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ICH GCP E6 R3: Impact on Clinical Operations

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ICH GCP E6 R3:
IMPACT ON CLINICAL OPERATIONS

Lucid Consulting presents an expert-backed view on the likely impact on clinical operations

The 3rd revision of the E6 foundational guidelines for Good Clinical Practice are expected to **become effective in April/May 2025**

We have brought together **experts in quality management and clinical operations** to review key updates and determine their likely consequences

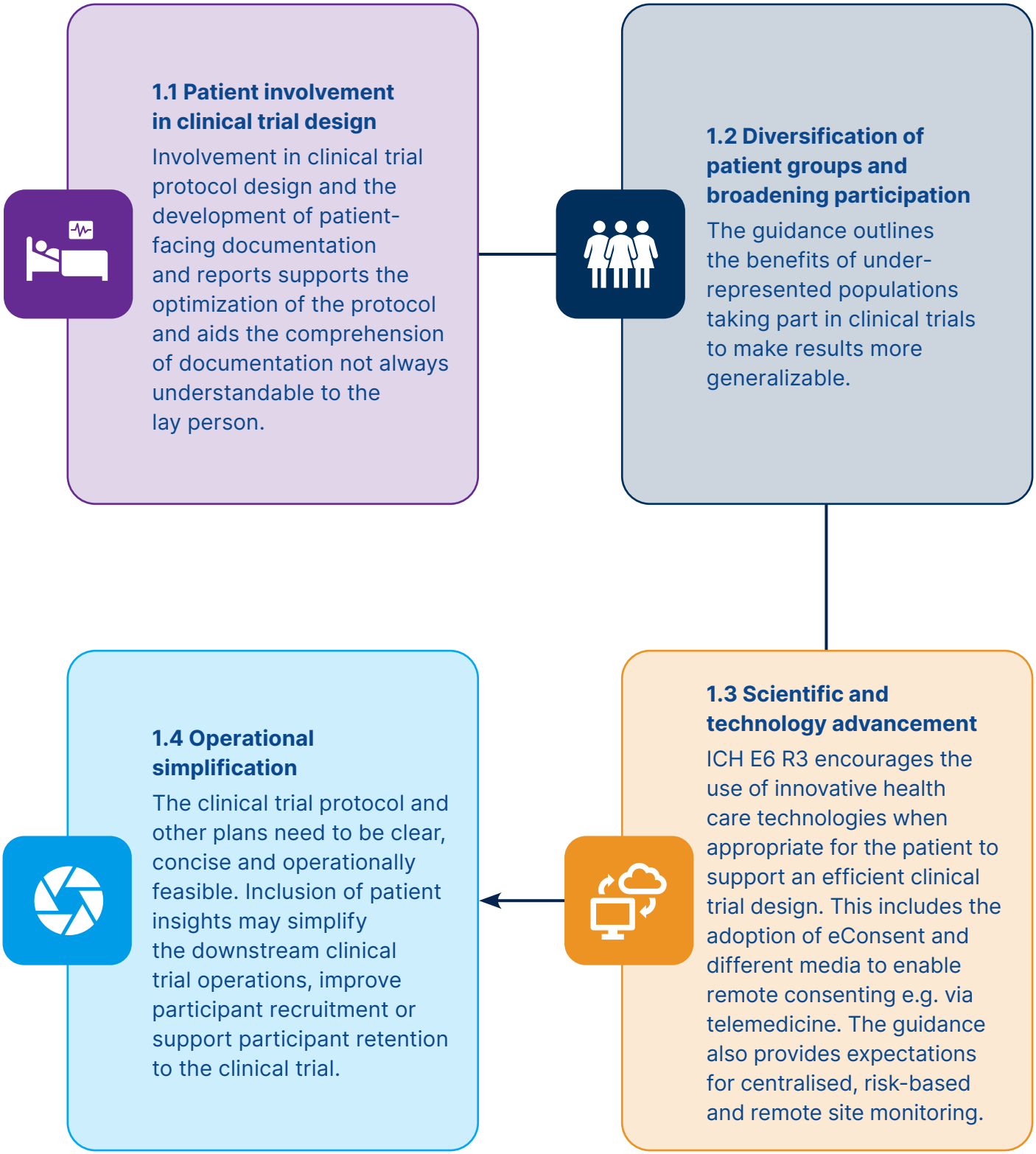
This document summarises our view on **likely operational impacts** of these updates for biopharmaceutical companies, sponsor-investigators, non-commercial sponsors, and contract research organisations

ICH E6 R3: 6 key changes	
1	The Principles section has been refined to be more comprehensive and patient-centric
2	The importance of Risk Based Quality Management (RBQM) comes to the forefront
3	Appropriate use of technology is encouraged
4	Proportionality of data reliability is open to interpretation
5	Public involvement in clinical protocol design and increased diversity of participants is expected
6	Changes to essential record requirements may reduce administration

Key update 1: The Principles section has been refined to be more comprehensive and patient centric (1/2)

Each of these provides sponsors with both opportunities and challenges. There will be a need to adapt and embed new behaviours, processes, and ways of working to support the adoption of these principles.

Key update 1: The Principles section has been refined to be more comprehensive and patient centric (2/2)



Key update 2: The importance of Risk Based Quality Management (RBQM) comes to the forefront

Quality by design was introduced by Juran in the 1970s and these concepts were introduced into international guidelines for the pharmaceutical industry between 2009 and 2012.

Within ICH E6 R3, there in an increased focus on planning which may result in extended timelines and effort when developing a high-quality clinical study protocol.

Biometrics will likely become more prominent in determining and accepting certain risks to data integrity. **Refinement of responsibilities** is likely required.

Approaches from **auditors and inspectors** will need to evolve to a **risk-based quality environment** to avoid expectation mismatch and unexpected findings.

Developing and implementing a robust RBQM approach can take several years. This may require **dedicated resources** which smaller companies may not have readily available.

The guidance expects **risk assessments must be robust, well-considered, and risks proactively mitigated** in an efficient and timely way.

Key update 3: Appropriate use of technology is encouraged

- ICH E6 R3 guidelines, for the first time, **encourage the appropriate use of technology e.g. wearables or sensors to develop an efficient approach to clinical trials**

Context

In "Decentralised Clinical Trials: Achieving Our Ambition" 2023, we outlined a series of opportunities and challenges, and conducted an examination of the value decentralised trials may create for patients, investigators and site staff, regulators and ethics committees, and sponsor companies

We also have taken the view that decentralised clinical trials is a collective term for a number of elements which a sponsor may, or may not, include in a clinical trial e.g. eConsent, telemedicine, wearables, behavioural nudges, ePRO/eCOA, direct-to-patient IMP and home health care

Future considerations

1. A pragmatic review of the **feasibility of technology use, current health equity between populations, and the risks and benefits to the patients** will be needed
2. Different indications, **patient groups, product formulations, interventions and procedures** will need to be considered when **assessing decentralised elements** and their applicability to a particular clinical study protocol
3. The industry will need to consider these assessments in a structured way and **develop clear criteria to support decision-making**

Key update 4: Proportionality of risk for data reliability is open to interpretation

- Within ICH E6 R3 there is the **clear expectation that those data and systems used within clinical trials are governed in a way that is proportionate to the risks for participants and the reliability of results**
- The data should be of sufficient quality to provide confidence in the results and to support decision making

General data-related changes

- In a recent white paper, we addressed the challenges for data governance as systems become more networked, **quantities of data increases exponentially and a reduction in the quality of data may be the new reality**
- The consequence of the ICH E6 R3 changes coupled with the change in scale and quality of data will prove challenging to interpret

Immediate changes

- Protocol design drives data so more time should be invested into data management, statistical planning and clinical operation strategy, determining critical systems and priority data. In the movement away from the "one-fits-all" approach this will be required for each individual clinical trial
- Initially we expect biopharmaceutical companies to operate in a similar way to the way they are operating under ICH E6 R2

Medium-term changes

- In the medium term, we expect sponsors to build a more standardised view of the more obvious higher and lower priority data
- There will continue to be data and systems which will need to be assessed on a case-by-case basis

Key update 5: Public involvement in clinical protocol design and increased diversity of participants is expected

- ICH E6 R3 guidelines **now specify that sponsors pre-define diversity requirements within the inclusion and exclusion criteria in the clinical trial protocol**, ensuring the rationale for these criteria are clearly described and documented
- This will encourage a **shift in mind-set to improve trial inclusion and the generalisability of results, considering health equity among target populations**

How might patients be involved?

Patients or patient advocates to review trial protocol and highlight undesirable aspects

Provision of plain language versions of informed consent documents and summaries

Trial designers developing a deeper understanding of the priorities of the patient medically and socially

Potential challenges from increased public involvement

Implementing these changes may negatively impact performance or cost of clinical trials due to the need to engage with less-experienced investigators, hospitals or R&D centres, in less traditional locations

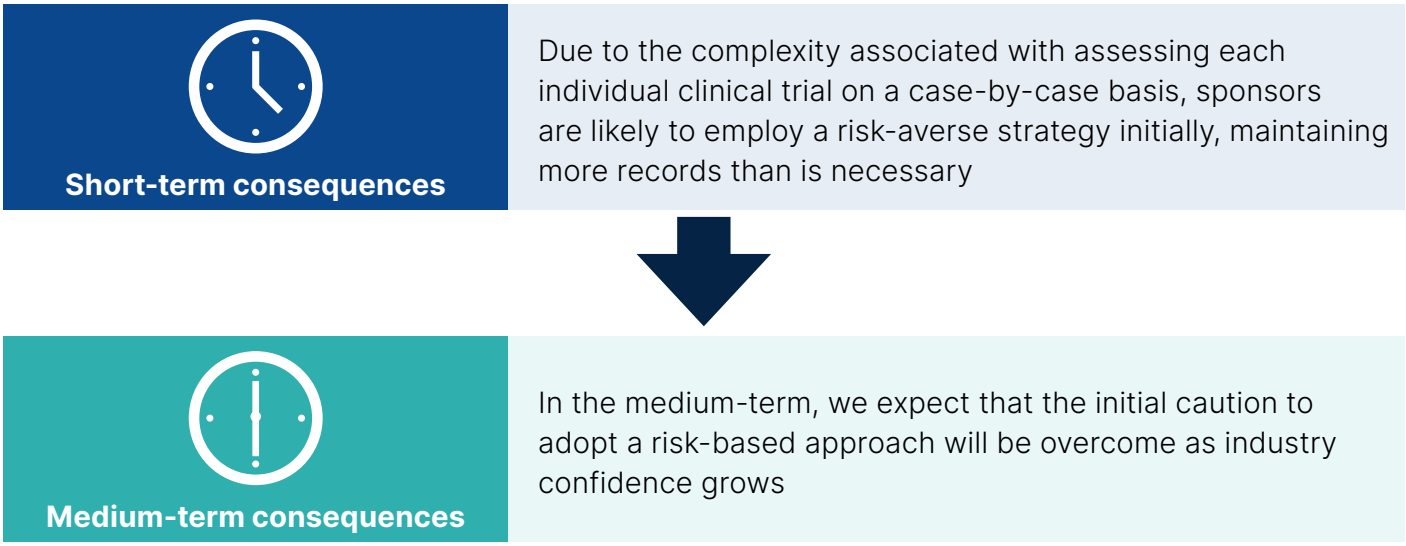
Increased engagement may result in longer start up and recruitment periods to ensure diversity, as well as the additional effort and time needed to generate RWD to better understand patient populations

Deciding when and how to implement such changes without having to update documentation or negatively impact timelines may prove challenging

Standard performance metrics e.g. active patients per site, or overall cost per site, will likely be inferior to benchmarks. Senior management will need to accept lower performance levels or will need to be reframe the metrics

Key update 6: Changes to essential record requirements may reduce administration

- ICH E6 R3 guidelines **for the first time includes two tables relating to essential records** to be captured before, during, and after a clinical trial (one for essential records and another for potential essential records)
- This change is intended to empower sponsors to streamline their approach to maintaining essential records



About Lucid Consulting

"Lucid Consulting is a consulting firm focused on the life sciences industry. We bring a combination of deep health & life sciences expertise with the capabilities, discipline and resources of a top-tier management consulting firm."

- We are focused on research, development and commercialization of biopharmaceutical products and services

R&D Operations | Clinical Development | Medical Affairs & HEOR | Regulatory | Safety and PV | Quality & Compliance

- Lucid Consulting provides a deep expertise and extensive experience drawn from both consulting and senior roles within industry
- We have extensive experience designing and implementing R&D operating models, decentralized clinical trials (DCT), quality management systems, integrated evidence generation and Medical Affairs plans
- We offer the ability to bring external perspectives, benchmarks and accelerators, from our experiences running complex transformational change programs, and deploy high-caliber teams in the disciplined and structured manner expected of a top-tier consulting firm

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We would like to recognise the contribution of Paul Hargreaves (Chief Development Officer, Board Member, Board Advisor and Consultant), Jean Samuel (former Chief Compliance Officer, Business Owner, and Quality & Compliance Advisor), and Gabrielle Marsh and Sophie Cancemi, both from Lucid Consulting.

About Lucid Consulting

Lucid Consulting is the consulting division in Lucid Group focused solely on the life sciences industry. We bring a combination of deep health & life sciences expertise with the capabilities, discipline and resources of a leading management consulting firm. Our consulting teams have worked extensively in R&D and Medical Affairs. We continue to focus on emerging trends, needs and best practices across the industry.