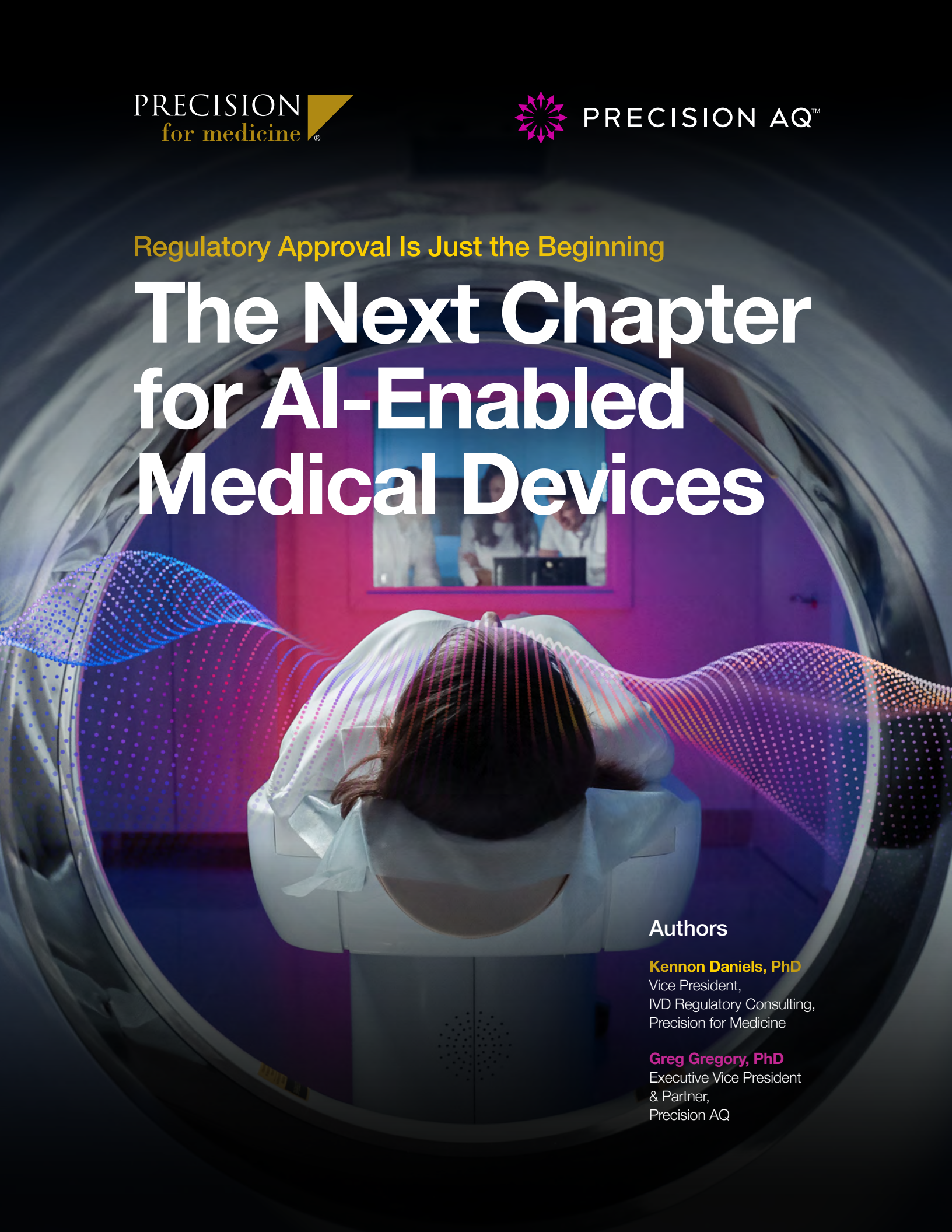
PRECISION for medicine®

PRECISION AQ™

Regulatory Approval Is Just the Beginning

The Next Chapter for AI-Enabled Medical Devices



Authors

Kennon Daniels, PhD
Vice President,
IVD Regulatory Consulting,
Precision for Medicine

Greg Gregory, PhD
Executive Vice President
& Partner,
Precision AQ

Table of Contents

Over the past year, we have shared perspectives on how health systems are using artificial intelligence (AI) to support clinical decision-making and how physicians are increasingly turning to tools like Open Evidence in daily practice.

In this article, we focus on a different but closely related inflection point: the rise of AI as a regulated medical device. As AI becomes embedded in diagnostics, imaging platforms, software as a medical device, and software-driven medical technologies, regulatory oversight and requirements bring new rigor and exposes new challenges around evidence, adoption, and commercialization.

2025

The Year Regulatory Expectations Caught Up to AI Innovation

For much of the last decade, AI innovation in healthcare moved faster than the regulatory frameworks designed to govern it. That dynamic began to change meaningfully in 2025.

Early last year, the U.S. Food and Drug Administration (FDA) released comprehensive draft guidance addressing artificial intelligence–enabled medical devices across the total product life cycle. For the first time, FDA brought together expectations spanning design, development, validation, deployment, cybersecurity, post-market monitoring, and change management into a single, cohesive regulatory construct. There were also recommendations on what should be included in the regulatory submission such as transparency of design and usability studies to evaluate human factors depending on final end user.

There is clear signal that AI-enabled devices are no longer an edge case. They are medical devices, subject to the same rigor around safety, effectiveness, regulatory, and quality system management system requirements such as ISO13485 and 21CRF820, requirements under 21 CFR Part 820 (transitioning to the new Quality System Management Regulation, which aligns with ISO 13485:2016, effective Feb 2, 2026) with additional regulatory scrutiny. AI introduces unique risks such as model bias, opacity, use in unsupported patient populations, and performance drift which can all result in false negative or positive outputs.

FDA also reinforced the role of Predetermined Change Control Plans (PCCPs) as a mechanism for managing adaptive algorithms post-clearance. Rather than freezing models at launch, PCCPs allow manufacturers to define in advance with FDA's agreement, the scope and governance of future updates, provided changes remain within validated boundaries. From a regulatory perspective, this is a pragmatic step that enables innovation while maintaining control by the regulators.

Yet as regulatory expectations became clearer, a parallel reality began to emerge.

What FDA Approved and What That Signals

By the end of 2025, FDA had authorized well over a thousand AI-enabled medical devices across a range of specialties. While growth continued broadly, authorizations remained heavily concentrated in a few areas.

Radiology continues to dominate, accounting for roughly three quarters of FDA-authorized AI devices. Imaging has served as the proving ground for medical AI, supported by clear intended uses, structured data, established workflows, and well-defined clinical endpoints. Growth has also continued in cardiology, neurology, pathology, and ophthalmology, although many tools still rely on image or signal-based inputs.

What is evolving is the type of AI FDA is willing to clear.

In 2025, FDA demonstrated increased comfort with:

Predictive and prognostic AI, not just detection

Tools that shape clinical decisions rather than simply assist interpretation

AI embedded directly into hardware, instrument platforms for analysis of complex biomarkers, and procedural workflows

FDA's clearance of the following types of platforms Examples such as signal a regulatory willingness to clear higher-impact use cases when evidence is appropriately structured and risks are well characterized.

- AI platforms that estimate future disease risk from imaging alone signal a regulatory willingness to clear higher
- Standalone software as a medical device that analyzes predetermined inputs from the patient's electronic health record to generate a risk score for disease progression within 24 hours of patient assessment

Most AI enabled medical devices have entered the market through the de novo or 510(k) pathways and are regulated as Class II devices. In the early stages of FDA oversight, a greater proportion of AI and machine learning technologies were reviewed through the PMA pathway as Class III devices. PMA submissions remain relatively uncommon and reserved for higher-risk intended uses.

The majority of these medical devices have hit the market through the de novo or 510(k) regulatory submission pathway which is Class II. Early on the majority were approved through the PMA pathway as a Class III device. Over the past five years, there have only been a handful of higher risk AI/ML devices signifying FDA's drawing a line for higher-risk AI/ML devices, especially those that directly guide time-critical treatment decisions or control/drive therapy delivery, where the tolerance for error is lower and the evidence bar is correspondingly higher.

FDA's drawing a line for those devices that guide treatment decisions or even provide the treatment such as external defibrillation of individuals who are exhibiting symptoms of cardiac arrest.

Yet as authorization volumes continue to rise, it has become increasingly clear that regulatory success alone is no longer a reliable predictor of real-world adoption.

That momentum is not limited to FDA authorizations. In early 2026, the Advanced Research Projects Agency for Health (ARPAH) announced a new initiative, ADVOCATE, aimed at developing the first FDA-authorized agentic AI system capable of providing continuous cardiovascular disease management. Unlike the current AI tools, ADVOCATE is designed to autonomously manage all elements of care such as medication adherence, appointments, diet, and exercise, while operating under an explicit regulatory pathway and in close coordination with FDA.

The structure of the program reflects how seriously ARPAH is treating both regulatory and real-world constraints. ADVOCATE includes patient-facing clinical AI agents, a supervisory agent responsible for monitoring safety and effectiveness, and deployment across diverse healthcare organizations for holistic clinical care. The program also highlights unresolved challenges: real-world healthcare data are often incomplete, inconsistent, or captured for billing rather than clinical decision-making. Oversight becomes particularly complex when ground truth is unavailable in real time, forcing difficult tradeoffs between human review and automation.

That ARPA H is explicitly funding this work, while engaging closely with FDA, underscores a growing recognition that regulatory authorization, evidence generation, and implementation strategy must evolve together rather than sequentially.

Clearance Is Not the Finish Line

Regulatory clearance answers a necessary question: Is this device safe and effective for its intended use?

It does not answer other questions that ultimately determine whether an AI-enabled medical device will succeed:

- Does it meaningfully change clinical decisions?
- Does it improve outcomes, efficiency, or both?
- Who pays for it, and under what mechanism?
- How does it fit into existing workflows and incentives?

Health systems evaluating AI-enabled medical devices have grown more discerning. Algorithmic performance alone is no longer sufficient. Instead, stakeholders are increasingly focused on whether a tool reduces variation in care, enables earlier or more confident decisions, improves workforce efficiency, and aligns with quality metrics and value-based care objectives.

This gap between clearance and adoption has become one of the defining challenges for AI in medical devices.

The Evidence Bar Is Expanding

A significant part of this challenge lies in how evidence is generated.

FDA's risk-based framework appropriately emphasizes safety and effectiveness, often allowing retrospective analyses, enriched data sets, or surrogate endpoints particularly for lower-risk devices. These approaches may be sufficient for 510(k) clearance, but they are often insufficient for payer confidence, guideline inclusion, or health-system investment decisions.

As AI-enabled devices move closer to diagnostic and therapeutic decision-making, stakeholders increasingly expect evidence of impact on downstream decisions, performance across diverse populations and care settings, and ongoing real-world monitoring rather than reliance solely on premarket validation.

From an IVD and companion diagnostics perspective, many AI-enabled tools are beginning to function as diagnostics without a specimen. They stratify risk, guide care pathways, and shape treatment decisions—without fitting neatly into traditional evidence or reimbursement frameworks.

This tension is becoming increasingly visible as AI tools influence clinical behavior without a corresponding strategy for value demonstration.

Why Go-to-Market Strategy Must Start Earlier

These dynamics place new pressure on commercialization planning.

Historically, many device developers treated regulatory approval as the primary hurdle, with go to market strategy following close behind. For AI enabled medical devices, that sequencing is increasingly risky.

Today, successful programs align regulatory, evidence, pricing, and reimbursement strategies much earlier in development. This includes designing validation studies that support both 510(k) clearance and payer dialogue; anticipating how value will be communicated to nontechnical stakeholders; understanding how AI fits into existing coding, coverage, and payment pathways; and planning for education and trust-building around transparency and bias.

Reimbursement remains fragmented, particularly outside of imaging, but momentum is building. CMS and commercial payers are beginning to recognize select AI-enabled services through addon payments, temporary codes, or inclusion within bundled care models. Still, coverage decisions often lag authorizations, and evidence expectations continue to evolve.

Differentiation in a Crowded AI Landscape

As the number of AI enabled medical devices grows, differentiation has become another challenge.

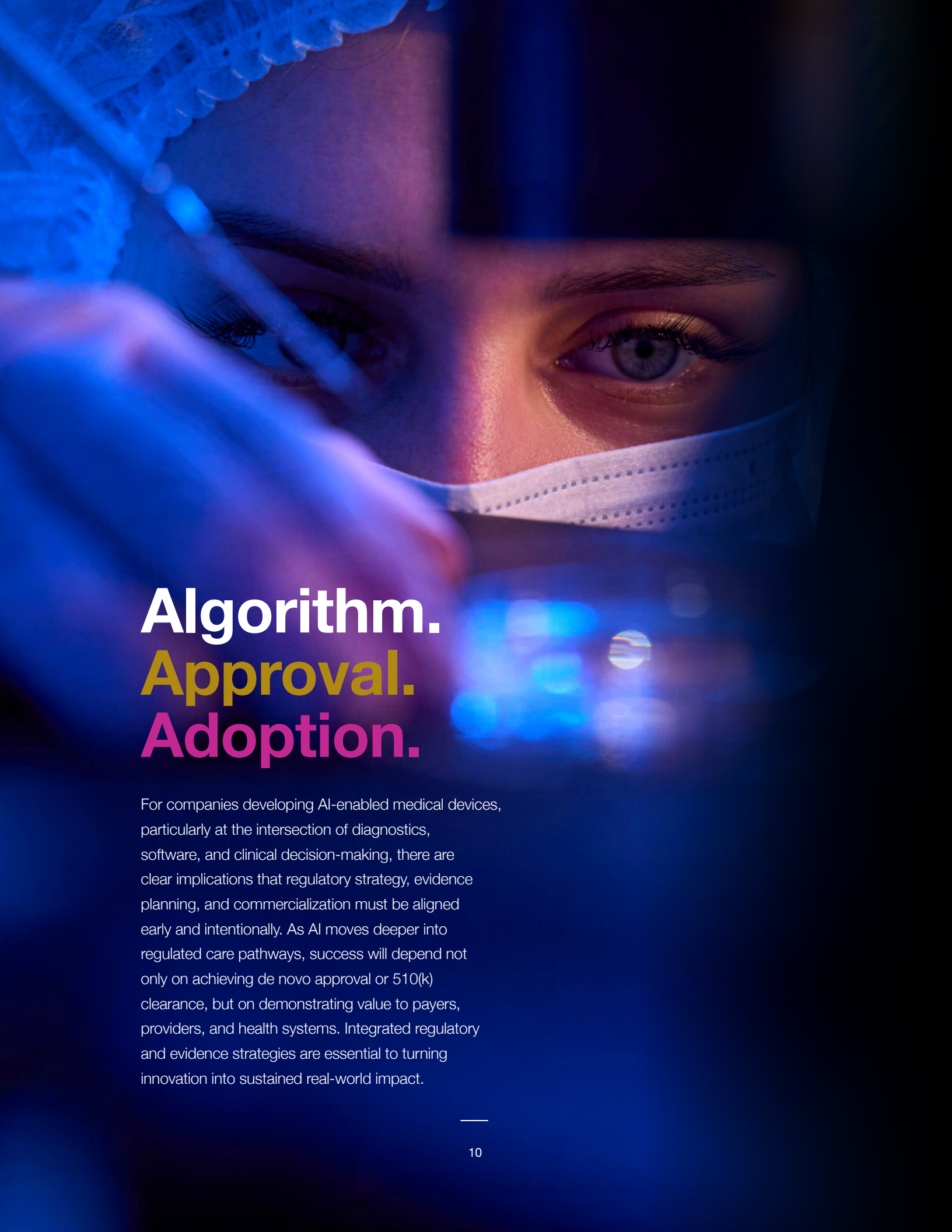
Clinicians and administrators face increasing cognitive overload, with many tools promising marginal gains in accuracy or efficiency. In this environment, success will favor companies that can clearly articulate what decision is changed (and for whom), why that change matters clinically and operationally, and how performance is monitored and maintained over time.

Transparency, explainability, and post-market accountability once viewed primarily as regulatory obligations are increasingly commercial differentiators.

From Regulatory Success to Real World Impact

FDA has taken meaningful steps to modernize the regulation of AI-enabled medical devices. The 2025 guidance clarified expectations on transparency of design, validation requirements, cybersecurity, and usability which reduced uncertainty. Programs such as ARPAH's ADVOCATE illustrate how quickly AI is moving toward higher-risk, more autonomous use cases even as regulatory and evidentiary expectations for these technologies are still being defined. But regulatory clarity does not guarantee adoption.

The next chapter of AI in medical devices will be defined less by approval counts and more by integration into real clinical and economic decision-making. That requires manufacturers to think beyond algorithms and design evidence, value propositions, and engagement strategies that resonate with regulators, payers, health systems, and clinicians alike.



Algorithm. Approval. Adoption.

For companies developing AI-enabled medical devices, particularly at the intersection of diagnostics, software, and clinical decision-making, there are clear implications that regulatory strategy, evidence planning, and commercialization must be aligned early and intentionally. As AI moves deeper into regulated care pathways, success will depend not only on achieving de novo approval or 510(k) clearance, but on demonstrating value to payers, providers, and health systems. Integrated regulatory and evidence strategies are essential to turning innovation into sustained real-world impact.

Authors

Kennon Daniels, PhD
Vice President,
IVD Regulatory Consulting,
Precision for Medicine
Kennon.Daniels@precisionformedicine.com

Greg Gregory, PhD
Executive Vice President
& Partner,
Precision AQ
Greg.Gregory@precisionaq.com

PRECISION for medicine®

precisionformedicine.com

PRECISION AQ™

precisionaq.com

Download your digital copy

Rev. 01