TESTING FOR PLASMA CELL DISORDERS
Simplifying a Complex Medical Journey
ADVANCING PATIENT CARE WITH SUPERIOR TESTING

As a pioneer in the field, Mayo Clinic plays an integral role by developing new tests to help align patients with new therapies for plasma cell disorders. Our algorithmic approach ensures that the right tests are ordered at the right time, and that health care providers get clinically actionable answers for their patients faster. And testing with Mayo Clinic means 24/7 access to our physician and laboratory experts, who are leaders in their fields.

Experience industry-leading turnaround times

Leverage convenient, cost-effective testing that delivers clinically relevant information

Access award-winning 24/7 support
WITH YOU EVERY STEP OF THE WAY

Appropriate diagnosis and monitoring of plasma cell disorders require a comprehensive and often complex testing approach. Our testing and expert support are designed to simplify the patient journey and give health care providers the critical answers they need—all in one place.

SCREENING
A groundbreaking method to accurately identify monoclonal proteins and determine risk of progression.

DIAGNOSIS
A simplified approach to risk stratification and diagnosis using the Mayo Stratification for Myeloma and Risk-Adapted Therapy (mSMART).

MONITORING
Accurate monitoring of patients to determine response to therapy and risk of relapse.
When a patient presents with a monoclonal protein (M-protein) disorder, the answer is not always multiple myeloma. From the more common diagnosis of monoclonal gammopathy of undetermined significance (MGUS), to rarer findings such as amyloid light-chain (AL) amyloidosis or POEMS syndrome, it is becoming more recognized that plasma cell neoplasms are not just one disease, and they are characterized by marked protein, cytogenetic, molecular, and proliferative heterogeneity. Clinicians are increasingly challenged to provide answers in this rapidly changing environment. Advances in testing methodologies, novel therapies, and individualized treatment regimens continually add to the complexity of helping patients. Whether you’re screening, diagnosing, or monitoring patients, we offer leading-edge testing while keeping patient care local.
### Monoclonal Protein Isotype

<table>
<thead>
<tr>
<th></th>
<th>Monoclonal Gammopathy of Undetermined Significance (MGUS)</th>
<th>Smoldering Multiple Myeloma (SMM)</th>
<th>Multiple Myeloma (MM)</th>
<th>Amyloidosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence in Patients with Monoclonal Gammopathy</td>
<td>58%</td>
<td>4%</td>
<td>17%</td>
<td>10%</td>
</tr>
<tr>
<td>Progression to Multiple Myeloma</td>
<td>10–15% (within 10 years) 25–30% (within 20 years)</td>
<td>50% (over 5 years)</td>
<td>NA</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Bone Marrow Monoclonal Plasma Cells</td>
<td>&lt;20%</td>
<td>&gt;20%</td>
<td>≥10%*</td>
<td>Any %</td>
</tr>
<tr>
<td>Serum M-Spike</td>
<td>&lt;3g/dL</td>
<td>&gt;2g/dL</td>
<td>Variable (typically ≥3g/dL)</td>
<td>Any amount</td>
</tr>
<tr>
<td>End-Organ Manifestations (CRAB)**</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Variable organ involvement dependent on affected protein</td>
</tr>
<tr>
<td>Treatment Required</td>
<td>No</td>
<td>Clinical trials available</td>
<td>Yes, and can be guided by mSMART 3.0</td>
<td>Yes</td>
</tr>
<tr>
<td>Other Plasma Cell Disorders</td>
<td>Amyloidosis, lymphoplasmacytic disorders, plasmacytoma, and POEMS syndrome</td>
<td>Plasma cell leukemia</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

* OR PATIENTS WITH ANY OF THESE:
- >60% plasma cells
- >100 kappa/lambda free light chain ratio
- >1 MRI lesion

** KEY
- C - Hypercalcemia
- R - Renal insufficiency
- A - Anemia
- B - Bone lesions
SCREENING

MASS-FIX: A GROUNDBREAKING APPROACH TO IDENTIFY MONOCLONAL PROTEINS

For patients at risk of plasma cell disorders, early identification is critical to ensure better outcomes. Coined as MASS-FIX, our innovative approach uses matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF MS), and marks the first major breakthrough in multiple myeloma screening since gel electrophoresis was developed in 1967.

Now included in International Myeloma Working Group recommendations
MASS-FIX is now included in International Myeloma Working Group recommendations as an accepted method for screening of M-proteins.

By weighing M-proteins, this method overcomes electrophoresis’s limitations in detection and provides the most accurate understanding of a patient’s M-proteins. This novel testing also helps health care providers understand their patients’ risk of progression to multiple myeloma or AL amyloidosis. This level of insight is not possible via traditional testing methods.

SENSITIVE
Surpassing immunofixation methodology

SPECIFIC
Confirming IgG kappa mass causation throughout monoclonal therapy

RAPID RESULTS
One-day turnaround time

Diagnosis of plasma cell neoplasms using MASS-FIX and bone marrow morphology puts patients on a path to individualized treatment. Proper risk stratification is a crucial first step in that process.
TESTING FOR SCREENING

DMOGA | Monoclonal Gammopathy Screen, Serum

Analytic time: 2 days
Appropriate ordering scenario
Identifying the presence of MGUS and assessing the risk of progression to multiple myeloma.

PEISO | Protein Electrophoresis and Isotype, Serum

Analytic time: 2 days
Appropriate ordering scenario
Diagnosis of monoclonal gammopathies, when used in conjunction with serum free light chain studies performed at client site.

SPEP | Electrophoresis, Protein, Serum

Analytic time: Same day/1 day
Appropriate ordering scenario
Screening patients with suspected monoclonal gammopathies and diagnosing monoclonal gammopathies, when used in conjunction with MALDI-TOF MS and free light chains.

FLCS | Immunoglobulin Free Light Chains, Serum

Analytic time: Same day/1 day
Appropriate ordering scenario
Monitoring serum from patients with monoclonal light chain diseases without a M-spike on protein electrophoresis. May be useful as a diagnostic test in patients in whom there is a suspicion of primary systemic amyloidosis, light chain deposition disease, or non-secretory myeloma.

MALD | M-Protein Isotype, Matrix-Assisted Laser Desorption-Ionization Time-of-Flight Mass Spectrometry, Serum

Analytic time: Same day/1 day
Appropriate ordering scenario
When protein electrophoresis and free light chain testing is performed in house. M-protein isotyping by MASS-FIX only.
DIAGNOSIS AND RISK STRATIFICATION

AN ALGORITHMIC APPROACH TO GUIDE DIAGNOSIS

Our updated approach to fluorescence *in-situ* hybridization (FISH) testing takes into account the fact that multiple myeloma is increasingly recognized as more than one disease, and is characterized by cytogenetic, molecular, and proliferative heterogeneity. While novel agents and combinations are rapidly redefining the treatment paradigm, patient outcomes vary based on risk stratification.

Created in conjunction with Mayo Clinic’s multiple myeloma clinical practice, mSMART uses flow cytometry, FISH, and the latest consensus to determine a patient’s genetic risk of developing multiple myeloma to better inform individualized treatment plans and provides clinicians with a comprehensive and correlated patient profile.

**MSMRT | mSMART Algorithmic Testing, Bone Marrow**

*Appropriate ordering scenario*
- At diagnosis of multiple myeloma and every 12 months if appropriate to assess potential disease progression.
- Order within 12 months only when disease progression is suspected.

*Included*
- Plasma cell DNA content and proliferation flow cytometry testing (PCPRO) provide plasma cell clonality, plasma cell proliferation, DNA index, and percent polyclonal plasma cells in total plasma cells.
- Updated algorithms can reduce unnecessary FISH testing by 20%.
- Newly implemented cell sorting methodologies provide optimal results for patients and clinicians.
- Standardized panels for diagnostic and progression testing.
- Focus on utilization management with additional FISH testing only performed when appropriate.

**PCPDS | Plasma Cell Proliferative Disorder, FISH, Bone Marrow**

*Appropriate ordering scenario*
- At diagnosis of multiple myeloma and every 12 months if appropriate to assess potential disease progression.
- Order within 12 months only when disease progression is suspected.

*Included*
- Updated algorithms can reduce unnecessary FISH testing by 20%.
- Newly implemented cell sorting methodologies provide optimal results for patients and clinicians.
- Standardized panels for diagnostic and progression testing.
- Focus on utilization management with additional FISH testing only performed when appropriate.
The mSMART algorithm stratifies patients into standard or high-risk categories.

**Traditional Approach**

- **Chromosome Analysis**
- **FISH**
- **Flow Cytometry**

Physician consolidates test results

Physician selects appropriate treatment options

**Mayo Clinic Approach**

- **mSMART 3.0** (Includes flow cytometry and FISH testing)

Risk stratification (standard or high)

mSMART 3.0 incorporates all testing into one patient profile and interpretive report. Learn more at [msmart.org](http://msmart.org).

**Traditional testing poses some risks**
- Wrong risk stratification identified
- Suboptimal treatment option selected
- Wasted health care expenses
- Studies have shown chromosome testing does not yield additional information—not necessary unless other disease states are suspected
- Potential for conflicting stratification results from multiple test methodologies

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**Our comprehensive FISH menu includes:**

<table>
<thead>
<tr>
<th>Initial panel</th>
<th>Reflex testing</th>
<th>Follow-up testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Includes testing for the following abnormalities using the probes listed.</td>
<td>Based on the results from the initial panel, reflex testing may be performed to identify the following abnormalities using the probes listed.</td>
<td>For follow-up samples, only the following probes will be tested.</td>
</tr>
<tr>
<td>17p−, TP53/D17Z1</td>
<td>t(11;14), CCND1/IGH</td>
<td>TP73/1q22</td>
</tr>
<tr>
<td>1q gain, TP73/1q22</td>
<td>t(14;16)(q32;q23) IGH/MAF</td>
<td>TP53/D17Z1</td>
</tr>
<tr>
<td>14q32 rearrangement, IGH</td>
<td>t(4;14)(p16.3;q32) FGFR3/IGH</td>
<td>MYC</td>
</tr>
</tbody>
</table>
MONITORING

ARMING PROVIDERS WITH ACCURATE TESTING FOR PATIENT MONITORING

Since the early 2000s, the average length of survival from time of diagnosis has more than tripled to more than five years. While the use of monoclonal therapies has benefited patients greatly, it presents a unique challenge for laboratories as these therapies can cause interference with traditional gel immunofixation testing methods. The MASS-FIX methodology easily overcomes this issue for a majority of patients.

Now included in International Myeloma Working Group recommendations
MASS-FIX is now included in International Myeloma Working Group recommendations as an accepted method for monitoring of M-proteins.

The most accurate testing for monitoring
The new MASS-FIX testing method provides:

- Increased sensitivity for early identification of myeloma relapse.
- Verifying if a patient’s IgG kappa mass is caused by monoclonal therapeutics or residual disease.
- Convenient, cost-effective, and clinically relevant information.
- Industry-leading turnaround times for results.

**TMOGA | Monoclonal Gammopathy Monitoring, Serum**

**Analytic time:** Same day/1 day

**Appropriate ordering scenario**
Determining if IgG kappa mass changes are caused by monoclonal therapeutics or residual disease.

**MALD | M-Protein Isotype, Matrix-Assisted Laser Desorption-Ionization Time-of-Flight Mass Spectrometry, Serum**

**Analytic time:** Same day/1 day

**Appropriate ordering scenario**
When protein electrophoresis and free light-chain testing is performed in house. M-protein isotyping by MASS-FIX only.
Providing a complete picture

Using MASS-FIX methodology provides a deeper understanding and accurate differentiation of a patient’s M-spike from monoclonal therapeutic interference from drugs like daratumumab, as illustrated in the example below.

![Graph showing IgG kappa with daratumumab](image)

Figure 1. IgG kappa with daratumumab
**MONITORING**

**Minimal residual disease testing**
As more effective therapies have become available, the average overall survival length for newly diagnosed multiple myeloma patients has more than tripled since the early 2000s.

Detecting minimal residual disease in bone marrow samples during treatment or after therapy has become increasingly important. Patients who do not achieve a minimal residual disease (MRD) negative status and will relapse faster and have a shorter survival length.

With a sensitivity of $10^{-5}$, our EuroFlow MRD test meets the guidelines recommended by the International Myeloma Working Group, the National Comprehensive Cancer Network, and the International Clinical Cytometry Society. Additionally, because most clinical trials require the use of MRD testing with at least a $10^{-5}$ sensitivity, approaches that overcome the current limitations of conventional flow cytometry must be used.

**MRDMM | Multiple Myeloma Minimal Residual Disease by Flow, Bone Marrow**

- **Analytic time:** 2–4 days
- **Appropriate ordering scenario**
  Assessing the level of MRD after completion of therapy to aid in prognosis and treatment planning.
When should I order this test?

<table>
<thead>
<tr>
<th>CONSIDER ORDERING</th>
<th>DO NOT ORDER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Once a patient is immunofixation negative on both serum and urine samples, the most frequent ordering scenarios for MRD testing include:</td>
<td>This test <strong>should not</strong> be ordered in situations of known relapse or diagnosis. For these situations, please see the following tests in our test catalog:</td>
</tr>
<tr>
<td>▸ To assess response to therapy in the setting of a clinical trial.</td>
<td>▸ <strong>Plasma Cell DNA Content and Proliferation</strong>, Bone Marrow (Mayo ID: PCPRO)</td>
</tr>
<tr>
<td>▸ As a prognostic indicator of future disease progression and overall survival time, post chemotherapy or autologous stem cell transplantation.</td>
<td>▸ <strong>Mayo Algorithmic Approach for Stratification of Myeloma and Risk-Adapted Therapy Report</strong> (Mayo ID: MSMRT)</td>
</tr>
<tr>
<td>▸ As follow-up testing for complete remission patients who are not MRD negative, but remain immunofixation negative.</td>
<td></td>
</tr>
</tbody>
</table>
MULTIPLE MYELOMA

**CLINICAL REFERENCES**


**Publications on MASS-FIX Testing**


**Publications on MRD Testing**


For more information on plasma cell disorder testing, visit news.mayocliniclabs.com/hematology.