

October 19, 2026

Dr. Michelle Tarver, Director, Center for Devices and Radiological Health
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

RE: ACRO comment on FDA CDRH Discussion Paper *Considerations for the Regulation of Generative AI-Enabled Medical Devices: Discussion Paper and Request for Feedback*
[Docket FDA-2026-N-7874]

Dear Dr. Tarver,

Founded in 2001, the Association of Clinical Research Organizations (ACRO) is a non-profit trade association representing the world's leading clinical research and technology organizations, which provide specialized services that are integral to the development of drugs, biologics, and medical devices that enable patients to live longer, healthier, and more productive lives. ACRO members provide a wide range of specialized services across the entire spectrum of drug development—from preclinical, proof of concept, and first in human studies through post-approval, pharmacovigilance, and health data research. ACRO member companies employ more than 470,000 people worldwide and conduct research in every global region.

ACRO is pleased to provide feedback on this CDRH Discussion Paper and commends CDRH for seeking early stakeholder input. Because generative artificial intelligence (“GenAI”) is evolving rapidly, ACRO encourages CDRH to favor flexible, pragmatic, principles-based approaches that provide sponsors with clarity and predictability while avoiding recommendations that are impractical, unduly burdensome, or likely to become quickly outdated. Our key messages are set out below.

1. ACRO welcomes the two-axis risk framework, which aligns with FDA’s approach for drugs and biologics

CDRH proposes a two-axis risk framework that considers the device’s “activity” (ranging from informational/non-directive to fully autonomous action-taking) and the “consequences” of relying on an incorrect output (ranging from limited to severe). This CDRH two-axis risk framework builds upon, and converges with, the two-axis framework outlined in the 2025 FDA draft guidance on *Considerations for the Use of Artificial Intelligence to Support Regulatory Decision-Making for Drug and Biological Products*, which presents a two-axis Model Risk Matrix based on “model influence” and “decision consequence.” ACRO believes this alignment makes sense. The underlying principles (how much an AI output drives a decision or action, and the consequences if that output is wrong) apply irrespective of whether the AI is part of a medical device or supports drug and biologic development. A consistent approach across FDA centers will also benefit sponsors, CROs, and technology developers that work across product types.

ACRO encourages CDRH to maintain the framework as a flexible, organizing heuristic within existing device classification, benefit-risk, and risk-management principles, rather than as a new GenAI-specific classification scheme. Other factors, such as the detectability and reversibility of errors, human oversight, and downstream safeguards, may also be relevant and could be treated as contextual considerations rather than additional fixed criteria. Likewise, the intended user (patient, generalist, or specialist) may be relevant context but should not, on its own, determine a function’s risk. ACRO would welcome additional discussion and communication from FDA regarding how CDRH, CDER, and CBER will keep their frameworks aligned as each is finalized.

2. ACRO supports a technology-neutral approach that builds on existing FDA frameworks

ACRO strongly supports CDRH's statement that FDA regulates medical devices, not GenAI as such. The use of GenAI should not, by itself, determine a device's classification, regulatory pathway, or evidentiary requirements; these should continue to rest on intended use, clinical context, and risk. Future policy should build on existing frameworks, including those for AI-enabled device software functions, PCCPs, quality systems, cybersecurity, and Good Machine Learning Practice, with targeted additions only where GenAI introduces risks those frameworks do not already address. The same principle should apply to agentic functionality, which should be assessed based on what the system is permitted to do and the consequences of error rather than the "agentic" label, and to multi-function products, where oversight should continue to apply at the device-function level.

3. ACRO supports flexible and risk-proportionate premarket evaluation

ACRO welcomes CDRH's recognition that conventional testing approaches may not suit GenAI-enabled devices and that clinical confirmation may not require a prospective clinical study in every case. The competency-based approach of benchmarking followed by clinical confirmation may be useful for some devices. However, given how quickly GenAI is evolving, ACRO encourages CDRH to present it as one of several acceptable approaches rather than a required sequence or checklist. In particular, ACRO recommends that CDRH clarify in future communications that (1) benchmarking elements are a menu from which sponsors select based on intended use and risk; (2) sponsor-developed benchmarks and datasets are acceptable when shown to be fit for purpose; (3) independent third-party testing or adjudication is an option rather than a default requirement; and (4) the choice of comparator (e.g., a clinical reference standard, standard of care, unaided user, or human-device team performance) follows the intended use rather than defaulting to physician performance.

ACRO members have extensive experience designing and conducting clinical studies for devices, drugs, and biologics, and stand ready to work with CDRH on practical, scientifically sound approaches to clinical confirmation, including the appropriate use of real-world data and data collected outside the United States.

4. ACRO supports risk-based, pragmatic postmarket monitoring and change control

ACRO supports a total product life cycle approach and agrees that postmarket evidence can complement, but should not replace, the premarket evidence needed to provide a reasonable assurance of safety and effectiveness. Re-benchmarking, sample-based clinician review, and drift monitoring may each be useful, but none should be universally required; manufacturers should be able to set the scope, frequency, and triggers for monitoring based on device risk and identified failure modes. Similarly, evaluation after a modification should be proportionate to its reasonably foreseeable impact, and PCCPs should be able to define a bounded range of anticipated changes without specifying every future technical implementation. ACRO requests FDA to clarify how it will distinguish *expected* variability in generative outputs, on the one hand, from performance degradation that affects safety or effectiveness, on the other. We ask the Agency to clarify its expectations for manufacturers using third-party foundation models, which should reflect the information and controls reasonably available to them.

5. ACRO supports voluntary Foundation Model Master Files

ACRO sees value in voluntary Foundation Model Master Files as a way to reduce duplicative submissions and give FDA reviewers consistent information. Participation should remain voluntary; the absence of a Master File should not disadvantage a sponsor that can support its submission with device-level evidence; and a Master File should not be viewed as FDA qualification or endorsement of the underlying model.

ACRO also encourages CDRH to continue working with international regulators, including through the International Medical Device Regulators Forum (IMDRF), to promote convergence on terminology, validation, and change-management expectations. Given the pace of change in GenAI, ACRO believes that high-level, principles-based policy, supplemented by illustrative examples and early engagement through the Q-Submission program, will serve patients better than detailed, prescriptive requirements that may quickly become outdated.

ACRO appreciates this opportunity to comment and welcomes continued engagement with CDRH on this important topic. Please do not hesitate to contact ACRO (knoonan@acrohealth.org) if we can answer any questions or provide additional information.

Respectfully submitted,

Karen Noonan
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