AMWA JOURNAL V41 N2 / 2026

GLOBAL MEDICAL COMMUNICATION

Will the Food and Drug Administration's New Standard of Requiring Only One Trial for a New Drug Application / Biologic License Application Have Repercussions for Medical Communicators?

Thomas M. Schindler / RSW – RegulatoryScienceWriting, Biberach, Germany

On February 19, Prasad and Makary published a "Sounding Board" opinion piece in the *New England Journal of Medicine* (NEJM).[1] They announced that the Food and Drug Administration (FDA) will move away from its long standing practice of requiring 2 well-controlled clinical trials for marketing approval. From now on, a single pivotal trial—supported by "additional evidence" (for example, biomarker data, mechanistic evidence, real-world data, or postmarketing surveillance)—will become the new default for many drug approvals.

The authors point to the FDA's September 2023 draft guidance, "Demonstrating Substantial Evidence of Effectiveness with One Adequate and Well Controlled Clinical Investigation and Confirmatory Evidence."[2] That document already outlined the conditions for a "one trial to NDA/BLA" pathway. The key message of the rather forceful NEJM piece is that this approach will become the default, not the exception—although noting that the FDA can still ask for 2 independent trials (for example, when the effect size is modest or the mechanistic rationale is weak).

So far, the response has been muted. There has been no official reaction from regulators outside the United States, no major commentary in leading medical journals, and little public input from industry leaders or trade associations. Surprisingly, the NEJM piece has not sparked meaningful debate in medicine, academia, or global regulatory circles. One reason may be that Prasad and Makary presented the shift as a fait accompli, rather than a proposal. In addition, other regulators (for example, the European Medicines Agency [EMA], the Medicines and Healthcare products Regulatory Agency [MHRA], and the Pharmaceuticals and Medical Devices Agency [PMDA]) already accept single pivotal trials in defined circumstances. As industry generally welcomes greater flexibility in evidentiary standards, it may therefore have adopted a "silence is golden, but my eyes still see"[3] attitude.

What does this mean for medical writers and medical communicators? Based on the limited commentary available, 2 broad views have emerged.

VIEW 1: FEWER PIVOTAL TRIALS COULD MEAN LESS WRITING WORK

If the pharmaceutical industry adopts one pivotal trial as the norm, clinical development programs may involve fewer studies—potentially reducing writing and publication opportunities.

- Fewer trials would mean fewer core study documents to produce (for example, protocols, informed consent forms, statistical analysis plans, committee charters, and clinical study reports).
- Medical communication could also be affected: fewer trials can translate into fewer publications, conference abstracts, posters, and related materials.
- If the policy encourages more programs to advance toward FDA submission, reduced trial document work could be partly offset by an increased volume of New Drug Application and Biologic License Application dossiers.
- With fewer trials in scope, some submission packages may also become simpler—at least in terms of the number of studies they need to cover.

A key issue, therefore, is whether the new default actually reduces the number of pivotal trials run. In oncology and rare diseases, single trial approvals and expedited pathways are already common, so the incremental impact may be limited. As of May 10, 2026, oncology accounts for 26.8% and rare diseases for 0.3% of all "actively recruiting" and "not yet recruiting" trials on ClinicalTrials.gov. By contrast, for mass market therapies in cardiovascular (11.8%) and respiratory (7.8%) diseases, sponsors may be more willing to streamline development—potentially leading to fewer trials.

VIEW 2: THE WRITING WORKLOAD MAY SHIFT RATHER THAN SHRINK

Under a one pivotal trial model, dossiers may need a clearer and more defensible narrative to meet the "substantial evidence" standard. In practice, that could mean more

ISSN 2163-5315

emphasis on justification, integration of supporting evidence, and cross module consistency.

- Module 2 may need to be more explicitly argumentative: the Clinical Overview and Clinical Summaries would need to explain why a single pivotal trial is adequate.
- A mechanistic rationale, pharmacokinetic and pharmacodynamic dose-response relationships, external controls, and/or real-world evidence may need to be tightly integrated and mapped to the pivotal trial's limitations.
- Expectations for statistical defensibility may rise (for example, clearer multiplicity control, stronger missing data strategies, more sensitivity analyses, and more extensive use of Bayesian approaches).
- The safety narrative may need to be strengthened, including clearer plans and commitments for post-marketing activities.
- With greater emphasis on mechanistic plausibility, stronger alignment across CMC (chemistry, manufacturing, and controls), nonclinical, and clinical sections may be needed, with explicit links between the mechanism of action and expected clinical effect.
- Because both the 2023 draft guidance and the NEJM piece emphasize early and frequent agency engagement, interactions with the FDA may need to be described more comprehensively—and reflected consistently across the full document set.

Even so, it remains unclear how consistently the FDA will apply a one trial default in practice. Sponsors may also hesitate to adopt a strict "one trial only" strategy for global programs: regulators in Europe and Asia could still expect more comprehensive evidence in some settings. One potential compromise is geographic tailoring—running a second pivotal trial primarily outside the United States whereas keeping the US submission focused on a single trial plus confirmatory evidence.

Prasad and Makary also point out that, if fewer trials are conducted, scrutiny of the remaining pivotal trial will increase. Medical writers describing such trials will therefore benefit from revisiting core Good Clinical Practice (GCP) principles and include illustrations of the following: "… the use of a contemporary control group (…), the nature of the control group (…), the prespecification of a hypothesis, the choice of a primary end point, the concordance with biologic correlates (…), alignment of intermediate end points, statistical power, blinding, concealment, independent review, whether post-protocol therapy is on par with the U.S. standard of care, the use of concomitant therapy, inclusion criteria, exclusion criteria, randomization, run-in periods, how missing data are handled, and many additional factors[1]".

In addition to more intense scrutiny, the value of evidence generated outside traditional clinical trials is likely to rise. Prasad and Makary note that "this reform is being rolled out synchronously with the agency's post market initiative to collect robust data on all drugs and devices." However, they provide few specifics on how this initiative will be implemented or how such data will be weighed in individual decisions.

In summary, a shift toward a one pivotal trial default could affect regulatory medical writers in both the *amount* and the *type* of work available—potentially reducing some trial level deliverables while increasing the need for integrated, persuasive submission narratives. Because the policy's real-world application is still evolving, medical writers should watch this space closely and be ready to adapt.

Author declaration and disclosures: *The author notes no commercial associations that may pose a conflict of interest in relation to this article.*

Author contact: *RegulatoryScienceWrite@web.de*

References

1. Prasad V, Makary MA. One pivotal trial, the new default option for FDA approval - ending the two-trial dogma. *N Engl J Med*. 2026;394(8):815-817. doi:10.1056/NEJMsb2517623
2. Food and Drug Administration, Oncology Center of Excellence (OCE), Center for Biologics Evaluation and Research (CBER), Center for Drug Evaluation and Research (CDER). *Demonstrating Substantial Evidence of Effectiveness With One Adequate and Well-Controlled Clinical Investigation and Confirmatory Evidence: Guidance for Industry*. US Department of Health and Human Services; 2023.
3. The Tremeloes, "Silence is golden, but my eyes still see"; song by Bob Crewe and Bob Gaudio; record issued by CBS Records in the UK and Epic Records in the US and Canada April 21st, 1967

Postscript: Unexpectedly, on May 12th, 2026, Martin A Makary resigned from his position as FDA Commissioner.