# Test Definition: QMPSS

Monoclonal Protein Study, Quantitative, Serum

## 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 IMMG or IGA) | Yes |
| IGM | Immunoglobulin M (IgM), S | Yes, (Order IMMG or IGM) | Yes |
| IGG | Immunoglobulin G (IgG), S | Yes, (Order IMMG 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 Serum total; 2 separate plastic vials, each containing 1 mL serum
**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)
-Kidney Transplant Test Request

### Specimen Minimum Volume

Serum: 2 Plastic vials, each containing 0.75 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 | |
| | Ambient | 7 days | |
| | Frozen | 28 days | |

## Clinical & Interpretive

### Clinical Information

Monoclonal gammopathy is a general term that 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 [polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, skin changes] syndrome) 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 that 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 either 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.

The Mayo Clinic MASSFIX (immunoenrichment-based matrix-assisted laser desorption/ionization time-of-flight mass spectrometry [MALDI-TOF-MS]) method has demonstrated to be more analytically and clinically sensitive than IFE in detecting M-proteins. MASSFIX results have also been shown to better predict patient's progression free survival time than IFE in treated MM patients. In addition, MASSFIX can detect M-proteins with glycosylated light chains, which were demonstrated to be a risk factor for AL amyloidosis, cold agglutin disease, and MGUS progression. When 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 that consist of only light chains are best quantified using serum free light chains measurements.

If a M-protein pattern is detected by the Mayo Clinic MASSFIX or serum FLC measurements, a diagnosis of a monoclonal

gammopathy is 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 suggest 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 be reduced 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. For more information see https://istopmm.com/riskmodel/

### Reference Values

Monoclonal-protein Isotype Flag:
Negative
Interpretation:
No monoclonal protein detected.

IMMUNOGLOBULIN G:
0-<5 months: 100-334 mg/dL
5-<9 months: 164-588 mg/dL
9-<15 months: 246-904 mg/dL
15-<24 months: 313-1,170 mg/dL
2-<4 years: 295-1,156 mg/dL
4-<7 years: 386-1,470 mg/dL
7-<10 years: 462-1,682 mg/dL
10-<13 years: 503-1,719 mg/dL
13-<16 years: 509-1,580 mg/dL
16-<18 years: 487-1,327 mg/dL
> or =18 years: 767-1,590 mg/dL

IMMUNOGLOBULIN A

0-<5 months: 7-37 mg/dL
5-<9 months: 16-50 mg/dL
9-<15 months: 27-66 mg/dL
15-<24 months: 36-79 mg/dL
2-<4 years: 27-246 mg/dL
4-<7 years: 29-256 mg/dL
7-<10 years: 34-274 mg/dL
10-<13 years: 42-295 mg/dL
13-<16 years: 52-319 mg/dL
16-<18 years: 60-337 mg/dL
> or =18 years: 61-356 mg/dL

IMMUNOGLOBULIN M:
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 is 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 FLCS / Immunoglobulin Free Light Chain, Serum.
-Patients with IgD or IgE can be followed using quantitative IgD or IgE measurements (IGD / Immunoglobulin D [IgD], Serum; IGE / Immunoglobulin E [IgE], Serum).
-Patients with monoclonal Ig heavy chains (gamma, alpha, and mu) can be detected by the Mayo Clinic MASSFIX 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 immunofixation electrophoresis can have positive results on the Mayo Clinic MASSFIX test 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 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.
-Mayo Clinic MASSFIX testing will not quantitate albumin, alpha-1-trypisin, 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 free light chain (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 FLC 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

Results determined by assays using different manufacturers or methods may not be comparable.

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

Immunoglobulins A, G, and M
In this Siemens Nephelometer II method, the light scattered onto the antigen-antibody complexes is measured. The intensity of the measured scattered light is proportional to the amount of antigen-antibody complexes in the sample under certain conditions. If the antibody volume is kept constant, the signal behaves proportionally to the antigen

volume.

A reference curve is generated by a standard with a known antigen content on which the scattered light signals of the samples can be evaluated and calculated as an antigen concentration. Antigen-antibody complexes are formed when a sample containing antigen and the corresponding antiserum are put into a cuvette. A light beam is generated with a light emitting diode, which is transmitted through the cuvette. The light is scattered onto the immuno-complexes that are present. Antigen and antibody are mixed in the initial measurement, but no complex is yet formed. An antigen-antibody complex is formed in the final measurement.

The result is calculated by subtracting the value of the final measurement from the initial measurement. The distribution of intensity of the scattered light depends on the ratio of the particle size of the antigen-antibody complexes to the radiated wavelength.(Siemens Nephelometer II, Siemens, Inc.; Version 2.4, 07/2019)

Monoclonal Protein Isotype
This test is performed with immunoaffinity purification followed by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) analysis. For the immunoaffinity purification, patient serum is applied to 5 separate immunoaffinity resins specific to immunoglobulin G, A, M, K, and L. Unbound protein is washed away and the isolated immunoglobulins are broken down into their reduced forms 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
Mayo Clinic Laboratories - Rochester Superior Drive

## 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 |