monitoring of monoclonal gammopathies, when used in conjunction with free light chain studies

This test alone is **not considered** an adequate screen for monoclonal gammopathies.

### Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
QMPTS	Quantitative M-protein Isotype, S	No	Yes
IGA	Immunoglobulin A (IgA), S	Yes, (Order IMMIG or IGA)	Yes
IGM	Immunoglobulin M (IgM), S	Yes, (Order IMMIG or IGM)	Yes
IGG	Immunoglobulin G (IgG), S	Yes, (Order IMMIG or IGG)	Yes
TMAB1	Therapeutic Antibody Administered?	No	Yes

### Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
IFXED	Immunofixation Delta and Epsilon, S	Yes	No
IGD	Immunoglobulin D (IgD), S	Yes	No
IGE	Immunoglobulin E (IgE), S	Yes	No

### Testing Algorithm

This test includes quantitation of monoclonal-protein isotype and immunoglobulins G, A, and M.

If a light chain is identified without a corresponding heavy chain during initial testing, then immunofixation with immunoglobulin D (IgD) and immunoglobulin E (IgE) will be performed at an additional charge.

If a monoclonal IgD or IgE is identified during initial testing, then IgD or IgE testing will be performed at an additional charge.

For more information see:

[-Multiple Myeloma: Laboratory Screening](#)

[-Amyloidosis: Laboratory Approach to Diagnosis](#)

[-Acquired Neuropathy Diagnostic Algorithm](#)

**Special Instructions**

- [Amyloidosis: Laboratory Approach to Diagnosis](#)
- [Multiple Myeloma: Laboratory Screening](#)
- [Acquired Neuropathy Diagnostic Algorithm](#)

**Method Name**

QMPTS: Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS)

IGG, IGA, IGM: Nephelometry

TMAB1: Patient Information

**NY State Available**

Yes

**Specimen****Specimen Type**

Serum

**Additional Testing Requirements**

Quantitation of monoclonal protein alone is not considered an adequate screen for monoclonal gammopathies. When screening a patient or establishing a first-time diagnosis for a monoclonal gammopathy, order FLCS / Immunoglobulin Free Light Chains, Serum in addition to this test.

**Specimen Required****Supplies:** Sarstedt Aliquot Tube, 5 mL (T914)**Collection Container/Tube:****Preferred:** Serum gel**Acceptable:** Red top**Submission Container/Tube:** Plastic vial**Specimen Volume:** 2 mL total in 2 separate plastic vials, each containing 1 mL**Collection Instructions:** Centrifuge and aliquot serum into 2 plastic vials, each containing 1 mL**Forms**

If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:

-[Hematopathology/Cytogenetics Test Request](#) (T726)-[Renal Diagnostics Test Request](#) (T830)-[General Request](#) (T239)**Specimen Minimum Volume**

1.5 mL

**Reject Due To**

Gross hemolysis	OK
Gross lipemia	Reject
Gross icterus	OK

## Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	28 days	
	Frozen	28 days	
	Ambient	7 days	

## Clinical & Interpretive

### Clinical Information

Monoclonal gammopathy is a general term which includes a spectrum of diagnoses including malignancies of plasma cells or B cells (eg, multiple myeloma [MM], Waldenstrom macroglobulinemia, plasmacytoma, and B-cell lymphomas and leukemias), symptomatic disorders directly related to the M-protein (eg, immunoglobulin light chain [AL] amyloidosis, light chain deposition disease, cryoglobulinemia, monoclonal gammopathy of clinical significance [MGCS], monoclonal gammopathy of renal significance [MGRS], monoclonal gammopathy of thrombotic significance [MGTS] and POEMS syndrome [polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, skin changes]) and asymptomatic premalignant conditions (eg, monoclonal gammopathy of undetermined significance [MGUS] and smoldering MM). While the identification of the monoclonal gammopathy is a laboratory diagnosis, the specific clinical diagnosis is dependent on several other laboratory and clinical assessments.

Monoclonal proteins (M-proteins) are the marker of monoclonal gammopathies. An M-protein is defined by the presence of a monoclonal immunoglobulin which is expressed above the polyclonal background. The International Myeloma Working Group (IMWG) guidelines state that to adequately document the presence of a monoclonal protein, a serum protein electrophoresis (SPEP), serum free light chain (FLC) analysis, and serum immunofixation electrophoresis (IFE) or serum mass spectrometry, should all be used. If AL amyloidosis is suspected, a 24-hour urine monoclonal protein study should be performed when all serum testing is negative.

Mass-Fix has been demonstrated to be more analytically and clinically sensitive than IFE in detecting M-proteins. Mass-Fix results have also been shown to better predict patient's progression free survival time than IFE in treated MM patients. In addition, Mass-Fix can detect M-proteins with glycosylated light chains, which were demonstrated to be a risk factor for AL amyloidosis, cold agglutinin disease, and MGUS progression. When matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) results are combined with quantitative immunoglobulin measurements, the assay can replace traditional SPEP for M-protein quantitation for common M-protein isotypes IgG, IgA, and IgM. M-proteins, which consist of only light chains are best quantitated using serum free light chains measurements.

If a M-protein pattern is detected by Mass-Fix or serum FLC measurements, a diagnosis of a monoclonal gammopathy is

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established. The patient should be assessed clinically for symptomatic conditions such as multiple myeloma and the other diagnoses listed above. Once symptomatic disease is ruled out, a diagnosis of MGUS can be established. The IMWG guidelines suggests follow-up M-protein testing at 6 months for the first two years following a MGUS diagnosis. If the M-protein concentration remains stable over this period (ie, less than 0.5 g/dL increase) and the patient remains asymptomatic, testing can reduce to once per year.

The Iceland Screens, Treats, or Prevents Multiple Myeloma (iStopMM) study involving 75,422 participants has online resources to predict the chance that a bone marrow biopsy will have greater than 10 percent plasma cells given the isotype, M-protein concentrations, free light chain ratio and total IgG, IgA, and IgM. This could be an important resource for physicians trying to decide if their patient should have a follow up bone marrow evaluation (<https://istopmm.com/riskmodel/>).

**Reference Values**

Monoclonal-protein Isotype Flag:

Negative

Interpretation:

No monoclonal protein detected.

IgG:

0-&lt;5 months: 100-334 mg/dL

5-&lt;9 months: 164-588 mg/dL

9-&lt;15 months: 246-904 mg/dL

15-&lt;24 months: 313-1,170 mg/dL

2-&lt;4 years: 295-1,156 mg/dL

4-&lt;7 years: 386-1,470 mg/dL

7-&lt;10 years: 462-1,682 mg/dL

10-&lt;13 years: 503-1,719 mg/dL

13-&lt;16 years: 509-1,580 mg/dL

16-&lt;18 years: 487-1,327 mg/dL

&gt; or =18 years: 767-1,590 mg/dL

IgA:

0-&lt;5 months: 7-37 mg/dL

5-&lt;9 months: 16-50 mg/dL

9-&lt;15 months: 27-66 mg/dL

15-&lt;24 months: 36-79 mg/dL

2-&lt;4 years: 27-246 mg/dL

4-&lt;7 years: 29-256 mg/dL

7-&lt;10 years: 34-274 mg/dL

10-&lt;13 years: 42-295 mg/dL

13-&lt;16 years: 52-319 mg/dL

16-&lt;18 years: 60-337 mg/dL

&gt; or =18 years: 61-356 mg/dL

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**IgM:**

0-<5 months: 26-122 mg/dL  
5-<9 months: 32-132 mg/dL  
9-<15 months: 40-143 mg/dL  
15-<24 months: 46-152 mg/dL  
2-<4 years: 37-184 mg/dL  
4-<7 years: 37-224 mg/dL  
7-<10 years: 38-251 mg/dL  
10-<13 years: 41-255 mg/dL  
13-<16 years: 45-244 mg/dL  
16-<18 years: 49-201 mg/dL  
> or =18 years: 37-286 mg/dL

**Interpretation****Monoclonal Gammopathies:**

- A monoclonal IgG or IgA of greater than 3 g/dL is consistent with multiple myeloma (MM).
- A monoclonal IgM of greater than 3 g/dL is consistent with macroglobulinemia.
- A monoclonal IgG, IgM, or IgA of less than 3 g/dL may be consistent with monoclonal gammopathy of undetermined significance (MGUS), light chain (AL) amyloidosis, well as other monoclonal gammopathies of clinical significance.
- If the initial identification of a serum M-spike is greater than 1.5 g/dL, then order a follow-up MPU / Monoclonal Protein Studies, 24 Hour, Urine to evaluate renal impairment due to the M-protein
- If the initial identification of an IgM, IgA, or IgG M-spike greater than 4 g/dL, greater than 5 g/dL, and greater than 6 g/dL, respectively, then SVISC / Viscosity, Serum should be ordered to rule out hyperviscosity syndrome.
- Patients with monoclonal light chain diseases who have no serum or urine M-spike may be monitored with the quantitative serum free light chain (FLC) assay.
- Patients with IgD or IgE can be followed using quantitative IgD or IgE measurements.
- Patients with monoclonal Ig heavy chains (gamma, alpha and mu) can be detected by the Mass-Fix assay.
- A small subset of MM patients (<1%) have malignant plasma cells that do not secrete an M-protein. Thus, these non-secretory MM patients need additional clinical testing to establish the diagnosis.
- Patients with normal serum protein electrophoresis and IFE can have positive results on Mass-Fix testing due to the increased sensitivity of the assay.

**Detection of Therapeutic Monoclonal Antibodies:)**

- Patients who are receiving therapeutic monoclonal antibodies (t-mAb) therapies can have a "pseudo" monoclonal protein (M-protein) depending on the level of the t-mAb in the blood. These t-mAb have predictable light chain mass to charge values. The lab has a limited (but expanding) number of t-mAb for which a comment is provided. If an M-protein is detected with a mass, isotype, and concentration similar to a t-mAb in the database, a comment is added to the report : "A monoclonal [isotype] is present with a light chain mass suggestive of [t-mAb name]. If the patient is not on [t-mAb name] the monoclonal [isotype] is indicative of a monoclonal gammopathy. Given that some M-proteins mass, isotype, and concentration will match a t-mAb, it is possible that the named t-mAb is not present and is in fact a low-level M-protein associated with a monoclonal gammopathy. If the patient has no history of taking the named t-mAb, then the reported M-protein is likely associated with a monoclonal gammopathy."
- In studies performed at Mayo Clinic, it is possible to see daratumumab for 9 months after the cessation of treatment.
- Mass-fix testing will not quantitate albumin, alpha-1-trypsin, alpha-2-macroglobulins or the beta fractions.

**MGUS Prognosis:**

- Low-risk MGUS patients are defined as having an M-spike of less than 1.5 g/dL, IgG monoclonal protein, and a normal FLC K/L (kappa/lambda) ratio (0.25-1.65), and these patients have a lifetime risk of progression to MM of less than 5%.
- High-risk MGUS patients (M-spike >1.5, IgA or IgM, abnormal FLC ratio) have a lifetime risk of progression to MM of 60%.

**Other Abnormal Findings:**

- IgG, IgA, and free light chain M-proteins with reported light chain glycosylation have demonstrated to be a risk factor for AL amyloidosis.
- IgM M-proteins with light chain glycosylation have been demonstrated to be associated with cold agglutinin disease.
- Persistent elevated immunoglobulin levels are consistent with autoimmune disease, IgG4 related disease and liver failure.

**Cautions**

Quantitation of IgD, IgE, free kappa and free lambda monoclonal proteins cannot be performed by this assay. Free light chain M-proteins should be quantified using FLCs / Immunoglobulin Free light Chains, Serum. IgD and IgE should be quantified using IgD / Immunoglobulin D (IgD), Serum; or IgE / Immunoglobulin E (IgE), Serum.

**Clinical Reference**

1. Rajkumar SV, Kyle RA, Therneau TM, et al. Serum free light chain ratio is an independent risk factor for progression in monoclonal gammopathy of undetermined significance. *Blood*. 2005;106(3):812-817
2. Katzmann JA, Dispenzieri A, Kyle RA, et al. Elimination of the need for urine studies in the screening algorithm for monoclonal gammopathies by using serum immunofixation and free light chain assays. *Mayo Clin Proc*. 2006;81(12):1575-1578
3. Mills JR, Kohlhagen MC, Dasari S, et al. Comprehensive assessment of M-proteins using nanobody enrichment coupled to MALDI-TOF mass spectrometry. *Clin Chem*. 2016;62(10):1334-1344
4. Milani P, Murray DL, Barnidge DR, et al. The utility of MASS-FIX to detect and monitor monoclonal proteins in the clinic. *Am J Hematol*. 2017;92(8):772-779. doi:10.1002/ajh.24772

**Performance****Method Description**

Monoclonal protein isotype by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) is performed with immunoaffinity purification followed by MALDI-TOF MS analysis. For the immunoaffinity purification, patient serum is applied to 5 separate immunoaffinity resins specific to immunoglobulins G, A, M, K, and L. Unbound protein is washed away and the isolated immunoglobulins are broken down in to their reduced to separate the heavy and light chains subunits to be analyzed via MALDI-TOF MS. The 5 separate spectra from each specimen immunopurification are overlaid and investigated for an overabundance of immunoglobulin and immunoglobulin light chain. Monoclonal protein peaks are integrated based on the modeled polyclonal background. The quantitative value is determined based on the percent area and nephelometric value of the corresponding immunoglobulin.(Milani P, Murray DL, Barnidge DR, et al. The utility of MASS-FIX to detect and monitor monoclonal proteins in the clinic. *Am J Hematol*.

2017;92(8):772-779. doi:10.1002/ajh.24772)

## PDF Report

No

## Day(s) Performed

Monday through Friday

## Report Available

2 to 4 days

## Specimen Retention Time

14 days

## Performing Laboratory Location

Rochester

## 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

0077U

82784 x 3

### LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
QMPSS	Quantitative M-protein Study, S	104266-2

Result ID	Test Result Name	Result LOINC® Value
IGA	Immunoglobulin A (IgA), S	2458-8
IGG	Immunoglobulin G (IgG), S	2465-3
IGM	Immunoglobulin M (IgM), S	2472-9
620875	M-protein GK	74862-4
620876	M-protein GL	74863-2

620877	M-protein AK	74864-0
620878	M-protein AL	74865-7
620879	M-protein MK	74866-5
620880	M-protein ML	74867-3
620881	Glycosylation	104267-0
620874	Flag, M-protein Isotype	94400-9
621012	QMPTS Interpretation	69048-7
TMAB1	Therapeutic Antibody Administered?	98855-0