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Hybrid Event

# **ICH R3 – changes for sites**

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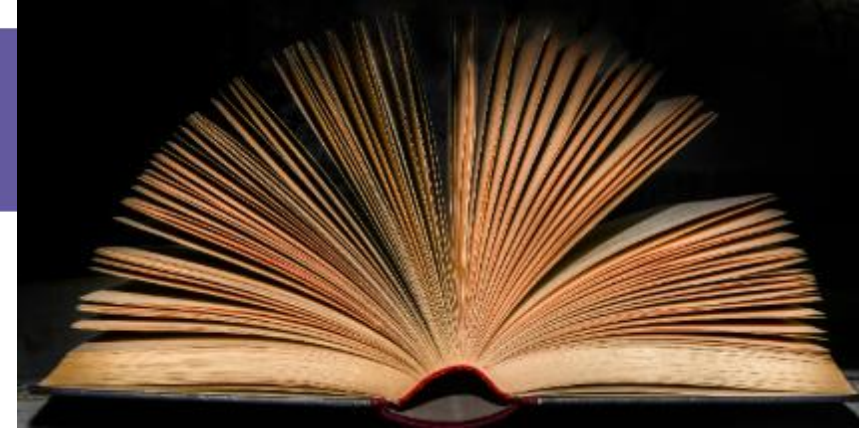




The changes reflect the following principles:

- **Flexibility for modern trial designs** (decentralized trials, hybrid designs, real-world evidence (RWE), adaptive and umbrella trials and new data sources. R3 is “media-neutral” and modular in structure to accommodate future technological/operational changes)
- **Data governance** (digital technologies, lifecycle of data)
- **Quality-by-Design** (proactive risk-based quality, pre-design quality into a trial to prevent errors)
- **Proportionality** and **fitness-for-purpose**, aiming to improve trial efficiency and extend the applicability of GCP to a broader range of trials. (emphasis on a ‘fit-for-purpose’ approach – data does not have to be error-free **if** it supports conclusions equivalent to those drawn from error-free data)
- **Critical-to-Quality factors built-in** (major safety endpoint, major efficacy endpoint), perform central monitoring and remote monitoring of non-critical data, risk thresholds and escalation mechanisms

\*Note: R3 includes: **14** “fit for purpose” + **30** “purpose” + **22** “proportionate”/“proportionately” + **10** “avoid unnecessary complexity” → move focus from “**Did we collect all the documents?**” to “**Are the important things controlled?**”



Includes the need for consent to be ‘**clear and concise**’

Confirmation that **electronic methods** can be used to obtain informed consent.

**Varied approaches** (e.g., text, images, videos and other **interactive methods**) may be used in the informed consent process.

Whether the informed consent process takes place in person or remotely, **the investigator should assure themselves of the identity** of the participant (or legally acceptable representative)

**New** information in the revised ICF should be **clearly identified**

The participant or the participant’s legally acceptable representative should receive a **copy (paper or electronic)** of the signed and dated informed consent form (*see also the frequent Protocol provisions stating “original at site”*). Signing 2 originals is not better because one does not know what info was actually given to the participant (flag of fraud).

Unfavourable medical events **occurring** in participants **before** the investigational product administration (e.g., during screening) should be considered and reported to the sponsor **if required by the protocol**.

All serious adverse events (SAEs) should be reported immediately to the sponsor (after the investigator **reasonably** becomes aware of the event).

**Removal** of the requirement for all SUSARs to be expedited to investigators and IRBs/IECs and introduction of *alternative arrangements* for safety reporting to regulatory authorities.

During and following a trial, the investigator/institution should ensure that **adequate medical care** is provided to a participant for **any AEs**, including clinically significant lab values, related to the trial.





**Payments to a participant** should be timely, **prorated and not contingent** on completion of the trial by the participant. Reasonable reimbursement of expenses incurred by participants, such as for travel and lodging, **is not coercive**.

Confirmation that **health professionals other than doctors** and dentists can have overall responsibility for trial-related medical care and decisions.

Expectations for transparency, including providing investigators with trial results and information **about the treatment taken by their participants**.

Support for **alternative approaches to IP management** and accountability.

Confirmation that **IP may be shipped to participants** and administered by site staff, participants, caregivers, or health professionals.

Clarification that services provider (vendor) quality management processes should be fit-for-purpose, but **not necessarily designed to be GCP compliant**.

**Monitoring** detailed and include site monitoring (on-site and/or remotely), centralized monitoring; central reading is another quality measure.

**Training** of the site team members: flexibility, fit to purpose (to role). Trial-related training should correspond to what is necessary for the person to fulfil their delegated trial-related activities that go beyond their usual training and experience. (e.g. Radiologists doing regular procedures do not need Protocol training).



“**Essential Documents**” evolves into “**Essential Records**” (which may include documents, data, metadata, communications, audit trails) and emphasizes the *process and rationale* (why decisions were made) not just documenting the “what”. Instead of only ensuring that each piece of paper is filed, we need to demonstrate how decisions were made, how risk was managed, how critical data were handled.

Expanded content on digital data requirements, including a new framework for determining **the essentiality** of trial records.

The original records should generally be retained by the responsible **party who generated them**.

When a copy is used to permanently replace the original essential record, the copy should fulfil the requirements for **certified copies**. (when the original is not present at either site or the sponsor)

Encouraged proportionality and clarified **acceptable ranges beyond which deviations** could represent systemic issues.

Avoid **unnecessary burden** on participants and investigators

**R3 inspections**/oversight will focus more on *how quality was built into the trial* (risk identification and mitigation, data governance, vendor oversight) rather than just “are all the documents present”.

Patient/Subject → **PARTICIPANT**



Thank you !