Infographic

MRD as a Primary Endpoint for Accelerated Approval in Multiple Myeloma

January
2026

A new regulatory milestone

The FDA published draft guidance on using minimal residual disease (MRD), also known as measurable residual disease, as primary endpoint to support the potential accelerated approval of novel treatments for multiple myeloma (MM).

Why this matters

- **Increasing survival and stronger response rates** make differentiation harder
- MRD enables earlier **differentiation** and can support faster **development timelines**

What the draft guidance enables

- **MRD negativity** in complete response may serve as a reasonably likely surrogate for progression-free survival for accelerated approval, provided evidentiary and assay validation standards are met

Trial design options in accelerated approval pathway

1 SINGLE-TRIAL MODEL

May enable **earlier submission and operational continuity**

MM Study 1 (randomized) → Assess MRD → Accelerated approval → Assess MRD, PFS, OS → Regular approval

2 DUAL-TRIAL MODEL

Can **reduce bias and provide greater flexibility** but increases complexity

MM Study 1 (randomized or single-arm) → Assess MRD → Accelerated approval

MM Study 2 (randomized) → Assess MRD, PFS, OS → Regular approval

PFS: Progression-Free Survival
OS: Overall Survival

MRD execution

- MRD timing, threshold, and population must be prespecified
- Statistical analysis plans must clearly define endpoints and analysis approach
- Assay processes must be controlled across the full workflow

Assay expectations

- Validation should demonstrate **accuracy, precision, detection limits, stability, and specificity**
- A **single validated technology** such as next-generation flow (NGF) or next-generation sequencing (NGS) should be used

Accelerated approval expectations

- **Confirmatory trials** are expected early, often before or at approval
- **Operational readiness and study feasibility** are assessed by regulators
- **On-going progress reporting** is required post-approval

MRD endpoint readiness in 5 steps

1. Define the MRD context of use
2. Prespecify endpoint timing and statistical analysis plan
3. Lock assay strategy and validation plan
4. Select an appropriate trial model
5. Engage FDA early in development

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