Accelsiors

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Go Beyond Serendipity

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Some of the most essential medicines didn't emerge from a straight line of hypothesis → experiment → success.

They came from attentive scientists and clinicians noticing something they weren't looking for.

These breakthroughs typically happened because someone noticed an anomaly, verified it, and connected it to an unmet medical need.

Analyzing serendipity reveals that "luck" in drug discovery isn't a random magic.
Still, it is often structured, favoring environments with careful observation, high-quality measurement, diverse expertise, and openness to revising hypotheses.

The stories that follow show 'iconic' examples when a surprising observation met with human curiosity, methods and persistence to test it.

Attila B. Kovacs (COO at Accelsiors CRO)

Molecule To Medicine – Stories From Drug Discovery And Development

The Pivot: How Development Strategy, Not Luck, Creates Second Lives for Drugs

For decades, the pharmaceutical industry has been captivated by the "Linear Myth", the idea of an unswerving path from target identification to clinical approval. This model suggests that if our molecular understanding is deep enough, the clinical outcome is a foregone conclusion. Yet, looking back at the history of medicine, we find that biology rarely follows a straight line.

In the mid-20th century, drug discovery was largely driven by bedside observation. As we moved into the era of high, throughput screening and genomics, we gained precision but often lost that crucial dialogue between the lab and the patient. Today, the most successful emerging biotechs are those that rediscover this balance, recognizing that a "failed" trial is often just an asset asking for a different direction.

Drug development does not fail because biology is unknown; it fails when teams misread the **kind of problem** they are facing. Below, we revisit five well, known drugs. Viewed not as historical accidents, but as **five distinct strategic pivots**, these cases illustrate how professional judgment transforms observation into value.

1. Signal-First Repurposing: Sildenafil

In the early 1990s, Pfizer researchers in Sandwich, Kent, developed sildenafil (UK, 92,480) as a treatment for angina pectoris. The hypothesis was scientifically sound: inhibit the PDE5 enzyme to enhance nitric oxide signaling and improve coronary blood flow. However, in Phase II trials, the molecule proved uncompetitive against existing cardiovascular therapies.

The program was not saved by a lab breakthrough, but by a reproducible clinical signal. Male participants across multiple sites consistently reported a specific side effect: improved erectile function. Pfizer did not discover a new mechanism, the PDE5 biology was already well, mapped. Instead, the team made a high, stakes strategic decision to abandon the crowded cardiovascular market and redesign the entire program around a different tissue where the biology expressed far higher value.

Why it worked

- A consistent, dose-related clinical signal.
- A known mechanism with tissue-specific relevance.
- Fast strategic realignment before the asset reached attrition.

Partner Insight: Recognizing Tissue-Specific Value

A "failed" primary endpoint is often where the most valuable data is hidden. We help our partners look beyond the initial hypothesis to identify where a known mechanism may express significantly higher value in a different tissue or patient population. Our role is to ensure that a clinical signal is met with the fast strategic realignment necessary to capture value before an asset stalls.

2. Intuition-First Repurposing: Thalidomide

The story of thalidomide is perhaps the most dramatic pivot in pharmaceutical history. Following the global tragedy of the 1950s, the drug was effectively exiled from pharmacopeia. However, in 1965, Israeli dermatologist Jacob Sheskin administered it off label to patients suffering from erythema nodosum leprosum (ENL), a debilitating inflammatory complication of leprosy.

Guided by the drug's known sedative and anti, inflammatory properties, Sheskin hypothesized it could dampen the severe immune activation of ENL. The response was rapid and reproducible, even though the molecular mechanism remained a mystery for another thirty years. It wasn't until the early 1990s that Celgene recognized Sheskin's intuition aligned with emerging cytokine biology. They rebuilt the program around immune modulation (suppressing TNF, α), eventually pivoting again into oncology to treat multiple myeloma.

Why it worked

- Hypothesis-driven clinical intuition in an area of high unmet need.
- Later mechanistic validation (cytokine modulation).
- Willingness to rebuild a development program around biology, not original intent.

Partner Insight: Bridging the Gap Between Intuition and Evidence

Scientific breakthroughs often outpace molecular validation. When clinical intuition suggests a new application, we provide the regulatory and safety framework to explore that signal responsibly. We specialize in rebuilding development programs around emerging biology, ensuring your asset evolves as the science matures.

3. Control-Driven Repurposing: Warfarin

Warfarin's journey began in the 1920s as the mysterious cause of "sweet clover disease," which led to fatal hemorrhages in cattle. By 1948, it was commercialized not as a medicine, but as a highly effective rat poison. While its mechanism, Vitamin K-antagonism, was understood, it was considered far too dangerous for human use.

The pivot occurred in 1951, when a U.S. Army inductee survived a suicide attempt involving a massive ingestion of warfarin. Clinicians observed that the drug's effects were delayed, easily measurable through prothrombin time, and, most importantly, reversible with Vitamin K. This shifted the development strategy from "toxicity" to "manageable anticoagulation". Warfarin was approved for human use in 1954 and gained global legitimacy after being used to treat President Eisenhower in 1955.

Why it worked

- Known mechanism with a measurable clinical effect.
- High-stakes observation proving the effect was reversible.
- Development built entirely around monitoring and reversal strategies.

Partner Insight: Engineering Safety into Efficacy

A mechanism becomes a medicine only when its boundaries are controllable. A "toxic" profile or narrow therapeutic window does not have to be a program killer. We focus on designing robust development strategies built around laboratory monitoring and reversal strategies, turning high-risk mechanisms into manageable clinical successes.

4. Formulation-Driven Repurposing: Minoxidil

In the 1970s, Upjohn developed minoxidil (Loniten) as a potent oral vasodilator for severe hypertension. Systemically, it was effective, but it was plagued by a side effect that many patients found distressing: hypertrichosis, or excessive hair growth.

Initially viewed as a liability, the Upjohn team recognized the biological plausibility of the effect, increased local blood flow, and follicular stimulation. The pivot was a masterclass in formulation strategy: by moving from an oral tablet to a topical solution, developers isolated the follicular benefit while avoiding the systemic hypotension that made the drug dangerous for non, hypertensive patients.

Why it worked

- A localized biological effect identified as an "adverse event".
- A strategic reformulation that decoupled therapeutic benefit from systemic liability.
- A clear tissue-level mechanism.

Partner Insight: Decoupling Benefit from Liability

Sometimes the most critical pivot is not the target itself, but how the molecule reaches it. When systemic side effects limit a drug's potential, we help partners evaluate formulation strategies that isolate biological effects to the target tissue. By separating benefits from liability through smart delivery, we can salvage assets that would otherwise be discarded.

5. Evolutionary Repurposing: Aspirin

Aspirin is the ultimate example of a drug that "evolved" into its second life. Originally launched by Bayer in 1899 as an analgesic, its cardiovascular benefits were not the result of a single trial, but of decades of longitudinal observation.

Clinicians began noticing lower rates of heart attacks in patients who took aspirin chronically for pain. It took decades for the molecular understanding, irreversible inhibition of COX, 1 in platelets, to catch up with the clinical reality. Because platelets cannot synthesize new enzymes, even a short, lived dose of aspirin produces a sustained antithrombotic effect. This translated a routine analgesic into one of the most successful preventative medicines in history.

Why it worked

- Decades of long-term population observation.
- Late-stage mechanistic understanding that explained a durable benefit.
- Successful translation from real-world practice to formal clinical strategy.

Partner Insight: The Power of Longitudinal Vision

Not every pivot happens in a single study; some emerge slowly and only become visible at scale. We assist our partners in translating real, world practice and long, term population data into formal clinical strategies. By maintaining a high, resolution view of how a drug behaves over time, we help you uncover durable benefits hidden in the data.

Building Medicines Through Judgment

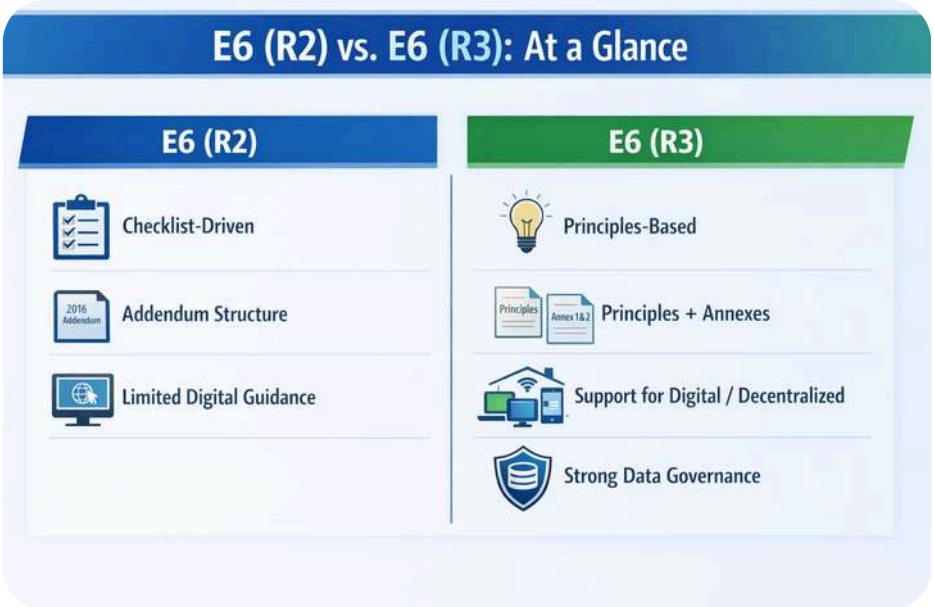
The success of these molecules was not a matter of luck. They reached patients because development teams had the clarity to recognize the specific nature of the pivot before them: whether it was driven by signal, intuition, control, formulation, or evolution.

For decision, makers in emerging biotech, the hardest question is rarely "What is the mechanism?". It is **"What kind of decision is this asking us to make?"**.

At Accelsiors, we don't just provide data; we work alongside you at those critical decision points where observation meets biology and strategy replaces inertia. We understand that while breakthroughs begin in the lab, enduring medicines are built through the weight of human judgment. We are here to ensure that when your molecule reaches that pivot, the path forward is clear.

Introduction to ICH E6 (R3): What's New and Why It Matters for Your Trials

As clinical development becomes more complex and digital, Good Clinical Practice (GCP) standards are evolving to keep pace. The updated **ICH E6 (R3)** guideline is a generational change in how trials are designed, run, and overseen.



For sponsors and partners working with Accelsiors, E6 (R3) is not just another regulatory update, it is the framework that will shape **trial quality, data integrity, and oversight** for the next decade.

This article introduces the core changes in E6 (R3), explains why 2025 is a pivotal year, and outlines how our integrated compliance program is preparing your trials for the new standard.

1. ICH E6 (R3) in 2025: A New GCP Baseline

ICH E6 (R3) modernizes the original GCP guideline from 1996 and its 2016 addendum (E6 (R2)). It is being finalized and adopted across regions, with **the EU bringing the overarching Principles and Annex 1 into effect on 23 July 2025**, replacing E6 (R2) as the applicable GCP standard for most interventional drug trials in that region.

Other ICH regions are moving in parallel. For example, the FDA has announced the availability of its draft E6 (R3) guidance and is aligning inspection expectations and sponsor obligations to the new framework.

For global trials, 2025 is therefore a **transition year**: sponsors, CROs, and sites are expected to migrate from an E6 (R2) mindset to an E6 (R3) model that is:

- **Principles-based** rather than checklist-driven
- **Risk-proportionate**, scaling controls to what truly matters
- **Digital-ready**, explicitly accommodating decentralized and technology-enabled trials

Accelsiors has been strengthening its Quality Management System (QMS) since 2020 in anticipation of these changes. E6 (R3) provides the formal reference standard that codifies many of these practices.

2. From Prescriptive Rules to Risk Based Quality

E6 (R3) replaces the more prescriptive tone of E6 (R2) with a **risk-based, Quality by Design (QbD)** approach. For sponsors, that means more focus on outcomes that matter, **participant safety and reliable data,** and less on low-impact administrative tasks.

Key shifts include:

Integrated risk-based QMS
Trials must be built on a structured QMS that includes proactive risk identification, assessment, and mitigation across the trial lifecycle. This is not optional; it is central to how regulators will assess GCP compliance.

Proportionality of controls
Controls (e.g., monitoring intensity, data checks, vendor oversight) should be **proportionate to the risk** to participants and critical data. High-risk elements get more attention; low-risk elements are managed appropriately but not overcontrolled.

Quality Tolerance Limits (QTLs) in context
E6 (R3) keeps the concept of QTLs but clarifies that minor deviations are acceptable if they are understood, managed, and documented. The emphasis shifts from "no deviations" to "effective, risk-based control of critical factors."

For sponsors working with Accelsiors, this translates into **more targeted oversight, clearer risk rationales, and quality plans that are easier to explain to regulators and internal stakeholders.**

3. Digital, Decentralized, and Data Driven Trials

E6 (R3) explicitly recognizes decentralized and hybrid trial models, digital tools, and advanced analytics. This is a major step forward from E6 (R2), which treated many of these topics peripherally.

Under E6 (R3):

Decentralized and hybrid designs (e.g., home visits, telemedicine, wearables, ePRO) are fully compatible with GCP, provided they are validated, appropriately monitored, and integrated into the quality plan.

Electronic data capture and eSource are treated on equal footing with paper, as long as systems are validated, audit trails are in place, and data integrity is maintained.

Remote and centralized monitoring are encouraged where they can improve error detection and efficiency.

This supports the kinds of solutions many sponsors now seek: **patient-centric, flexible trial models** that still satisfy regulators' expectations on data integrity and participant protection.

Accelsiors is using E6 (R3) as the blueprint for

- Enhanced computerized systems validation across EDC and eClinical platforms
- Refined centralized monitoring strategies for digital and decentralized trials
- Clearer data governance roles between sponsor, CRO, and technology vendors

Risk-Based Quality Framework

4. Structural Changes: Principles, Annex 1, and Annex 2

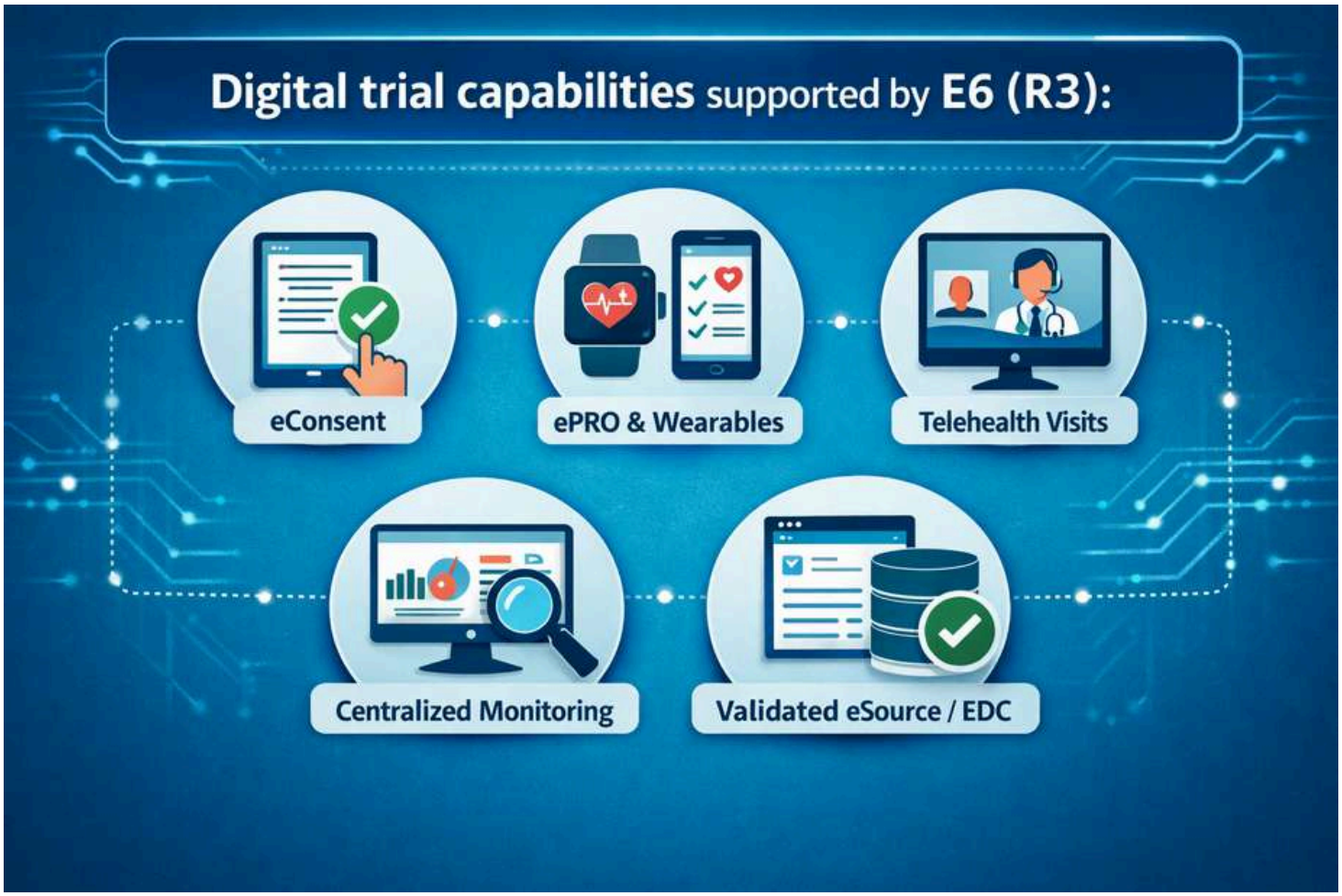
E6 (R3) is restructured into:

- **Overarching Principles** – applicable to all clinical trials, regardless of design
- **Annex 1** – detailed requirements for traditional interventional trials
- **Annex 2** – upcoming guidance for nontraditional/innovative designs (e.g., highly decentralized, pragmatic, or realworlddatarich trials)

For sponsors, this structure means:

- A **single set of principles** that can be applied consistently across portfolios
- Tailored considerations for complex designs without losing sight of core ethics and quality standards
- A clearer path to harmonizing practices across regions and study types

This is particularly important for global programs where Accelsiors supports **multiregional Phase II/III trials, platform trials, and complex hybrid designs.**



5. Why This Matters for You as a Sponsor

For our clients, the implications of E6 (R3) are concrete and strategic:

Higher confidence in data and inspections
A risk-based QMS aligned with E6 (R3) can reduce avoidable findings and improve preparedness for inspections and audits.

More efficient use of resources
Proportional control enables smarter allocation of monitoring and operational effort—particularly important in large, complex or decentralized studies.

Stronger, clearer oversight model
E6 (R3) clarifies responsibilities across sponsors, CROs, investigators, and vendors, with explicit attention to data governance. This helps set expectations and prevents gaps.

Better fit for modern trial designs
E6 (R3) endorses many of the practices (hybrid trials, remote assessments, digital consent) that sponsors are already asking for, making regulatory dialogue more straightforward.

Accelsiors is integrating E6 (R3) into our **quality, information security, and cyber resilience program**, alongside ISO 27001:2022 and the NIS2 Directive, to offer you a **cohesive compliance framework** rather than isolated initiatives.

6. How We Support You Through the Transition

As part of this series, we will detail how our teams are:

- Updating **risk-based quality plans** and monitoring strategies for E6 (R3)
- Aligning our **vendor oversight** and **data governance** practices to the new principles
- Integrating E6 (R3) requirements with **information security (ISO 27001:2022) and NIS2driven cyber resilience**

If you are planning a new program or adapting an ongoing trial, we can help you:

- Map your trial's **critical-to-quality factors** to E6 (R3) requirements
- Review your current protocol design and oversight model against the **new principles**
- Prepare a phased transition plan that minimizes disruption while maximizing regulatory readiness

Turn E6 (R3) Compliance into a Strategic Advantage

We are already working with sponsors to align protocols, monitoring plans, and vendor oversight with E6 (R3).

To discuss a trial-specific E6 (R3) readiness review or to see how our integrated framework (ICH E6 (R3) + ISO 27001:2022 + NIS2) can support your portfolio, contact us at bdglobal@accelsiors.com or visit www.accelsiors.com.

Key ICH E6 (R3) Takeaways for Your Clinical Programs

Modernized GCP

Principle-based, flexible, yet with clear expectations on quality, data integrity, and participant protection.

Risk-Proportionate Oversight

Monitoring, auditing, and controls scaled to what is truly critical to patient safety and data quality.

Digital & Decentralized Ready

Provides explicit support for hybrid trials, remote assessments, and electronic records.

Structured Responsibilities

Reinforced roles and shared data governance between sponsors, CROs, and investigators.

Global Harmonization

Facilitates acceptance of trial data across ICH regions and supports multiregional development strategies.

The Clinical Pulse - Industry News

The Accelsiors Clinical Pulse: Reader's Digest

In the rapidly evolving landscape of multiple sclerosis (MS) research and therapy development, timely and accurate diagnosis is essential for enabling early intervention with disease-modifying treatments. As a CRO specializing in neurology trials, Accelsiors remains at the forefront of supporting sponsors through these clinical advancements. The 2024 revisions to the McDonald criteria, the cornerstone for MS diagnosis, were finalized in 2024 and formally published in September 2025 in The Lancet Neurology and companion journals. These updates mark a significant evolution, shifting toward a more biomarker, driven, unified approach that applies across relapsing, progressive, pediatric, and late, onset presentations.

Here is what the industry is reading these month about this pivotal update:

1. Unified Diagnostic Framework

Source: The Lancet Neurology (October 2025)

The Gist: The 2024 criteria introduce a single, streamlined diagnostic algorithm that applies to all MS phenotypes (relapsing, remitting, primary progressive, and secondary progressive). A major change is the elimination of the strict requirement for dissemination in time (DIT) in many cases, diagnosis can now be made based on dissemination in space (DIS) alone when supported by strong paraclinical evidence (e.g., CSF biomarkers or advanced MRI). This removes the previous need for a second clinical attack or new MRI lesions over time in several scenarios.

Why it Matters: This enables earlier confirmation of MS, potentially shortening the time from first symptoms to treatment initiation by months. For clinical trials, it broadens the eligible patient pool and facilitates faster enrollment, especially in early-phase studies targeting disease modification.

2. Optic Nerve as the Fifth CNS Location

Source: *The Lancet Neurology (October 2025)*

The Gist: The optic nerve is now formally included as a fifth anatomical site for demonstrating dissemination in space (alongside periventricular, juxtacortical/cortical, infratentorial, and spinal cord). Lesions or evidence of optic nerve involvement can be confirmed via MRI, optical coherence tomography (OCT) showing retinal nerve fiber layer thinning, or visual evoked potentials (VEP) demonstrating delayed conduction.

Why it Matters: Optic neuritis is one of the most common initial presentations of MS. This change increases diagnostic sensitivity, particularly for patients with isolated visual symptoms, and could account for 15–20% of newly eligible cases in trials. It also requires sites to have neuro-ophthalmology capabilities for accurate screening.

3. Advanced MRI Biomarkers: Central Vein Sign and Paramagnetic Rim Lesions

Source: *The Lancet Neurology (October 2025)*

The Gist: The revisions incorporate the central vein sign (CVS), a vein running through the center of white matter lesions visible on susceptibility, weighted imaging (SWI), and paramagnetic rim lesions (PRLs), chronic active lesions with iron rims, as highly specific "rule, in" biomarkers. These are especially recommended for patients over 50 years old or those with vascular comorbidities to distinguish MS from mimics.

Why it Matters: These markers significantly improve specificity and reduce the risk of misdiagnosis in ambiguous cases. In trials, they serve as powerful tools for patient enrichment and endpoint protection, but require specialized MRI sequences and centralized reading to ensure data integrity.

4. Expanded Role of CSF Biomarkers

Source: *eBioMedicine (October 2025)*

The Gist: Kappa free light chains (κ-FLC) measured in CSF are now fully equivalent to oligoclonal bands (OCBs) for demonstrating intrathecal immunoglobulin synthesis and supporting DIT. The κ-FLC index (>6.1) is quantitative, automated, and faster than the traditional qualitative OCB assay via isoelectric focusing/Western blot. The criteria also provide guidance for pediatric and older adult populations.

Why it Matters: This biomarker shift reduces turnaround times (from days to hours), minimizes inter-rater variability, and lowers costs. It also decreases the need for repeat lumbar punctures in borderline cases, improving patient experience and screening efficiency in trials.

5. Balancing Progress with Caution

Source: *Nature Reviews Neurology (September 2025)*

The Gist: The revisions permit diagnosis of MS in select asymptomatic individuals with MRI findings consistent with MS (previously termed radiologically isolated syndrome/RIS) when additional paraclinical evidence (e.g., κ-FLC, CVS/PRL, or spinal cord lesions) is present. However, experts warn that this could lead to overdiagnosis, particularly in older adults or those with incidental findings unrelated to MS.

Why it Matters: While the change offers earlier access to therapies for at-risk patients, it requires careful clinical judgment to avoid enrolling non-MS patients in trials. This underscores the importance of specificity markers and centralized eligibility review to maintain trial validity and regulatory acceptance.

Accelsiors' 2026 MS Trial Playbook >> Download now

For a deeper operational dive into implementing these revisions, such as site selection for VEP/OCT capabilities, central lab validation for κ, FLC (>6.1 index), centralized imaging review for CVS/PRL, endpoint recalibration to protect against dilution (e.g., incorporating PIRA or NEDA, 4), and ICH, E6(R3) alignment via Critical to Quality (CtQ) factors and Risk, Based Quality Management (RBQM), see our 2026 MS Trial Playbook.

The Playbook includes a 10, Point Protocol Audit Checklist to stress, test your studies. It also features a hypothetical case study demonstrating how harmonizing the 2024 criteria with R3 principles accelerated recruitment by 18% while maintaining data integrity. In conclusion, the 2024 McDonald criteria and ICH, E6(R3) together create a powerful opportunity for faster, more precise, and patient-centric MS trials. Accelsiors is fully equipped to help sponsors navigate this convergence through strategic protocol design, biomarker validation, and regulatory compliance.

We invite your feedback on how these updates may influence your studies. Please connect with our medical affairs or project management teams.

Contact us

Talent & Tomorrow

Launching a Career as a CRA in CNS Research , Focus on Multiple Sclerosis

The drug development industry is evolving rapidly, and few areas offer more excitement and impact than central nervous system (CNS) research. With breakthroughs in neurodegenerative and autoimmune conditions like multiple sclerosis (MS), the demand for skilled professionals is soaring. If you're a young talent eyeing a career as a Clinical Research Associate (CRA) and passionate about CNS trials, now is an ideal time to prepare.

CRAs in CNS, especially MS studies, play a pivotal role as the "eyes and ears" of sponsors, ensuring trials run ethically, safely, and with high, quality data. Unlike other therapeutic areas, CNS trials often involve complex endpoints (e.g., MRI assessments, cognitive scales, or disability progression measures), high placebo responses, and patient populations with cognitive or mobility challenges. Success requires a blend of scientific depth, regulatory expertise, and adaptability.

Here are the most important requirements for beginners aiming to thrive as a CRA in CNS/MS research:

Strong Scientific Foundation in Life Sciences or Related Fields

A bachelor's degree in life sciences (biology, neuroscience, pharmacology, or nursing) is typically the minimum entry requirement. Advanced degrees (master's or PhD) are highly valued, especially in CNS, related fields, as they provide deeper understanding of neurobiology, immunology, and disease mechanisms. In MS trials, familiarity with key concepts, like dissemination in space/time, biomarkers (e.g., kappa free light chains), and advanced MRI techniques (central vein sign, paramagnetic rim lesions), gives you an edge.

Why it matters: CNS protocols involve nuanced endpoints (e.g., Expanded Disability Status Scale, MS Functional Composite). Scientific knowledge helps you interpret data, discuss protocols with investigators, and identify protocol deviations early.

Mastery of Good Clinical Practice (GCP) and ICH E6(R3)

ICH E6(R3), effective since mid, 2025, shifts from rigid "checkbox" compliance to Quality by Design (QbD), Risk, Based Quality Management (RBQM), and Critical to Quality (CtQ) factors. As a beginner CRA, you must understand how to:

- Identify CtQ elements (e.g., accurate MRI sequence use or biomarker data integrity).
- Apply risk, proportionate monitoring (e.g., centralized vs. on, site).
- Ensure data governance for complex CNS biomarkers.
- Entry, level CRAs often start with intensive GCP training; certifications like ACRP's CCRA® or SOCRA's CCRP® boost credibility.

Why it matters: In CNS trials, where patient burden is high and misdiagnosis risks exist (e.g., under the 2024 McDonald criteria), RBQM helps focus on high, impact areas like eligibility verification and endpoint reliability.

Hands, On Clinical Research Experience (Start Entry, Level)

Pure "book knowledge" isn't enough, most successful CRAs begin as Clinical Research Coordinators (CRCs), Clinical Trial Assistants (CTAs), or in site roles. This builds practical skills in patient interaction, data entry, and protocol execution. For CNS, experience with neurological assessments (e.g., EDSS scoring, cognitive testing) or MRI coordination is invaluable.

Why it matters: MS trials involve vulnerable patients with relapsing, remitting or progressive forms. Early experience helps you empathize with participant challenges and build strong site relationships.

Technical and Digital Proficiency

Modern CRA roles demand comfort with EDC systems, eCOA/ePRO tools, remote monitoring platforms, and centralized data review. In CNS trials, digital biomarkers (e.g., wearables for progression, independent relapse activity) and decentralized elements are increasingly common.

Why it matters: ICH E6(R3) promotes technology to reduce burden, CRAs who can navigate these tools efficiently stand out.

Soft Skills: Communication, Adaptability, and Attention to Detail

Strong interpersonal skills are essential for building trust with investigators, coordinators, and patients. CNS trials require sensitivity to cognitive/emotional challenges. Organizational prowess helps manage multiple protocols, travel, and competing priorities.

Why it matters: CRAs in MS studies often travel extensively and handle complex data, adaptability ensures smooth site visits and timely issue resolution.

Bonus Resource: Downloadable Glossary for CRAs in CNS/MS Research

To help you build your vocabulary quickly, we've prepared a basic Glossary of Key Terms & Acronyms in MS Clinical Trials. This free downloadable asset covers essential concepts from the 2024 McDonald criteria, biomarkers, and trial, specific terms. It's a valuable starting point for interviews, training, or daily work in CNS studies.

Ready to take the next step?

- Schedule a free 30, minute career consultation with our Talent & Development team to discuss your path into CRA roles.
- Submit your CV for our entry, level CRA or CTA opportunities in CNS trials.
- Ask us anything, email your questions about ICH E6(R3), MS biomarkers, or starting in clinical research to **info@accelsiors.com**.

The future of CNS drug development depends on dedicated professionals like you. Keep learning, stay curious, and embrace the complexity, your impact on patients with MS could be profound.

Download the glossary

Unsure if this is for you? Move ahead to take a look of what it's like.

We're here to support emerging talent and help you build a rewarding career in drug development.

Term/Acronym	Definition
CNS	Central Nervous System, The brain, spinal cord, and optic nerve.
MS	Multiple Sclerosis, A chronic autoimmune disease of the CNS causing demyelination and inflammation.
DMT	Disease, Modifying Therapy , Drugs that alter MS disease course (e.g., ocrelizumab, fingolimod).
EDSS	Expanded Disability Status Scale , Standardized scale to measure disability in MS patients.
PRL	Paramagnetic Rim Lesions , Chronic active MRI lesions with iron rims; highly specific for MS (2024 McDonald criteria).
CVS	Central Vein Sign , MRI biomarker showing a central vein in white matter lesions; improves specificity.
κ, FLC	Kappa Free Light Chains , CSF biomarker equivalent to oligoclonal bands for intrathecal synthesis.
RBQM	Risk, Based Quality Management , ICH E6(R3) approach focusing monitoring on high, risk areas.
CtQ	Critical to Quality , Key data elements critical to trial integrity and patient safety.
PIRA	Progression Independent of Relapse Activity , Disability worsening without relapses.

This glossary is designed as a quick reference, download the full version for more terms, sources, and examples!

>> It is a living document, feel free to suggest additions!

Download the full PDF for printable version, examples, and quick, reference tips.

For career guidance or opportunities in MS/CNS research, contact talent@accelsiors.com.

The Patient Voice

Integrating Patient Perspectives in CNS Research with a Focus on Multiple Sclerosis

In the evolving landscape of central nervous system (CNS) clinical research, particularly for multiple sclerosis (MS), patient-centricity has shifted from a buzzword to a strategic imperative. For clinical research professionals, sponsors, investigators, and CRO teams, incorporating the patient voice isn't just about enhancing satisfaction; it's about redesigning trials to address the unique burdens of CNS conditions like MS, where cognitive, mobility, and emotional challenges amplify traditional trial hurdles. True patient-centricity moves beyond superficial "friendliness" (e.g., polite site interactions or simplified forms) to a systemic re, architecture that embeds patient insights from protocol design to closure, ultimately improving enrollment, retention, data quality, and regulatory success.

Drawing from regulatory mandates like the FDA's Patient-Focused Drug Development (PFDD) guidance, EMA's Engagement Framework, and ICH E8(R1)'s Quality by Design (QbD) principles, this approach ensures trials are not only scientifically robust but also feasible and meaningful for patients. At Accelsiors, our branded ProPATIENT Solutions™ framework exemplifies this, providing a structured methodology to integrate patient perspectives proactively. As detailed **on our website**, ProPATIENT applies PFDD principles to align trial elements with patient needs, leveraging real-world data, simulations, and advocacy partnerships to optimize outcomes, particularly vital in CNS/MS trials where progressive disability and variable symptoms demand flexibility. Here are key considerations for research professionals incorporating patient-centricity in CNS/MS studies:

Understanding Unique MS Patient Burdens

MS patients often face unpredictable relapses, fatigue, cognitive fog, and mobility limitations, making rigid trial protocols unsustainable. Traditional designs exacerbate these, requiring frequent site visits or burdensome assessments that lead to high dropout rates (up to 30% industry, wide). Patient-centricity starts with early co, creation: Engage MS patients and caregivers via advisory boards to refine endpoints (e.g., prioritizing Progression Independent of Relapse Activity [PIRA] over relapse, focused metrics) and minimize non, essential procedures. ProPATIENT's proactive planning pillar ensures that feasibility assessments incorporate these insights, reducing amendments and delays.

Leveraging Biomarkers and Decentralized Elements

With the 2024 McDonald criteria emphasizing biomarkers such as kappa free light chains (κ, FLC) and MRI markers (central vein sign, paramagnetic rim lesions), MS trials can now diagnose earlier, but this requires study designs that accommodate asymptomatic or early, stage patients. Professionals must integrate decentralized clinical trial (DCT) components, telehealth, home, based assessments, or wearables for real, time monitoring, to ease travel burdens, a top MS patient concern. ProPATIENT's data, driven execution uses recruitment simulations and hybrid designs to predict and mitigate retention risks, aligning with FDA DCT guidance for more inclusive CNS studies.

Enhancing Retention Through Holistic Support

In MS, emotional and financial toxicities (e.g., costs of missed work or assistive devices) compound physical challenges, driving attrition. A patient, centric approach provides radical transparency: Use plain, language communications, regular progress updates, and lay summaries of results to build trust. ProPATIENT's collaborative partnerships pillar fosters ongoing feedback loops with MS advocacy groups (e.g., National MS Society), enabling stipends, logistical aid, and emotional support tailored to progressive phenotypes like primary progressive MS (PPMS).

Regulatory and ROI Alignment

Regulators demand patient relevance as a quality metric, ICH E8(R1) defines "fitness for purpose" to include low, burden designs. For professionals working in central nervous system and multiple sclerosis research, this translates into clearly articulating value creation. Engaging patients early in development can significantly enhance asset value and deliver exceptionally strong returns on investment. ProPATIENT embeds Critical to Quality principles within contemporary regulatory frameworks (ICH E6(R3),), applying Risk, Based Quality Management (RBQM) to concentrate efforts on the areas that matter most, such as biomarker reliability, ultimately supporting trials that are both compliant and operationally efficient.

Future, Proofing with Technology

Emerging tools like AI for protocol optimization and digital twins for in silico simulations hold promise for MS, predicting outcomes without overburdening patients. Professionals should adopt these within a patient, centric framework to enhance personalization, such as virtual control arms for rare MS variants. ProPATIENT positions Accelsiors as a mid, sized CRO agile enough to embed these innovations from inception.

For a deeper dive into distinguishing true patient-centricity from "friendliness," including regulatory frameworks, ROI models, and our ProPATIENT blueprint, download our white paper: The Patient-centricity Imperative: Moving Beyond “Friendly” to Architect the Future of Clinical Research. This comprehensive guide aligns perfectly with CNS/MS applications, emphasizing systemic redesign to de, risk trials. **Click here to download the white paper (PDF)**.

Ready to embed patient-centricity in your next MS trial?

Schedule a free consultation on ProPATIENT Solutions™, submit your protocol for review, or ask questions at **bdglobal@accelsiors.com**.
We're here to partner in accelerating CNS research.

Interactive Case Studies

Navigating MS Trial Challenges for Emerging Biotechs

Let’s imagine you are the Head of Clinical Operations at an emerging biotech company. You're often tasked with stretching limited resources while delivering high-impact results in complex areas like multiple sclerosis (MS). Drawing from our 2026 MS Trial Playbook, which harmonizes the 2024 McDonald criteria with ICH E6(R3) for robust trial design, we've crafted two interactive case studies. These scenarios are designed to engage you in decision-making: Read the problem statement, consider the solution options, then review our recommended solution with justifications. Tailored for your role, they emphasize decision-making, risk mitigation, budget optimization, and regulatory alignment to accelerate your pipeline.

These case studies reflect real-world applications from our playbook, empowering you to lead with precision. For personalized guidance, schedule a free protocol review or playbook consultation at **bdglobal@accelsiors.com**.

Case Study 1:
Overcoming Recruitment Bottlenecks in a Phase II Relapsing MS Trial

Problem Statement

Your company is developing a novel disease, modifying therapy (DMT) for relapsing, remitting MS (RRMS). The trial protocol, designed under the 2017 McDonald criteria, is 14 months in and trending 30% behind enrollment targets. High screen failures stem from "insufficient evidence of dissemination in time (DIT)", requiring a second clinical attack or indeterminate oligoclonal bands (OCBs), leading to a narrow patient pool and frustrated sites. With a tight budget and investor pressure, each delay risks funding shortfalls. How do you pivot to widen the funnel without compromising data integrity?

Solution Options (Choose One and Compare to Our Recommendation Below)

A. Maintain the 2017 criteria and intensify site training/recruitment efforts (e.g., add more sites).

B. Amend the protocol to incorporate the 2024 McDonald criteria (e.g., optic nerve as fifth site, κ, FLC for DIT) but without updating monitoring plans.

C. Fully harmonize with 2024 criteria and ICH E6(R3) by designating biomarkers as Critical to Quality (CtQ) factors and implementing Risk, Based Quality Management (RBQM).

D. Switch to a fully decentralized trial model without criteria updates.

Justification:

- **Option A** risks ongoing delays and escalating costs (e.g., 113% spike in amendments from protocol complexity, per playbook data), without addressing the root diagnostic shift.
- **Option B** broadens eligibility but invites regulatory risks like misdiagnosis in older patients, lacking R3's data governance.
- **Option D** overlooks MS, specific needs like biomarker validation.
- **Option C** aligns with the playbook's "Protocol Pivot" strategy: Amend to accept optic nerve involvement (via VEP/OCT) and κ, FLC (>6.1 index) for faster DIT confirmation, reducing screen failures by 22% (as in our hypothetical case). Integrate R3 via CtQ identification (e.g., centralized MRI review for CVS/PRL) and RBQM (targeted monitoring on eligibility), boosting recruitment by 18% while ensuring compliance. This approach de-risks the trial, protects statistical power against endpoint dilution (e.g., lower ARR in early patients), and yields ROI through fewer amendments, critical for lean operations.

Recommended Solution:

Option C, Full Harmonization with 2024 Criteria and ICH E6(R3)

Case Study 2:
Ensuring Data Integrity and Patient Retention in a Progressive MS Study

Problem Statement

Your company is advancing a therapy for secondary progressive MS (SPMS), incorporating advanced MRI biomarkers from the 2024 McDonald criteria. Early data show variability in paramagnetic rim lesions (PRL) readings across sites, raising misdiagnosis risks for patients with comorbidities. Retention is dropping (25% attrition) due to burdensome site visits amid fatigue and mobility issues. With limited funding, you need to safeguard endpoint reliability (e.g., PIRA) while embedding patient-centricity to meet FDA/EMA mandates, without inflating costs.

Solution Options (Choose One and Compare to Our Recommendation Below)

A. Rely on local site radiologists for biomarker interpretation and add patient "friendliness" perks (e.g., travel reimbursements).

B. Centralize imaging review but maintain traditional monitoring, ignoring patient burdens.

C. Implement centralized "Gatekeeper" monitoring under ICH E6(R3), plus decentralized elements tailored to MS patient needs, incorporating patient, centric frameworks like ProPATIENT Solutions™.

D. Outsource to a large CRO for standard operations without customization.

Justification:

- **Option A** risks data inconsistencies (e.g., over, interpreted artifacts) and superficial fixes that don't address MS, specific emotional/financial toxicities, leading to sustained attrition.
- **Option B** secures data but ignores retention, potentially diluting endpoints like NEDA, 4. Option D may lack agility for emerging biotechs, adding overhead without MS expertise.
- **Option C** draws from our playbook's "Centralized Gatekeeper" and patient, centric pillars: Use ProPATIENT's proactive planning to integrate patient feedback (e.g., advisory boards for hybrid DCTs like home, based EDSS assessments), reducing travel burdens while aligning with FDA DCT guidance. Combine with R3's RBQM, designate PRL/CVS as CtQ factors for AI, assisted central review, ensuring "pure" MS cohorts and zero audit findings on eligibility. Justifications include 750x ROI from early engagement (per CTTI/Tufts), playbook, proven 22% attrition reduction, and compliance with ICH E8(R1)'s "fitness for purpose." This optimizes budgets by focusing resources on high, risk areas, accelerating timelines, and enhancing asset value in progressive MS.

Recommended Solution:

Option C, Embed ProPATIENT Solutions™ with R3, Aligned Monitoring

References

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