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White Paper

What Is ICH GCP, and How Does It Impact Clinical Planning?

Plus, the *recipe* for successful implementation



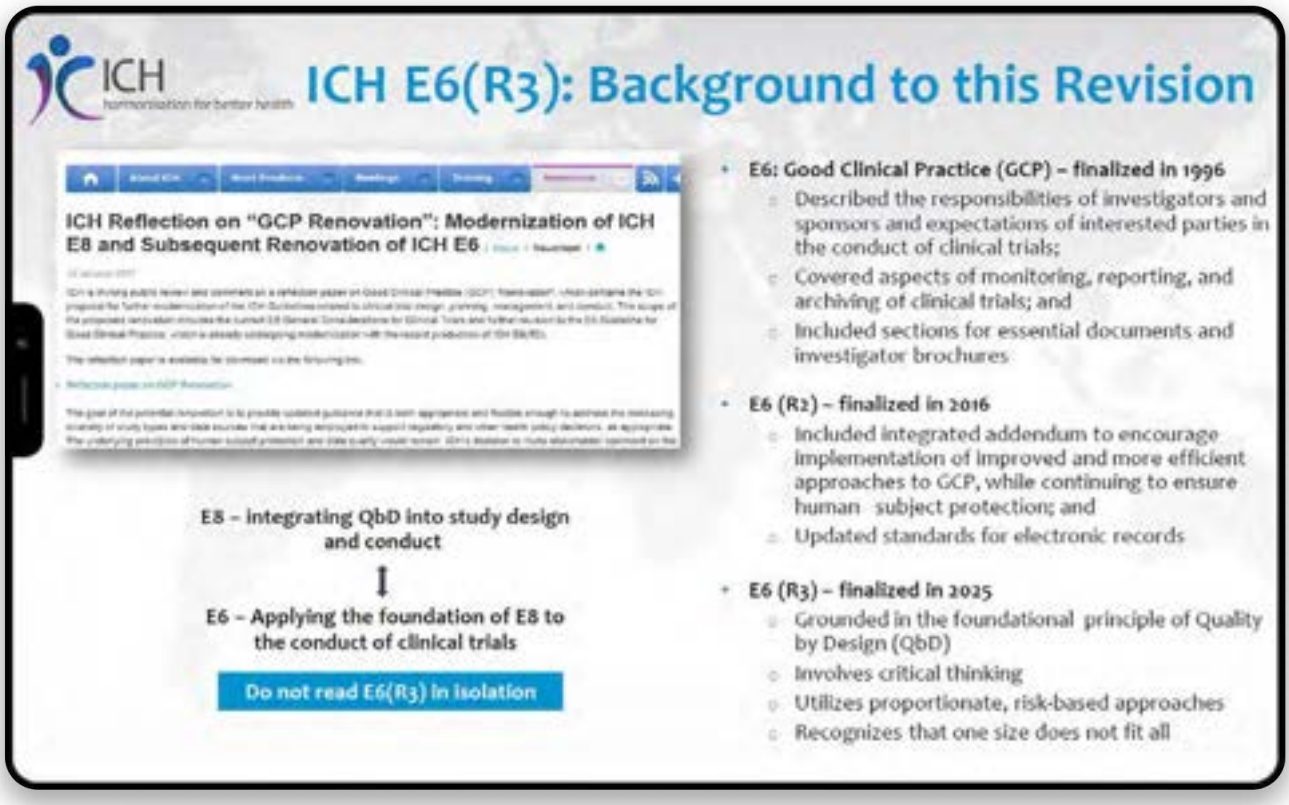
September 2025

Introduction

The International Council for Harmonisation (ICH) has updated its Good Clinical Practice (GCP) guideline, effective July 23, 2025. ICH GCP is an international, ethical, scientific, and quality standard for the conduct of trials that involve human participants. Clinical trials conducted in accordance with this standard will help to assure that the rights, safety, and well-being of trial participants are protected; that the conduct is consistent with the principles that have their origin in the Declaration of Helsinki; and that the clinical trial results are reliable.[1]

Put in place 30 years ago, the guideline was designed to make patient safety paramount, says Claire Riches, Citeline VP of Clinical Solutions. She says data integrity was always a critical component of GCP, to ensure that confidentiality was maintained, that data were being used for the right purposes, and that the minimum data needed were collected.

When the guideline was first put in place, Riches notes, everything was recorded on paper and conducted in person. There were no such things as electronic health records (EHR) or electronic diaries. Technological advancements such as these necessitated that the guideline be updated along the way. "The guideline was so out of date compared to what we have access to now," Riches says. She adds that the latest update is fit for purpose on "how we run trials today and what we have access to," with a focus on risk assessment and proportionality.



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While E6(R3) focuses on operational quality, says Dan Roach, Project Manager, External Engagement, TransCelerate BioPharma, its alignment with ICH E8(R1) encourages broader stakeholder engagement — including patients, healthcare professionals, and advocacy groups — to ensure trials are both scientifically sound and practically feasible. “This marks a departure from the more rigid, standardized approach of E6(R2), empowering teams to tailor trial design to the unique needs and risks of each study,” he says.

“ICH E6(R3) reshapes every phase of the clinical trial lifecycle,” Roach adds, “embedding a culture of quality and collaboration, prioritizing participant well-being and reliable trial data.”

“The buzzword … that everyone’s kind of grappling with is proportionality,” says Abigail Dirks, Data Scientist at the Tufts Center for the Study of Drug Development (CSDD). “Proportionality is really the pillar of risk-based quality management … to, first of all, think critically.



Dan Roach
Project Manager,
External Engagement,
TransCelerate BioPharma

ICH GCP is the foundation for clinical trial regulations in major regions including the US, EU, and Japan and has been updated over time to integrate modern trial practices and technologies. In short, ICH GCP sets the global gold standard for conducting ethical, scientifically sound clinical research.

The updated guideline reduces the number of principles to 11 (from 13 in the previous version), introducing principles on proportional risk and clear roles while refining others for clarity and efficiency. The majority of the updates apply to clinical planning, up until the first patient enrolled, Riches explains. She adds that the guideline also applies to trial execution, with the caveat that risk assessment should be conducted up front “so that it’s not just a tick-box exercise.”

Leslie Sam, president of the Leslie Sam and Associates consulting firm, agrees. “We’re



Leslie Sam
President
Leslie Sam and Associates

Key aspects of ICH E6(R3) GCP

- Protecting the rights, safety, and welfare of human subjects
- Ensuring scientific validity and credibility of clinical trial data
- Defining roles and responsibilities of investigators, sponsors, ethics committees, and monitors
- Mandating informed consent and confidentiality
- Emphasizing quality systems and risk-based management throughout the trial process

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moving away from this checkbox mentality. It's a good place to start, but you should have two to three questions under every checkbox."

"One of the interesting parts of the update to the guidance," Dirks says, "is the way that they formatted it. They were really intentional about the format." The guidance includes key principles as well as a set of annexes. The key principles are requirements, while the annexes provide options on how it could be implemented.

Dirks says there was an essential document section that at one point was being used as a sort of checklist. "And so they reformatted how that's listed, so it doesn't appear like a checklist. It doesn't mean that you need to check off every single one of those documents. You just need to have documents to support the type of decisions you're making throughout the trial."

Other foundational aspects are now codified in R3, says Sam. "Now the expectations are clear."

Failure to comply with the guideline can result in a clinical trial being halted, a completed trial restarted, or lack of approval for a drug. "It's a really strict framework," Riches says.

Why is the guideline being revised?

The updated ICH E6(R3) guideline, effective from July 23, 2025, focuses on modernizing the conduct of clinical trials with several prominent themes:

Flexibility and adaptability

The guidance promotes flexible, fit-for-purpose trial designs that can incorporate innovative methodologies and technologies, including decentralized and digital health approaches, to improve efficiency and effectiveness.

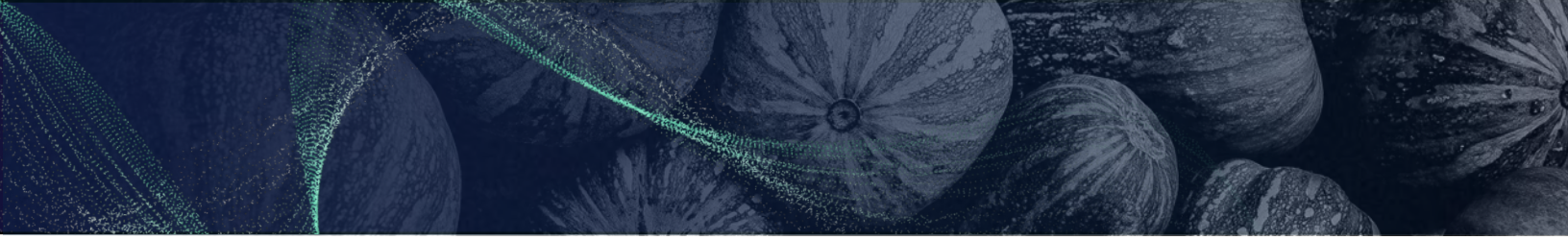
Using the analogy of meal planning and prep, Riches says, "If I'm setting my weekly menu, these are the *exact ingredients* I need as opposed to buying everything in the store — most of which have no bearing on the *recipe* — and then deciding what I'm going to cook. If I need 10 ingredients, I'm not going to buy 15. The extra five are just nice to have."



Claire Riches
VP, Clinical Solutions
Citeline

The same logic, she says, can be applied to clinical trials. "It's all about saving time, doing what you need to get a good outcome. Sponsors should use the parts of the guideline that are relevant to their specific trial." And, by limiting to essential elements, trials will not overburden sponsors, sites, and patients unnecessarily. "You'll still get the same result at the end of the day," Riches says. "That is, new drugs coming to market quicker but without all the unnecessary 'ingredients.'"

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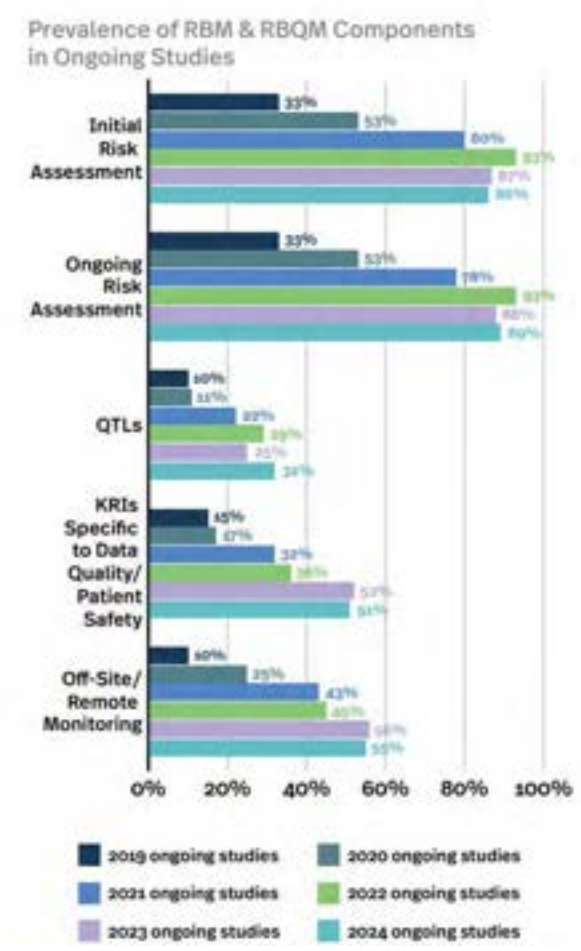
Roach says the renewed focus on flexibility allows teams to operate more efficiently, reduce administrative burden, and respond dynamically to emerging challenges, building on the foundations laid in E6(R2) with greater clarity and emphasis.

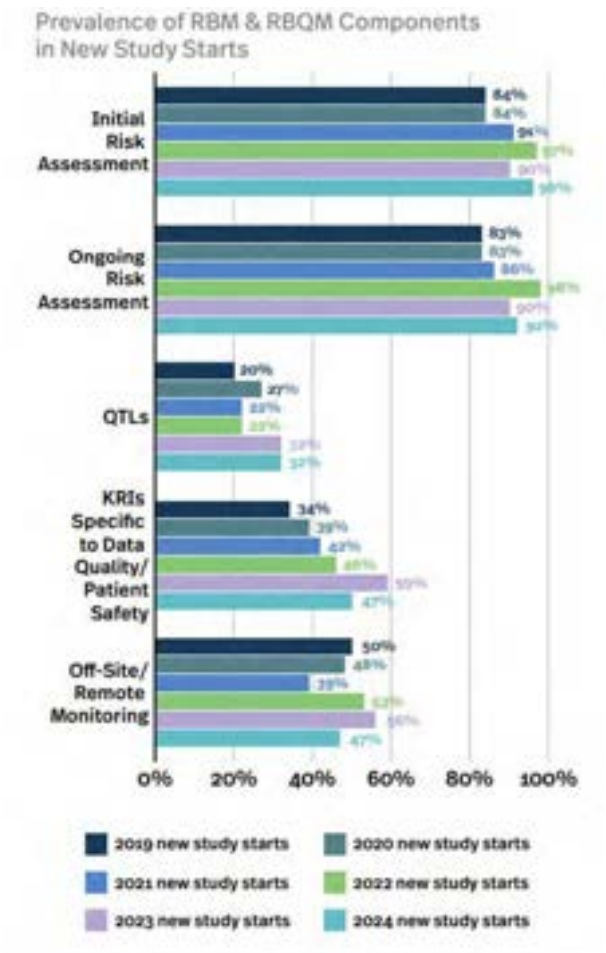
Enhanced risk-based quality management (RBQM)

Another area emphasized in the updated guideline is RBQM throughout the trial lifecycle. The focus is on assessing risks proactively and applying proportionate controls to protect participant safety and data integrity.

The new guideline promotes building quality from the beginning, says Sam, former director of global quality systems at Eli Lilly. She notes that the guideline did not introduce the concept but simply reinforces it.

Sam, a Six Sigma Black Belt, packs a punch when she talks about quality in clinical trials. She says it's all about leveraging Critical to Quality (CTQ) factors to help build studies in a way that enables a quality focus for good decision-making, risk monitoring, assessment, and analysis. "I think we still have a ways to go in understanding what those CTQs mean," she says, adding that this rests on sponsors'





Source: ACRO RBQM Landscape Summary Report, June 2025

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shoulders to design, but sites and contract research organizations (CROs) must weigh in as well.

A high-performing culture of quality is essential, Sam says. At Lilly she was one of a handful of GCP professionals in the manufacturing organization. "At the time, they operationalized quality different from clinical. It was more objective/quantitative. In clinical everything we do is prefaced by 'it depends,' because it's not a one-size-fits-all — it takes judgment and critical thinking."

Revisiting her analogy, Riches says risk assessment is akin to meal planning. When making a new recipe, you must decide if the *cost of the ingredients, time, and effort* are worth it — before even taking the first bite.

"Quality is still at the core of everything we do," Riches says, but adds that the focus is now on the key elements determining that quality. Sponsors will have to document the reasons supporting their decisions. "It's like showing how you got to the answer in math. Regulators will be looking at how you show your work, revealing that you had quality in mind from the start."

"I think one of the key parts … is doing this from the beginning of the trial. So starting with design, gaining input from stakeholders, including sites, including patients, including regulatory," the Tufts CSDD's Dirks says. "This is thinking about quality by design from the beginning."

Previously, Sam says, "risk discussions typically focused on operational risks, not the GCP risks related to patient safety and data reliability. R3 bridges that gap, providing the missing link — gives direction and focus and it expands on QbD [Quality by Design], fit-for-purpose, and risk-based approaches."

Advanced data governance

ICH E6(R3) introduces comprehensive data governance requirements to ensure data integrity, traceability, and security, addressing the use of electronic data capture, storage, and processing technologies.

Roach says E6(R3) strengthens expectations for data governance by emphasizing the importance of safeguarding blinding, managing metadata, and ensuring data integrity throughout the trial lifecycle, from capture through archival or destruction.

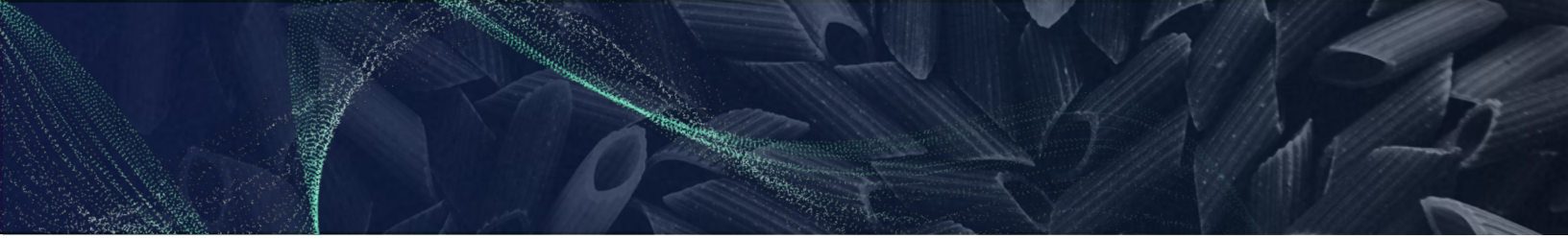
As she mentioned earlier, Riches says if a sponsor shows its work, it must also show which data sources it used. "Those sources must be extremely high quality, and the conclusions and insights drawn from the data must be robust. It's important for sponsors to know where their data is coming from, and that the quality is paramount."

Dirks agrees, referring to the process as data storytelling. It's about being able to explain to someone in simple terms where the data are from, how those data have been processed,



Abigail Dirks
Data Scientist,
Tufts Center for the Study of Drug Development

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and how they've changed to be able to get to those insights in a way that's for a broader audience, not for a data science audience.

Riches continues her meal-prep analogy: "If you buy poor ingredients, your meal won't taste as good as if you bought high-quality ingredients." Regulators want to know:

What's the *recipe*?

Where did you get those *great ingredients*?

As with a math problem, can you replicate your answer? While there may be a couple of ways to solve that problem, the solution must be rooted in principles/guidelines. With traceability, the sponsor must be able to recreate that scenario for regulatory authorities so that if they followed the same path, they would come to the same conclusion.

In terms of security, sponsors must ensure that data they are receiving are from reputable sources, not sold from unapproved sources, and not duplicate data. They also must ensure that consent was given at the time of data collection.

Patient-centric approaches

The guideline encourages patient involvement in trial design, reducing participant burden, enhancing engagement and retention, and using digital tools to improve the overall trial experience. Unfortunately, Riches says, the role









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of the patient (and caregiver) was somewhat of an afterthought.

"You have to get their input and doing that early in the trial and early in protocol design," says Dirks.

Many protocol amendments occur, Riches says, because once the trial is launched there is minimal involvement with the patient population. While facilitating that communication takes time and money, the reality is that protocol amendments are more costly overall. According to a study by the Tufts CSDD, the median direct cost to implement a substantial amendment was $141,000 for a Phase II protocol and $535,000 for a Phase III protocol.[2]

"Recruitment strategies under E6(R3) are shaped by a commitment to inclusivity and meaningful engagement," Roach says. "The guideline supports innovative trial designs and technologies that expand access and reduce barriers to participation. By encouraging reduction of unnecessary exclusion criteria and promoting diversity in trial populations, E6(R3) helps ensure recruitment efforts are equitable and representative."

Riches says it is important to look at the bigger picture: "Patients ultimately want access to new drugs quicker and at a lower price point, but without sacrificing safety and efficacy." Overall efficiency means shorter R&D timelines, which translate to lower prices and accelerated availability for patients. "Everybody wins," she says. "The pharmaceutical company, the payers, the patients."

She notes that "a lot of things are being done for the sake of being done. It's about trimming that fat, that white space." For example, five blood draws vs. 14. "What is the bare minimum we need to maintain safety and efficacy?".

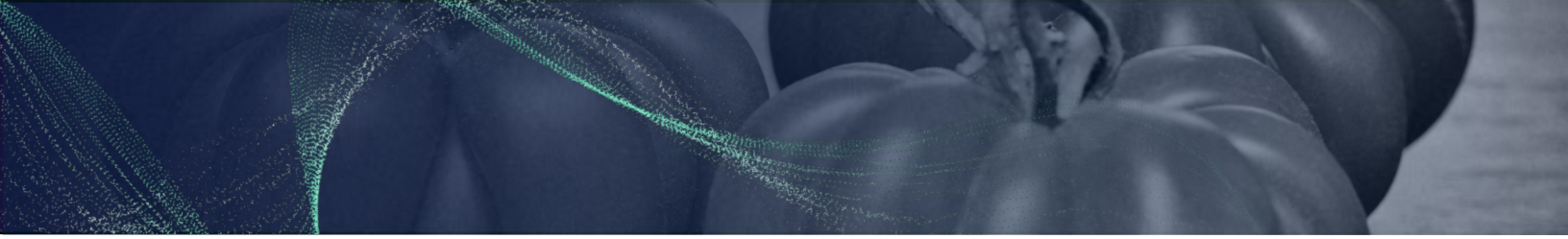


Cutting cost doesn't equate to skimping on quality To continue her meal prep analogy, Riches says that, in the long run, you end up spending less on 20 *quality ingredients* to make five delectable meals than if you purchased 100 mediocre ingredients to cobble together more "meh" meals.

Likewise, Riches compares dinner guests to patients. If you know who you're cooking for, you'll tailor the meal toward them.

The same can be said for meeting patients where they are. If you're planning a meal for an evening when everyone works late, the meal must be quick and easy to make. If trial

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participants work full time, mobile testing might be a more convenient option for them.

The updated guideline also positively impacts patient engagement, recruitment, and retention. "We're building more trust with patients so they're more likely to participate in clinical trials," Riches says. "If you've got an outdated framework, it doesn't build trust. The thread of trust runs all the way through, whether it's the company developing the drug, the investigator running the trial, or the participants themselves."

Clearer roles and responsibilities

For those seeking clarification of stakeholder roles, the updated guidance provides clearer definitions and expectations around the responsibilities of sponsors, investigators, ethics committees/independent review boards (IRBs), CROs, and service providers, fostering better collaboration and accountability.

Riches says collaboration is key. "No drug comes to market without multiple stakeholders being involved." She notes that the previous guideline was a bit vague; they now drill in to ensure accountability across the board.

Continuing her cooking analogy, Riches says multiple stakeholders is like having *too many cooks in the kitchen*. "You must align on who's doing what/when/how. You don't want to end up one night with no one cooking or cook a meal for 20 and only one shows up."



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Who will be impacted by the new guideline?

The new ICH E6(R3) guideline will impact a broad range of stakeholders involved in clinical trials, including:

Sponsors

Sponsors retain full responsibility for trial oversight, even when delegating tasks to CROs or other service providers. They must implement strong risk-based quality management, proactive risk identification, and comprehensive data governance, and use advanced technologies like electronic consent and remote monitoring. In addition, sponsors will need to update internal procedures and systems to meet new quality and data integrity standards.

Today, even more stakeholders are involved in the clinical trial process, such as data providers and technical partners. “We need to bring them into the fold as well,” Riches says. “They’re the ones who really hold the key to efficiency.”

Increasing the stakeholder pool with companies that hold real-world data (RWD), Riches says, introduces a new, really valuable ingredient that will help improve the quality and taste of the recipe. “It’s a good reset to make sure we bring the right people to the table.”

CROs and service providers

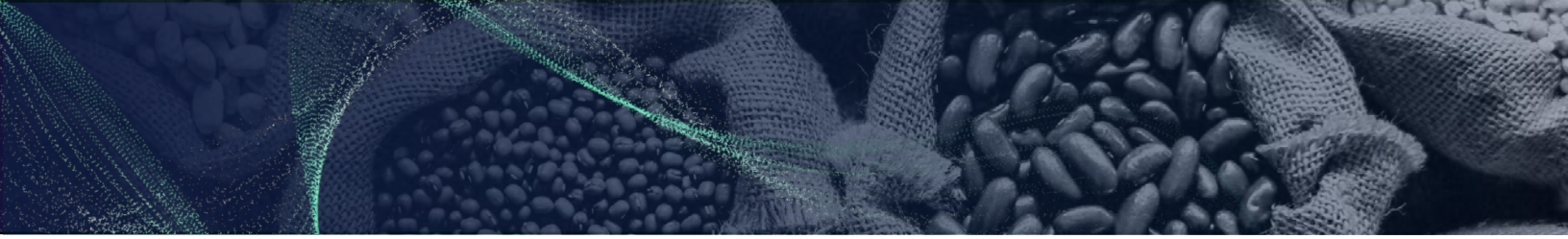
CROs and service providers must adapt to enhanced oversight and risk-management expectations. In line with the updated guideline, they will need to innovate their processes and technologies and support sponsors in maintaining trial quality and compliance. Sponsors rely heavily on CROs, which “must be in lockstep with the guideline,” Riches says.

While ICH E6(R3) does not define service providers in a dedicated section, Roach says, it reinforces the importance of clear documentation of roles, responsibilities, and delegated activities across all parties involved in a trial. “The expectations set out in E6(R3),” he says, “call for service providers to operate transparently and uphold high standards for data integrity and participant protection, contributing to a cohesive quality management system.”

Dirks says continuing to innovate while remaining compliant is one challenge sponsors



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are facing. She adds that the FDA, in a recent roundtable on the updated guideline, emphasized that the intention of the update was to allow for flexibility of innovation. The industry is trying to implement new digital health technologies, Dirks says, so it must thoughtfully consider how it implements those technologies in a way that makes sense.

Sponsors would be well advised to engage providers early in the process, during the strategy phase, particularly those involved with technology. "As a world, we've embraced technology, we've embraced AI," Riches says.

"I would be remiss if I didn't mention AI," Sam says. "Until we start to see evidence of how those AI-type solutions are governed," she adds, the jury is out "to determine how far we can go."

Riches compares kitchen tools like the microwave and air fryer to AI in clinical trials: "It's all about getting the same results and doing it quicker and more economically."

Investigators and clinical trial sites

Investigators have clearer responsibilities regarding recruitment capabilities and trial conduct. They must demonstrate realistic recruitment plans, ensure patient safety, and comply with enhanced data management measures.

Historically, when selecting investigators for a trial, Riches says, sites automatically go back to the investigator pool they know. All too often, she adds, investigators fall short of the numbers they say they can recruit and underestimate what it takes to run the trial.

Riches says RWD can improve recruitment by targeting investigators with eligible patients. "We no longer have to rely on a hit-and-hope type of process."

"Trial sites," Roach says, "are encouraged to adopt fit-for-purpose approaches that emphasize processes and documentation critical to trial quality. ICH E6(R3) moves away from the prescriptive requirements of E6(R2), aiming to reduce unnecessary complexity and administrative burden. The guideline provides clearer expectations for site-level documentation, monitoring, and investigator responsibilities, enabling more efficient and focused operations that align with the trial's specific needs."

Ethics committees and IRBs

Ethics committees benefit from the increased clarity and adaptability introduced in ICH E6(R3), says Roach.



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The roles of both ethics committees and IRBs are clarified with increased expectations for reviewing recruitment materials and consent processes, including oversight of digital recruitment and consenting methods.
"It's a very delicate balance running trials," Riches says. "You have humans you've got to keep safe. It's about maintaining those core principles while making it an easier process."

Patients and healthcare providers (HCPs)

The guideline promotes patient-centric approaches, encouraging patient involvement in trial design and enrollment to improve engagement and retention. Healthcare providers play a role in identifying and referring eligible patients for clinical trials.

"Patient power is massive," Riches notes.

Regulators

Like ethics committees, regulators benefit from the increased clarity and adaptability, says Roach. "The guideline supports global applicability and accommodates evolving trial models, including digitization, variable consent approaches, and flexible oversight mechanisms. While maintaining robust standards for participant safety and data reliability, E6(R3) facilitates innovation in trial design and conduct, helping regulatory bodies and ethics committees respond effectively to modern trial complexities."

Regulatory bodies across ICH regions (EU, US, Japan, etc.) are adopting and adapting the guideline at different paces. For example, the EU and Switzerland began implementation July 23, 2025; the US and UK are expected to follow

Clinical trial disclosure is one area directly affected by the updates.
Key disclosure impacts for clinical trial sponsors include:

Transparency as a GCP principle

Disclosure of results is now a fundamental ethical requirement — not just a regional compliance obligation. This includes most Phase I trials that may have previously been excluded from regulatory requirements.

Scalable disclosure and dissemination

Meeting global requirements will require updated processes and technologies to manage language versions, track communications, and ensure broad accessibility.

Treatment disclosure pathway

Sponsors must establish clear processes for informing participants and investigators about treatment assignments after unblinding.

Plain-language mandate

Participants who receive results should have them in accessible, nontechnical language.

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suit by the end of 2025/early 2026. However, many regulatory agencies are already informally following the guideline. Why? The updates now provide a fit-for-purpose guideline that can be used for company audits and drug approvals.

"The new GCP guideline aligns transparency expectations with ethical principles like the Declaration of Helsinki, creating a unified global approach that provides consistency across all markets," says Francine Lane, Citeline Head of Transparency. "Sponsors who have already embraced comprehensive transparency will find themselves well-positioned, while those with more limited approaches may need to expand their disclosure practices to meet these elevated global standards."

Sam says it would be helpful for regulatory agencies to share examples of good/better/best compliance. "As an ecosystem, we're not getting the feedback," she notes. "Until then, advancing quality will remain a challenge — but one best addressed through shared learning and collaboration."

"It's all about transparency," Riches says. "Transparency breeds trust at the end of the day. The insights are more valuable because there is a trust base."

This article offers a more detailed look at the impact of GCP on clinical trial disclosure.

Other stakeholders

This includes technology providers, data managers, and patient advocacy groups that support the ecosystem of clinical research, as the guideline emphasizes integration of technology and patient focus across the clinical trial process.

Riches emphasizes the importance of patient advocacy groups. "A lot of patients can't advocate for themselves," she says. "They are the collective voice of the patient."

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"ICH E6(R3), alongside ICH E8(R1), offers the industry a chance to move beyond compliance and embrace a shared commitment to quality," Roach says. "These guidelines invite us to design trials that are efficient, purposeful, and centered on the well-being of participants.

"With this revision to Good Clinical Practice, collaboration is essential," he says. "When sponsors, sites, service providers, regulators, and participants work together, sharing insights, embracing innovation, and valuing diverse perspectives, we can create trials that are not only more inclusive and transparent, but also more impactful. By working together, we can accelerate the development of safe and effective therapies and reinforce public trust in clinical research. This collective momentum will help advance global health and deliver outcomes that truly matter to the communities we serve."

In summary, the ICH E6(R3) guideline affects nearly all participants in clinical trials by requiring a culture of quality, transparency, advanced risk management, and patient centricity, fostering collaboration and technological innovation for safer, more efficient, and participant-friendly trials.

The updated guideline reflects a paradigm shift toward modern, flexible, patient-focused clinical trials with integrated risk management and leveraging digital innovation to maintain quality and safety in an evolving clinical research landscape. The updates underscore the need for an integrated, data-driven approach to clinical trials.

See how Citeline's end-to-end suite of solutions help sponsors meet the new requirements.

Additional resources

Several resources are available for those wanting to understand the intricacies of the guideline. TransCelerate BioPharma, a nonprofit catalyst for change in clinical research, houses a **library of assets** — including a webinar, use cases, and toolkit — on navigating ICH E6(R3). It also offers more than 2,300 self-attested GCP courses, with criteria updated to reflect the latest changes in ICH E6(R3).

The Association of Clinical Research Professionals (ACRP) offers an **online course** on ICH E6(R3) that is recognized by TransCelerate BioPharma Inc. as evidence of GCP training. The course is free for ACRP members and available for a fee to non-members.

Additional **ICH E6(R3) resources** are available from the Association of Clinical Research Organizations (ACRO), including data lifecycle, data flow and technology frameworks; data matrix and data flow templates; and a safeguarding blinding considerations tool.

The Global Health Training Centre — funded by WHO-TDR, WWARN, EACCR, the Bill and Melinda Gates Foundation, and the University of Oxford — offers a free, eight-module **course on ICH E6(R3)**. In addition to the foundation, its courses are made possible by the World-Wide Antimalarial Resistance Network and The East African Consortium for Clinical Research.

The Collaborative Institutional Training Initiative (CITI) offers courses in ethics, research, meeting regulatory requirements, responsible conduct of research, and more. Its **ICH E6(R3) course** is a fee-based course, with varying costs for organizations and individuals.

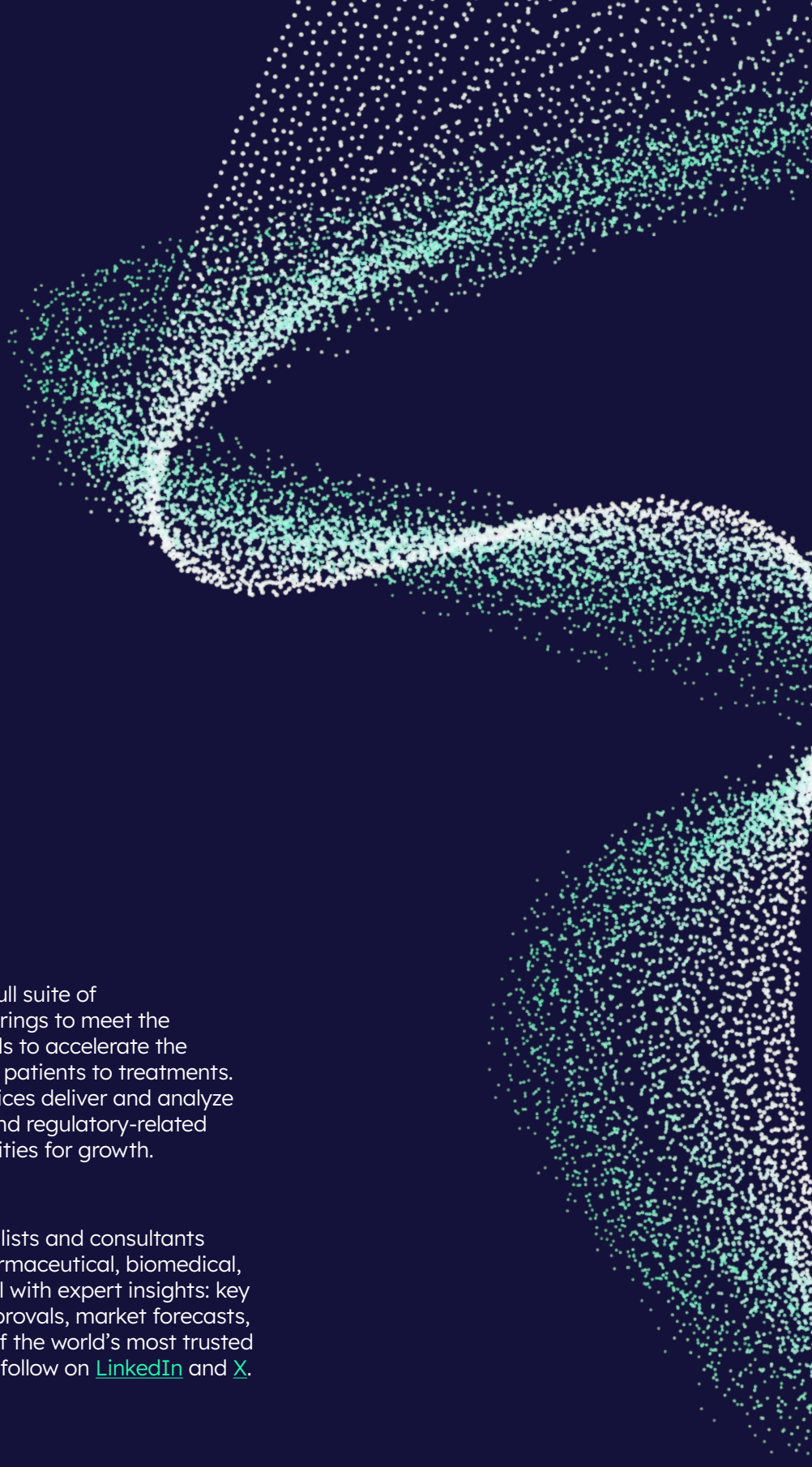
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