

viedocTM

Viedoc Regulatory Compliance

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Document History

Version	Author	Date	Change
1	Alan Yeomans	2019-05-08	Initial version – based on the 2019 release of eCF Requirements.
2	Alan Yeomans	2020-03-16	Updated with the 2020 release of eCF Requirements. Company name changed to Viedoc Technologies.
3	Alan Yeomans	2021-03-17	Updated with the 2021 release of eCF Requirements.
4	Alan Yeomans	2022-04-06	Updated with the 2022 release of eCF Requirements.
5	Alan Yeomans	2023-03-24	Updated with the 2023 release of eCF Requirements.
6	Marialuisa Baldi	2023-12-05	Update with the 2023.3 release of eCF Requirements.

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1 PURPOSE

This document describes how Viedoc Technologies ensures regulatory compliance for Viedoc.

1.1 Scope

Viedoc is a global eClinical Suite, used in over 70 countries around the world. Viedoc must comply with all international and national regulatory requirements for computerised systems used in clinical trials in those countries where it is used. Although regulation of the clinical research industry is performed by national regulatory bodies (the FDA, EMA, PMDA, NMPA, MHRA, etc.) there is a high degree of cooperation between the different national authorities.

2 PROCEDURE

Viedoc is developed using agile methods and tools with frequent new releases. Viedoc is a multi-tenant Software-as-a-Service (SaaS) solution. It is vital that every new release is compliant with all applicable regulatory requirements.

A regulatory test suite of automated test scripts is run as part of the validation of each release of Viedoc. These test scripts must be passed to demonstrate regulatory compliance.

The test scripts are based on the eCF Requirements for the use of electronic data in clinical research published by the eClinical Forum. The eClinical Forum is a non-commercial think-tank and a global consortium of organizations involved in clinical research. Its members include global pharma companies, CROs, and suppliers to the clinical research industry. For more information about the eClinical Forum and the eCF Requirements see appendix A, “Requirements for Electronic Data for Regulated Clinical Trials”.

The eCF Requirements address all types of electronic systems and electronic data used in clinical research. Not all of these are relevant for Viedoc, but the majority are. Some of the requirements are functional, while others are procedural. The functional requirements affecting Viedoc are included in and validated by the regulatory test suite.

Of the 36 requirements included in the 2023 release of the eCF requirements (see appendix A):

- 23 requirements are applicable or partly applicable to EDC/eCRF systems such as Viedoc.
An example of such a requirement is C04:
“System has an audit trail to include recording date/time/originator of any data creation, change, or deletion.”
- Viedoc has an audit trail.
- 6 requirements are valid but are not solved within Viedoc (or entirely within Viedoc). They are solved by another component of the system (e.g. the server operating system).
An example of such a requirement is C26:
“There are sufficient system and/or process controls for backup and recovery procedures.”
- This is handled in the IT environment, and not by Viedoc.
- 2 requirements are not valid for eCRF/EDC systems such as Viedoc or are procedural requirements for the sponsor and/or site.
An example of such a requirement is C02:
“Specified de-identified data can be extracted for clinical research.”
- This is a requirement that is valid for EHR systems, but not Viedoc.

- 11 requirements are procedural requirements concerning the use of the system or procedures at Viedoc Technologies.

An example of such a requirement is C29:

“There are sufficient process controls for the system covering Business Continuity to manage disruptive incidents.”

- This requirement is covered by Viedoc Technologies SOPs.

3 DETAILS

Requirements that are listed as “Applicable to Viedoc” below are included in the regulatory test suite that is a part of testing of every release of Viedoc.

Id	eCF Requirement	Applicability to Viedoc
C01	System has the ability to store and retrieve data items in a way that is attributable to a trial/data subject.	Applicable to Viedoc.
C02	Specified de-identified data can be extracted for clinical research.	Not applicable to Viedoc – this is a requirement for EHR systems.
C03	System has capability of storing data related to subject consent and should not allow data collection until the subject consent is confirmed.	Applicable to Viedoc.
C04	System has an audit trail to include recording date/time/originator of any data creation, change, or deletion.	Applicable to Viedoc.
C05	The audit trail includes the reason for changes /deletions.	Applicable to Viedoc.
C07	Audit trail information is readable and readily available.	Applicable to Viedoc.
C08	System does not allow new audit trail information to over-write existing (previous) Information and cannot be altered without detection.	Applicable to Viedoc.
C10	There is a process to ensure that case records and any subsequent modifications are reviewed and approved by the investigator.	Applicable to Viedoc.
C11	There is a system and/or process to ensure the investigator has control of and continuous access to all essential records (data and documents) generated by the investigator/institution/patient before, during and after the trial.	Applicable to Viedoc.
C13	Controls exist such that the ability to change system settings is limited to authorized personnel.	Applicable to Viedoc for Study settings. With respect to Viedoc hosting this is a non-functional requirement handled by IT operations procedures.
C14	System uses a standard time reference such that the local time can be derived.	Applicable to Viedoc.
C16	The system has the ability to create, maintain, apply and revoke the roles, access permissions and capabilities of each user that accesses the system, such that users have access only to those system features and functions to which they have been granted access.	Applicable to Viedoc.

C17	There is a policy and training that instructs users not to share their access mechanisms (e.g. usernames and passwords, or access keys) or to leave their account open for others to use. A shared account (group account) is not appropriate.	Procedural requirement applicable to Viedoc if 2FA is employed. Non-functional requirement handled by site/sponsor operations procedures.
C18	The monitor, auditor and inspector can within a reasonable timeframe, obtain direct access to relevant clinical trial records in order to perform their regulatory duties.	Applicable to Viedoc.
C19	System limits the number of log-in attempts and records unsuccessful attempts.	Applicable to Viedoc.
C20	System records and notifies a system administrator of unauthorized access log-in attempts.	Applicable to Viedoc.
C21	There are system and process access control mechanisms that follow current physical and logical information security best practices.	Applicable to Viedoc.
C22	System feature to allow automatic logoff or other access lock (such as password protected screen saver) after a set period of time of inactivity.	Applicable to Viedoc.
C23	The system must have the ability to provide a history of all individuals who have access to the system and their access privileges over time.	Applicable to Viedoc.
C24	System has the ability to produce a human-readable copy of data (which includes associated audit trails and any decoded data) in appropriate file formats that facilitate review, searching and analysis.	Applicable to Viedoc.
C25	Copies of electronic records must be certified copies if they are being used for regulatory purposes.	Applicable to Viedoc.
C26	There are sufficient system and/or process controls for backup and recovery procedures.	Procedural requirement handled by IT operations procedures.
C27	Documentation of the backup and recovery process can be produced for inspection by a monitor, auditor or inspector.	Procedural requirement handled by IT operations procedures.
C28	Process and/or system controls ensure that regulated data used for clinical research, including source data and metadata are enduring, continue to be available, readable and understandable and are retained in an archive for the legal period.	Applicable to Viedoc.
C29	There are sufficient process controls for the system covering Business Continuity to manage disruptive incidents.	Procedural requirement handled by Viedoc Technologies SOPs.

C30	There are sufficient process controls based on industry standards, covering Disaster Recovery Procedures.	Procedural requirement handled by Viedoc Technologies SOPs.
C31	There is a process to demonstrate that individuals who develop, maintain, or use the system should be qualified by having appropriate education, training, and experience to perform their assigned task.	Procedural requirement applicable to Viedoc for development and maintenance of the system. Non-functional requirement handled by user SOPs for study users.
C32	The development, hosting, deployment and change control of a computerised system has objective evidence that system components are traceable to requirements and have been validated based on risk, using good software lifecycle practices.	Procedural requirement handled by Viedoc Technologies SOPs.
C35	There are sufficient system and/or process controls to prevent or mitigate effects of malware: viruses, worms, or other harmful software code.	Procedural requirement handled by IT operations procedures.
C36	There are sufficient system and/or process controls over data transfers from/to other systems, including validation of data mapping and transfer, security of data in transit, and confirmation of receipt and continued availability of the audit trail.	Applicable to Viedoc for study data transfers. Procedural requirement handled by IT operations procedures.
C37	When service providers are used to provide GxP-related services, formal agreements must exist and include clear statements of the roles and responsibilities, management and oversight of the service provider (and their GxP-related providers).	Procedural requirement handled by Viedoc Technologies SOPs and vendor contracts.
C39	Signed electronic records shall contain information associated with the signing that clearly indicates all of the following: <ul style="list-style-type: none"> - The name of the signer - The date and time when the signature was executed - The meaning (such as creation, confirmation or approval) - Electronic signatures are permanently linked to their respective record 	Applicable to Viedoc.
C40	There is a process to ensure that in the event of a security incident that exposes privacy data, the Sponsor and/or Investigator shall notify the relevant Data Protection or other applicable authority.	Procedural requirement handled by Viedoc Technologies SOPs and vendor contracts.

C41	There is a process to evaluate and mitigate the risk and impact of changes to the computerised system taking into account changes to protocol (i.e. amendments and addendums), users, & roles on an ongoing basis.	Procedural requirement handled by site/sponsor operations procedures.
C43	There should be a process to periodically review and affirm the continued suitability of the computerized system taking into account the potential cumulative risks and impacts of changes to the system, requirements, version releases, and computing environment of the system.	Procedural requirement handled by Viedoc Technologies.
C44	For eTMF, the audit trail additionally captures accessing of records.	Applicable to Viedoc.

4 APPENDIX A

The document on the following pages can also be downloaded from the eClinical Forum's website, at eclinicalforum.org.

This document shows the derivation of each of the requirements in the eClinical Forum list, and which regulations they confirm compliance to. This way traceability to the underlying regulations can be seen.

The 2023.3 version of the eClinical Forum Requirements is only available to eClinical Forum members. The document below is the 2022 release which has now been released to the public, and not the 2023 release used for testing of Viedoc. The document below is missing some of the regulatory mappings and reformulations of some of the requirements (that do not change the basic meaning of the requirement). The additional regulations and guidelines that have been mapped in the 2023.3 release (and that have been included in the testing of Viedoc) but which are not included in the 2022 Public Release document below are:

- EU: EMA Recommendation Paper on Decentralised Elements in Clinical Trials (Dec 2022)
- EU EMA GCP Q&A B17. How can sponsors demonstrate oversight for those activities that are delegated by written contract? (December 2022)
- Japan: PMDA EDC Management Checklist (1-Jul-2021) – updated
- Japan: PIPC Act on the Protection of Personal Information (Act No. 57 of 2003;) Enforcement date: June 17, 2020; (Revised by Law No. 68 of 2022) – updated for new version
- EU: EMA Guideline on computerised systems and electronic data in clinical trials (September 2023)

Requirements for Electronic Data for Regulated Clinical Trials

“eCF Requirements”

Version:	PR2022.1
Date:	Public release of version 2022 was done in March 2023.
Status:	Publicly released version. This is the 2022 version. The 2023 version is available for eClinical Forum members only.
Author:	<p>eClinical Forum Regulatory Advisory Group (REG team)</p> <p>The eClinical Forum REG team that produced this version of eCF Requirements included regulatory expertise from these companies:</p> <p>Astellas, Boehringer Ingelheim, Bristol-Myers Squibb, Clario ERT, eClinical Solutions, Eli Lilly, Fasor, Medidata 3DS, Neptunus Data, Novartis, Oracle, Servier, Signant Health, THI Pharma Services, Viedoc Technologies</p>
Security:	This is a public release. Non-eCF Members are welcome to use and share as per License in Appendix 1.



DOCUMENT HISTORY

Date	Revision	Author	Changes
March 2018	MR2018	eCF Regulatory Expert Advisory Group (REG)	This document is updated annually, based on advisory group review and interpretation of information from regulatory authorities.
March 2019	MR2019		
March 2020	MR2020, PR2019		
March 2021	MR2021, PR2020		
March 2022	MR2022, PR2021		
March 2023	MR2023, PR2022		

Changes to eCF Requirements text from 2021 to 2022:

UR#	V2021 Text	V2022 Text
C04	System has an audit trail to include recording date/time/author of any data creation, change, or deletion.	System has an audit trail to include recording date/time/ originator of any data creation, change, or deletion.
C13	Controls exist such that the ability to change system standard settings is limited to authorized personnel.	Controls exist such that the ability to change system standard settings is limited to authorized personnel.
C14	System allows audit trail to utilize standard time-keeping method such that the local time can be derived.	System allows audit trail to utilize standard time- keeping method such that the local time can be derived.
C21	System enforces password or other access keys to be changed at established intervals.	The system enforces user authentication mechanisms that follow current information security best practices."
C22	System feature to allow automatic logoff or other data lock (such as password protected screen saver) after a set period of time of inactivity.	System feature to allow automatic logoff or other access lock (such as password protected screen saver) after a set period of time of inactivity.
C23	The system must have the ability to provide a cumulative directory of all individuals who have access to the system and their access privileges over time.	The system must have the ability to provide a history of all individuals who have access to the system and their access privileges over time.
C28	Process and/or system controls ensure data used for clinical research source data and metadata are enduring, continue to be available, readable and understandable and are retained in an archive for the legal period.	Process and/or system controls ensure that regulated data used for clinical research, including source data and metadata are enduring, continue to be available, readable and understandable and are retained in an archive for the legal period.
C32	There is a process to demonstrate that the development and hosting of the computerised system follows good	There is a process to demonstrate that the development, hosting and deployment of the computerised system follows good

	software lifecycle practices such that it is sufficiently validated.	software lifecycle practices such that it is sufficiently validated based on risk.
C41	The alignment of each protocol amendment with the associated trial-specific eSystem(s) should be evaluated and updated as needed.	The alignment of a trial-specific eSystem(s) with each protocol amendment should be evaluated and the system updated as needed
C42	A change to the core e-system should be evaluated to determine if it affects a trial-specific e-system. Updates should be made as needed.	A change to the core system should be evaluated to determine if it affects a trial-specific e-system configurations . Updates should be made as needed.
C43		New: There should be a process to periodically affirm the continued suitability of a deployed computerized system taking into account changes in risk, users, and protocol.
C44		New: For eTMF, the audit trail additionally captures accessing of records.

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1 About the eClinical Forum

The eClinical Forum (eCF) is a global not-for-profit and non-commercial, technology independent group representing members of the pharmaceutical, biotechnology, and allied industries. The eClinical Forum's mission is to serve these industries by focusing on those systems, processes and roles relevant to electronic capture, management and submission of clinical data. For further information visit the website at www.eclinicalforum.org.

The eClinical Forum has sought out opportunities to promote electronic capture since its inception in 2000. The cross-industry forum has a broad view of research with members - Sponsors, Contract Research Organizations (CROs), Technology vendors (both clinical research and healthcare), Academia, and Investigators - and with invited outreach opportunities with global Regulatory representatives.

The eClinical Forum is firmly committed to promoting electronic data in all areas of clinical research. The eClinical Forum endeavors to ease the pain of change by providing clear rationale on implications of regulatory guidance in this area.

1.1 DISCLAIMER, COPYRIGHT and LICENSE

The information presented in these works draws upon the combined current understanding and knowledge of the eClinical Forum on this topic and is provided as an aid to understanding the environment for electronic clinical research. While the information provided has been guided and reviewed by members of the eClinical Forum representing all areas of the pharmaceutical and associated support industry, the opinions of the author(s) and the eClinical Forum do not necessarily reflect the position of individual companies. Users should assess the content and opinions in the light of their own knowledge, needs and experience as well as interpretation of relevant guidance and regulations.

The information in these works does not represent legal advice.

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2 About the eCF Requirements

The eClinical Forum has produced a set of eCF Requirements, which are based upon statements in documents prepared and issued and/or recognized by regulatory authorities that pertain to the design, development, implementation, and management of electronic systems that support clinical research data, as well as those statements that pertain to the handling of data that will be used in a regulated clinical trial.

This is a significant accomplishment by the eClinical Forum’s “Regulatory Expert Group” (REG) as they have put in countless hours over several years to be able to produce such a comprehensive checklist for evaluating electronic systems that will manage data used in regulated clinical research, against regulations and guidance from FDA /United States, EMA/European Union, PMDA/Japan, NMPA/China, MHRA/Great Britain, and ICH (International Conference on Harmonization) among others. This work is a result of the vast experience of the REG members who come from a variety of different eCF Member companies. They have spent hours debating each regulation or guidance and how to word the eCF Requirements to meet the needs in the regulatory documents. If any one company were to undertake such a project, the hours spent would justify an eClinical Forum membership very quickly. *For this reason, this document release is for eClinical Forum members only.*

Each eCF Requirement has as its basis one or more statements from one or more of the documents prepared and issued by FDA, EMA, PMDA, MHRA, NMPA and ICH and others. See appendix 2 for this list of reference documents. We have made every attempt to make each Requirement as succinct as possible, containing a single requirement in each. In addition, we have reviewed many documents from regulatory agencies and associations that are leaders in regulatory insights for clinical research. In some cases, we determined, while valuable documents, did not specifically call-out expectations/laws/regulations/guidance what could be used as a basis for these eCF requirements. So that you may know the completeness of our work, we have included a list of these non-mapped documents in Appendix 3.

The eClinical Forum acknowledges that documents cited in this reference are utilized and applied by regulatory authorities in a variety of ways. For example, some regional regulatory authorities codified the ICH E6 Good Clinical Practice guidance to be binding; other regulatory authorities do not consider the ICH E6 document to be a regulatory document but instead consider it to be non-binding (to industry and the regulatory authority) guidance that represents best practices. These interpretations have been taken into consideration by eClinical Forum in defining the requirements set forth in this reference. To address this conundrum, eClinical Forum has adopted the following rule in determining its requirements:

- If *any* regulatory authority identifies a particular document as a regulatory requirement, we treat the statements in this document as a requirement.

The eClinical Forum recommends that users of this reference be guided by the regulations that impact the region(s) where electronic data and systems will be utilized and apply the eClinical Forum requirements accordingly. With the existence of a global marketplace, it is important to consider the regulatory requirements of all regions where data generated by electronic systems may be used for product marketing submissions or where clinical research is being conducted.

Users should be aware that local legislation may impose additional requirements or user obligations to those stated in the following eCF requirements. For example, local legislation governing data privacy or the use of electronic/digital signatures may also need to be considered.

We commit to updating these eCF Requirements as would be needed when updates are made to the underlying documents and/or new pertinent documents are released from any of the regulatory authorities and bodies listed in Appendix 2. We anticipate releasing updated eCF Requirements

once/year in the first quarter, in conjunction with our membership year, which begins in January. eClinical Forum member companies with paid annual membership fees are provided exclusive access to the updated eCF Requirements, while the previous year version may be released for non-member use via our website: www.eclinicalforum.org.

The eCF Requirements can be used to determine if systems which originate and/or manage data that will become part of a regulated clinical trial are consistent with regulatory requirements and recommendations. In particular, the eCF Requirements can be used to assist with self-assessment of systems, planning for system upgrades, writing RFIs, writing system requirements, writing system test scripts, etc. Depending on the type of system being evaluated, not all eCF Requirements may apply. It is up to the user of these eCF Requirements to review the underlying regulatory basis of any eCF Requirement that he/she deems may not apply to a particular system to determine if it should be included. When using to develop test cases, the user should review all statements from regulatory documents in the mappings to be sure test suites capture all items requested in these regulatory documents. *Please note that this is an eCF-Members-Only release; if using to produce test cases that will be documented in customer-facing (potentially non-eCF member) materials, please follow License for Fair Use in Appendix 1.*

In the case of evaluating Electronic Health/Medical Record systems (EHR/EMR systems), the eClinical Forum has provided a checklist, based on the eCF Requirements, to assist with this evaluation. It can be found on the eClinical Forum website in the eSRA tab¹ and is provided to all for free. The work that is published here is an extension of work previously published as HL7 EHRCR Functional Profile (2009), ANSI EHRCR Functional Profile (2010), EuroRec EHRCR Functional Profile (2010), EHRCR User Requirements (2011), eSource-Readiness Assessment: eSRA (2015-2022), Checklist for EDC Systems in Clinical Trials using Service Providers (2016).

3 eCF Requirements Release Schedule

The eCF Requirements are in a linked .pdf file such that one can easily review the Requirement and then the statements from regulatory authority documents used as a basis for the eCF Requirement. Each release is provided to eCF members with paid annual membership dues for the duration of that membership year (see rationale under “About the eCF Requirements”). It can be obtained by logging into the eCF website with member credentials and accessing the Members area. Public releases of the previous year eCF Requirements document will be done in the first quarter of the year, and can be obtained on the eCF website in the Downloads area: [Downloads \(eclinicalforum.org\)](http://www.eclinicalforum.org/downloads).

¹ The “eSource-Readiness Assessment”, or eSRA, can be downloaded for free from www.eclinicalforum.org/esra.

The linked .pdf file is provided in Appendix 5.

FEEDBACK: If you would like to provide feedback to these eCF Requirements or ask any questions, please submit in writing to REG@eclinicalforum.org. Please provide the eCF Requirements number and text your comments are referring to, as well as your contact information.

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Appendix 2: Basis for the 2022 Release

This release is based on the following documents that have been prepared and issued by regulatory authorities.

The below references are not all 'regulatory documents' as one customarily understands the phrase – some of them do not directly imply literal and strict observance by the Industry as do the FDA Code of Federal Regulations, EU Regulations/Directives and other national legislations. For instance, *FDA Guidance for Industry* documents and *EMA Reflection Papers* are offered as suggested best practices. In an effort to provide a homogenous template for quality designs and risk assessments, the eCF chose not to differentiate between Regulations and Best Practices in the naming convention for its statements and calls them all **eCF Requirements**; please refer to the Regulatory mapping section for each eCF Requirement in order to specifically assess the legal implications of non-conformance in your region.

The eCF Requirements Release 2022 are based on the following regulation and guidance documents. These eCF Requirements are a work-in-progress; we continue to evaluate and map new regulatory authority documents as they come into effect. It is our intent to release updated mappings yearly. Future releases will include additional regulatory authority document mappings.

Additions in the 2022 Version of this paper are highlighted in bold. Please note that during 2021 the eCF REG team spent significant time reviewing and commenting on the EMA Draft Guidance “Computerized Systems and Electronic Data in Clinical Trials”. For this reason, there was less time to review new documents for the V2022 of the eCF Requirements, however, no significant regulatory authority documents were released during this time.

United States (FDA)

- 21 CFR Part 312 (FDA regulatory requirement)
 - [21 CFR Part 312, Investigational New Drug Application;](#)
- 21 CFR Part 11 (FDA regulatory requirement)
 - [21 CFR Part 11 Electronic Records and Electronics Signatures](#)
- CSUCI
 - [Guidance for Industry: Computerized Systems Used in Clinical Investigations \(May 2007\);](#)
- FDA Risk Based Monitoring Guidance
 - [FDA Guidance for Industry: Oversight of Clinical Investigations – A Risk Based Approach to Monitoring \(August 2013\);](#)
- FDA eSource Guidance
 - [Guidance for Industry Electronic Source Data in Clinical Investigations \(September 2013\);](#)
- FDA Mobile Medical Applications Guidance

- [FDA Guidance Mobile Medical Applications Guidance –\(February 9, 2015\);](#)
- USA: HIPAA (HHS regulatory requirement)
 - [USA Health Insurance Portability and Accountability Act;](#)
 - This document was originally mapped as part of the HL7 Functional Profile project in 2010. It was reviewed again in light of current interpretations in 2019 and some mappings to eCF Requirements were adjusted.
- FDA EHR in CR Guidance
 - [FDA Use of Electronic Health Record Data in Clinical Investigations Guidance for Industry \(July 2018\);](#)
- [FDA 21 CFR Part 812 Investigational Device Exemptions \(Revised 1-April-2019\)](#)
- [FDA Use of Electronic Records and Electronic Signatures in Clinical Investigations under 21 CFR Part 11 – Questions and Answers; June 2017](#)
- [FDA & MHRA: Data Integrity in Global Clinical Trials: Discussions From Joint US Food and Drug Administration and UK Medicines and Healthcare Products Regulatory Agency Good Clinical Practice Workshop](#)
- [FDA Guidance Document: Use of Electronic Informed Consent in Clinical Investigations – Questions and Answers Guidance for Institutional Review Boards, Investigators, and Sponsors \(Dec 2016\)](#)

European Union (EMA)

- [EMA eSource Reflection Paper; Reflection paper on expectations for electronic source data and data transcribed to electronic data collection tools in clinical trials \(09-June-2010\);](#)
- [EU Directive 2005/28/EC: Laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products \(GCP Directive\).](#)
- [EU Directive 2001/20/EC: on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice and the conduct of clinical trials on medicinal products for human use \(Clinical Trials Directive\) \(superseded by Regulation \(EU\) 536/2014\).](#)
- EU Annex 11 (EU regulatory requirement)
 - [The Rules Governing Medicinal Products in the EU -Volume 4 - GMP Annex 11: Computerised Systems \(June 2011\);](#)
- Regulation (EU) 536/2014; Clinical Trials Regulation (EU regulatory requirement)

- [EU Regulation 536/2014 \(16 April 2014\) Articles 57, 58](#)
- [EMA Reflection paper on the use of interactive response technologies \(interactive voice/web response systems\) in clinical trials, with particular emphasis on the handling of expiry dates \(10-Dec-2013\);](#)
- [EMA Reflection paper on risk based quality management in clinical trials \(18-Nov-2013\);](#)
- EU GDPR: Regulation (EU) 2016/679
 - [EU General Data Protection Regulation \(25-May-2018\)](#)
- [REGULATION \(EU\) No 910/2014 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 23 July 2014 on electronic identification and trust services for electronic transactions in the internal market and repealing Directive 1999/93/EC;](#)
- [Guideline on the content, management and archiving of the clinical trial master file \(paper and/or electronic\) \(6-Dec-2018\)](#)
- [Notification to sponsors on validation and qualification of computerised systems used in clinical trials; QA 8 Contractual Arrangements with Vendors; April 2020](#)
- [Notification to sponsors on validation and qualification of computerised systems used in clinical trials; QA 9 Sponsor Validation of Vendor Systems; April 2020](#)
- [Q&A: GCP - What are the expectations of EU Competent Authorities concerning the use of electronic trial master files \(e-TMFs\)](#)
- [EMA Guideline on the content, management and archiving of the clinical trial master file \(paper and/or electronic\) \(Dec 2018\)](#)

Japan

PMDA

- ERES (Electronic Records / Electronic Signatures) Guidelines
- [Using electromagnetic records and electronic signatures for application for approval or licensing of drugs \(1-Apr-2005\)](#)
- [EDC Management Checklist \(1-Jul-2021\)](#)

JPMA (Agreed by Japanese manufacturers and accepted by PMDA)

- [Guidance for electronic trial data capturing of clinical trials \(01-Nov-2007\); JPMA;](#)
- [Supplement to the Guidance for Electronic Data Capture in Clinical Trials; JPMA \(10-Jan-2012\)](#)

Japan Personal Information Protection Commission

- [Act on the Protection of Personal Information \(02-Dec-2016; effective 30-May-2017\);](#)

China

Ministry of Public Security

- [Chinese Personal Information Security Specification \(1-May-2018\)](#)
- [China Electronic Signature Law - 中华人民共和国电子签名法. Electronic Signature Law of the People's Republic of China](#)
 - Note – we have used an unofficial English translation of this document. It is available to eCF members in the eCF Members section of our website.

National Medical Products Administration (NMPA)

- [Clinical Trial Data Management Guide \(non-official translation\)](#) (Judged by eCF REG review to have the same requirements for electronic data as ICH GCP, and therefore not separately mapped)

Great Britain Medicines and Healthcare products Regulatory Agency

- [MHRA & FDA: Data Integrity in Global Clinical Trials: Discussions From Joint US Food and Drug Administration and UK Medicines and Healthcare Products Regulatory Agency Good Clinical Practice Workshop](#)
- [MHRA Guidance on GxP Data Integrity, March 2018](#)

International:

ICH (International Council on Harmonisation)

- [International Council on Harmonisation Guideline for Good Clinical Practices E6 R2 \(9-Nov-2016\)](#); (considered regulatory requirement in EU)

ISO (International Organization for Standardization)

- [ISO 14155: Clinical investigation of medical devices for human subjects – Good clinical practice](#) (Judged by eCF REG review to have the same requirements for electronic data as ICH GCP, and therefore not separately mapped.)

Appendix 3: Documents Reviewed and Not Included as Basis for eCF Requirements

The eClinical Forum REG has reviewed many documents that, while providing value to the industry, do not provide specific basis for criteria for evaluating systems for clinical research. In order to provide a complete picture of the careful thought that has gone into the eCF Requirements, we offer this list of documents that eCF REG has reviewed and not used as a basis for eCF Requirements.

After much discussion, it was decided that the following types of documents would not be used as basis for the eCF Requirements.

- Documents pertaining to submission requirements
- Webinar slides and presentation notes from Regulatory Authorities
- Methodologies that are not legally mandated (e.g. ISO, GAMP, PDA, BSA, ACDM)
- Documents that are not freely available

In addition to documents in the above categories, the following documents were reviewed by REG and determined to be not appropriate for the eCF Requirements:

Source	Type	Version	Title	Keywords
EMA	Guide	May, 2020	EMA Guidance on remote GCP inspections during the COVID19 pandemic (18-May-2020)	<ul style="list-style-type: none"> -Inspection initiation -Impact analysis -feasibility assessment -Inspection preparation -Conduct of the inspection -Inspection reporting process
FDA	Guidance	Dec, 2009	Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims	<ul style="list-style-type: none"> -PRO Instrument -Content Validity -Conceptual Framework -Domain/Item Scoring -Recall Period -Respondent Burden -Reliability -Ability to Detect Change
FDA	Guidance	Feb, 2020	Providing Regulatory Submissions in Electronic Format – Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications Guidance for Industry	<ul style="list-style-type: none"> -eCTD -eCTD Backbone -Electronic Submissions -Waiver -File Formats
FDA	Guidance	Apr, 2005	Providing Regulatory Submissions in Electronic Format – Content of Labeling: Guidance for Industry	<ul style="list-style-type: none"> -Structured Product Labeling - SPL -Label Submissions -Electronic Labeling Rule
FDA	Guidance	Aug, 2003	Guidance for Industry Part 11, Electronic Records; Electronic Signatures – Scope and Application	
FDA	Guidance	Dec, 2017	Software as a Medical Device (SaMD): Clinical Evaluation; Guidance for Industry and Food and Drug Administration Staff; December 8, 2017	<ul style="list-style-type: none"> -Medical device -Mobile Medical Apps -SaMD
FDA	Notes	Sep, 2019	Policy for Device Software Functions and Mobile Medical Applications Sept 2019	<ul style="list-style-type: none"> -Device Software Functions -Mobile Medical Apps -Device regulatory requirements
FDA	Regulation	Revision Apr, 2020	21 CFR 50, Protection of Human Subjects	<ul style="list-style-type: none"> -Informed Consent -IRB -Risk
FDA	Regulation	Revision Apr, 2020	21 CFR 56, Institutional Review Boards	<ul style="list-style-type: none"> -Institutional Review Board -IRB

FDA	Regulation	Revision Apr, 2020	21CFR part 314.50 Application for FDA approval to market new drug	-NDA format -Labeling
FDA	Draft	Sep, 2019	Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act Guidance for Industry	-medical device
FDA	Draft Q&A	Mar, 2019	A Risk-Based Approach to Monitoring of Clinical Investigations Questions and Answers Guidance for Industry	-Risk-Based Monitoring -RBM -Risk Assessment -Centralized Monitoring
MHRA	Guide	Sep, 2018	Joint statement on seeking consent by electronic methods	-Consent -eConsent -Informed Consent
MHRA	Blog	Jul, 2015	MHRA Blog on Trial Master File	-TMF/ eTMF -Qualified Person (QP) -Key Decision Making -Trial Conduct
Japan PMDA	Guide	Apr, 2015	Technical Conformance Guide on Electronic Study Data Submissions (PFSB/ELD/OMDE Notification No. 0427001, April 27, 2015)	-Submissions -Electronic Study Data -Data Validation -SDTM -ADaM -Annotated CRF -Data Standards -eCTD
Japan PMDA	Q&A	Oct, 2010	Questions and Answers (O and A) regarding the Guideline on Management of Computerized Systems for Marketing Authorization Holders and Manufacturers of Drugs and Quasi-drugs (PFSB/CNB Administrative Notification October 21, 2010)	-Validation -Electronic Signatures -Business Continuity -Computerized Systems in GCP -System Retirement
Japan PMDA		June, 2014	Basic Principles on Electronic Submission of Study Data for New Drug Applications (PFSB/ELD Notification 0620-6, June 20, 2014)	-New Drug Application -NDA -Electronic Submission -Electronic Data -Data Standards -CDISC -XML
Japan PMDA		July, 2013	Basic Rules of the Risk-Based Approach to Monitoring Clinical Trials (PFSB/ELD Notification, 1 July 2013)	-SDV -Risk-based SDV -Clinical trial Quality

Japan PMDA		Apr, 2015	Notification on Practical Operations of Electronic Study Data Submissions (PFSD/ELD Notification 0427-1, April 27, 2015)	<ul style="list-style-type: none"> -Electronic data submissions -eCTD -CDISC data standards -Define-XML -New Drug Application
Japan PMDA	Guide	Oct, 2010	Guideline on Management of Computerized Systems for Marketing Authorization Holders and Manufacturers of Drugs and Quasi-drugs	<ul style="list-style-type: none"> -Drug Manufacturing -Manufacturing Quality Control -Manufacturing Quality Assurance -Computerized system lifecycle -GMP/GQP -Validation (PQ, OQ, IQ) -Operations Management -Document and Record Management
Brazil ANVIS A	Guide	Apr, 2020	Guide for Computerized System Validation	<ul style="list-style-type: none"> -Software/System Validation - Lifecycle -Risk Mgt -Backup -Migration -Retirement -Spreadsheet Validation
Non-Reg	Guide	Dec, 2019	SCDM: Good Clinical Data Management Practices	<ul style="list-style-type: none"> -GxP -Compliance -Data Quality -Electronic Edit Checks -Clinical Research Data -Data Management -Quality-by-Design -Risk-Based-Approaches -External Data -CRO, / Vendor Management -Certified-Clinical-Data-Manager
Non-Reg	Methodology		ECRIN (European Clinical Research Infrastructure Network) Requirements for Certification	<ul style="list-style-type: none"> -Europe -Investigator -Certification -Data Center -Training -Validation -Logical Security -Logical Access -IT Infrastructure -Business Continuity -Data Quality -Data Transfers -Data Storage -Long Term Retention -Subcontracting -Standards

NON-REG	Guide	Mar_2017	International Society of Pharmaceutical Engineering – GAMP Guide: Records and Data Integrity	<ul style="list-style-type: none"> -Quality Risk Management -Corporate Data Integrity Program -Risk Control Measures -Electronic Signatures -Paper Records and Hybrid Situations -User Requirements -Audit Trail -Audit Trail Review -Retention, -Archiving -Migration -Data Life Cycle -Inspection Readiness
NON-REG	Guide	Sep 2007	PIC/s Good Practices for Computerised Systems in Regulated 'GXP' Environments	
NON-REG	Guide	Jul 2021	PIC/S Guidance on Data Integrity (picscheme.org)	
ISO	Guide		ISO 14155 Clinical investigation of medical devices for human subjects – Good clinical practice	This document was compared to GCP; GCP has been mapped to eCF Requirements, so it is not necessary to also map ISO 14155
OECD	Guide	Sep 2021	Principals on Good Laboratory Practice and Compliance Monitoring	This is an excellent resource which we believe to be superior to other guidelines previously published.

Appendix 4: Abbreviations and Definitions

Abbreviations

Abbreviation	Meaning
ALCOA+	Attributable, Legible, Contemporaneous, Original, Accurate, Complete, Consistent, Enduring, Available When Needed
CFR	Code of Federal Regulations (US)
CRF	Case Report Form
CRO	Contract Research Organization
EDC	Electronic Data Capture
EHR	Electronic Health Record
EMA	European Medicines Agency
EMR	Electronic Medical Records
eSRA	eSource Readiness Assessment
EU	European Union
EuroRec	European Institute for Health Records
FDA	Food and Drug Administration (United States of America)
GCP	Good Clinical Practice
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
JPMA	Japan Pharmaceutical Manufacturers Association
NMPA	National Medical Products Administration (China)
PMDA	Pharmaceutical and Medical Devices Agency (Japan)

Definitions

Term	Definition
ALCOA+	<ul style="list-style-type: none"> ● Attributable ● Legible ● Contemporaneous ● Original ● Accurate ● Complete ● Consistent ● Enduring ● Available when needed
Audit trail / Audit log	A secure, computer generated, time-stamped electronic record that allows reconstruction of the course of events relating to the creation, modification, and deletion of an electronic record.
Certified Copy	A copy (irrespective of the type of media used) of the original record that has been verified (i.e., by a dated signature or by generation through a validated process) to have the same information, including data that describe the context, content, and structure, as the original.
Clinical trial	Any investigation in human subjects intended to discover or verify the clinical, pharmacological, and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy. The terms clinical trial and clinical study are synonymous.
Core system	A core system includes the application(s) that do not include the trial-specific configurations. It is what comes “out-of-the-box” with every study before any study-specific elements are added.
Contract Research Organization (CRO)	A person or an organization (commercial, academic or other) contracted by the sponsor to perform one or more of a sponsor’s trial related duties and functions. For the purpose of this document, the CRO acts as an extension of the sponsor.
EDC System	An Electronic Data Capture (EDC) system consists of a user interface, i.e., web pages and reports, programming logic (e.g., computer programs, scripts) and a repository of data (e.g., database) using services from Infrastructure Systems.

EMR / EHR	Electronic Medical Record, Electronic Health Record – for purposes of completing an eSRA assessment of your healthcare system, these terms are interchangeable
EHRCR	The global EHRCR Functional Profile Project is a collaborative effort to expand and adapt the functionality of EHR and associated systems, networks, and processes to support clinical research. The project is aimed at developing a Functional Profile that identifies critical capabilities for the conduct of clinical research utilizing EHR systems and establishes conformance to the HL7 EHR Functional Model and the Q-Rec EHR Certification Criteria. HL7 Health Level-7 refers to a set of international standards for transfer of clinical and administrative data between hospital information systems.
IoMT	Internet of Medical Things. The Internet of Medical Things (IoMT) is the collection of medical devices and applications that connect to healthcare IT systems through online computer networks. Medical devices equipped with Wi-Fi allow the machine-to-machine communication that is the basis of IoMT. ... IoMT is also known as healthcare IoT.
Investigator	A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.
IT, Site IT	Information Technology. IT should include a Data Privacy Officer and Records Retention staff particularly during set-up and maintenance of clinical research systems.
Research Protocol	(Also called Clinical Trial Protocol) A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents. Throughout the ICH GCP Guidance, the term protocol refers to protocol and protocol amendments.
SOP	Standard Operating Procedure
Sponsor	An individual, company, institution or organization that takes responsibility for the initiation, management and or/financing of a clinical trial.

Transient Data Collector	Devices, in that they acquire data, temporarily store it in files, but as part of normal workflow, pass the data onto databases before the process task is complete
Trusted Third Party	Third party entities who collect data on behalf of an investigator and maintain an independence from sponsor control.
Unsuccessful vs Unauthorized access attempt	This refers to questions 16 and 17. An “unsuccessful” access attempt refers to a legitimate user forgetting their access information (e.g., their username or password). An “unauthorized” access attempt refers to a non-user attempting to gain access (e.g., through hacking).

Appendix 5: ECF REQUIREMENTS Public Release V2022

(see next page)

eCF Requirement Report

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ID	Description	Version	Mapping Version
C01	System has the ability to store and retrieve data items in a way that is attributable to a trial/data subject.	1	12
C02	Specified de-identified data can be extracted for clinical research.	1	18
C03	System has capability of storing data related to subject consent and should not allow data collection until the subject consent is confirmed.	2	9
C04	System has an audit trail to include recording date/time/originator of any data creation, change, or deletion.	2	36
C05	The audit trail includes the reason for changes /deletions.	1	16
C07	Audit trail information is readable and readily available.	3	21
C08	System does not allow new audit trail information to over-write existing (previous) information and cannot be altered without detection.	2	15
C10	There is a process to ensure that eCRF entries and any subsequent modifications are reviewed and approved by the investigator.	2	11
C11	There is a system and/or process to ensure the investigator has control of and continuous access to their source data reported to the sponsor and the sponsor does not have exclusive control of those data.	4	21
C13	Controls exist such that the ability to change system settings is limited to authorized personnel.	3	9
C14	System allows audit trail to utilize a standard time such that the local time can be derived.	2	8
C16	The system has the ability to create, maintain and apply the roles, access permissions and capabilities of each user that accesses the system, such that users have access only to those system features and functions to which they have been granted access.	1	48

C17	There is a policy and training that instructs users not to share their access mechanisms (e.g. usernames and passwords, or access keys) or to leave their account open for others to use.	3	20
C18	The monitor, auditor and inspector can within reasonable timeframe obtain direct access to trial subjects records in order to perform their regulatory duties.	2	27
C19	System limits the number of log-in attempts and records unsuccessful attempts.	2	10
C20	System records and notifies a system administrator of unauthorized access log-in attempts.	1	12
C21	The system enforces user authentication mechanisms that follow current information security best practices.	3	12
C22	System feature to allow automatic logoff or other access lock (such as password protected screen saver) after a set period of time of inactivity.	2	5
C23	The system must have the ability to provide a history of all individuals who have access to the system and their access privileges over time.	3	8
C24	System has the ability to produce a human-readable copy of data (which includes associated audit trails and any decoded data).	2	13
C25	Copies of electronic records must be certified copies if they are being used for regulatory purposes	3	14
C26	There are sufficient system and/or process controls for backup and recovery procedures.	1	28
C27	Documentation of the backup and recovery process can be produced for inspection by a monitor, auditor or inspector.	1	9
C28	Process and/or system controls ensure that regulated data used for clinical research, including source data and metadata are enduring, continue to be available, readable and understandable and are retained in an archive for the legal period.	3	49
C29	There are sufficient process controls for the system covering Business Continuity.	2	16
C30	There are sufficient process controls based on industry standards, covering Disaster Recovery Procedures.	2	16
C31	There is a process to demonstrate that individuals who develop, maintain, or use the system have appropriate education, training, and experience necessary to perform their assigned task.	1	30
C32	There is a process to demonstrate that the development, hosting and deployment of the computerised system follows good software lifecycle	5	55

practices such that it is sufficiently validated based on risk.

C35	There are sufficient system and/or process controls to prevent or mitigate effects of viruses, worms, or other harmful software code.	1	9
C36	There are sufficient system and/or process controls over data transfers from/to other systems, including validation of data mapping and transfer, security of data in transit, and confirmation of receipt.	4	42
C37	When third parties are used to provide GxP-related services, formal agreements must exist and include clear statements of the roles and responsibilities of the third party.	4	29
C39	Signed electronic records shall contain information associated with the signing that clearly indicates all of the following: - The name of the signer - The date and time when the signature was executed - The meaning (such as creation, confirmation or approval) - Electronic signatures are permanently linked to their respective record	5	22
C40	There is a process to ensure that in case of data breach, the Sponsor and/or Investigator shall notify the relevant Data Protection supervisory authority.	2	4
C41	The alignment of a trial-specific eSystem(s) with each protocol amendment should be evaluated and the system updated as needed	3	14
C42	A change to the core system should be evaluated to determine if it affects trial-specific configurations. Updates should be made as needed.	4	19
C43	There should be a process to periodically affirm the continued suitability of a deployed computerized system taking into account changes in risk, users, roles and protocol.	3	7
C44	For eTMF, the audit trail additionally captures accessing of records.	2	4

Regulatory mapping for eCF Requirement ID C01

System has the ability to store and retrieve data items in a way that is attributable to a trial/data subject.

Regulation	Paragraph	Description
FDA 21 CFR Part 11 Q&A	Q18a	For the purposes of recordkeeping, audit trail, and inspection, each electronic data element should be associated with an authorized data originator.
FDA 21 CFR Part 11 Q&A	Q18b	If a study participant who is using the mobile technology actively participates in the performance measure by entering and submitting data to the sponsor's EDC system (e.g., when using an ePRO app or when performing visual acuity testing), the study participant should be identified as the data originator.
FDA 21 CFR Part 312	62b	An investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes. The case history for each individual shall document that informed consent was obtained prior to participation in the study.
Japanese APPI	Article 28	A principal may demand of a personal information handling business operator disclosing retained personal data that can identify him or herself.
FDA CSUCI	F2a	The computerized system should be designed in such a way that retrieved data regarding each individual subject in a study is attributable to that subject.
EMA eSource Reflection Paper	Topic 2a	Source data should be Accurate, Legible, Contemporaneous, Original, Attributable, Complete and Consistent. Accurate: The use of such instruments/systems should ensure that the data are at least as accurate as those recorded by paper means. The validity of the data capture process is fundamental to ensuring that high-quality data are produced as part of a trial. The process needs to ensure that all data required are captured and that data are captured in

a consistent manner. The coding process which consists in matching text or data collected on the CRF to terms in a standard dictionary, thesaurus or tables (e.g. units, scales, etc.) should be controlled. The process of data transfer between systems should be validated.

EMA eTMF Guideline	4.1.3b	The documentation in the investigator TMF includes some source documents containing personal data that enable the data subjects to be directly identified (i.e. direct identifiers of trial subjects).
EU Directive 2005 28	2.1.5	All clinical trial information shall be recorded, handled, and stored in such a way that it can be accurately reported, interpreted and verified, while the confidentiality of records of the trial subjects remains protected.
FDA eSource Guidance	Background	<p>Source data includes all information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical investigation used for reconstructing and evaluating the investigation. Access to source data is critical to the review and inspections of clinical investigations. The review of source data by both the FDA and sponsor is important to ensure adequate protection of the rights, welfare, and safety of human subjects and the quality and integrity of the clinical investigation data. Source data should be attributable, legible, contemporaneous, original, and accurate (ALCOA) and must meet the regulatory requirements for recordkeeping. Capturing source data electronically and transmitting it to the eCRF should:</p> <ul style="list-style-type: none"> - Eliminate unnecessary duplication of data - Reduce the possibility for transcription errors - Encourage entering source data during a subjects visit, where appropriate - Eliminate transcription of source data prior to entry into an eCRF - Facilitate remote monitoring of data - Promote real-time access for data review - Facilitate the collection of accurate and complete data
EU GDPR	Article 15	The data subject shall have the right to obtain from the controller confirmation as to whether or not personal data concerning him or her are being processed.
ICH GCP	2.10	All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification. ADDENDUM - This principle applies to all records referenced in this guideline, irrespective of the type of media used.
ICH GCP	4.9.0	The investigator/institution should maintain adequate and accurate source documents and trial records that include all pertinent observations on each of the site's trial subjects. Source data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry, and should be explained if necessary (e.g., via an audit trail).

ICH GCP	4.9.7	Upon request of the monitor, auditor, IRB/IEC, or regulatory authority, the investigator/institution should make available for direct access all requested trial related records.
ICH GCP	5.5.5	The sponsor should use an unambiguous subject identification code (see 1.58) that allows identification of all the data reported for each subject.
JPMA EDC Guidance	4.2.2	Clinical data captured can be displayed on screen or printed on paper as forms or inventory for each clinical case.
JPMA EDC Supplement	1.2a	...it is required to prepare necessary equipment (e.g. devices) and environment (e.g. internet line, telephone line) for data entry by subjects, make operational procedures for transmitting subject data to the operational database, operational procedures for providing the collected subject data to investigators. and sponsors, and also procedures for data retention after completion of the clinical trial and location of storage.
NMPA PISS	7.4	Personal information controllers should provide personal information subjects with access to the following information: a) the personal information or type of information it holds about the subject; b) the source of the above personal information and the purpose for which it was used; c) The identity or type of the third party who has obtained the above personal information.

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Regulatory mapping for eCF Requirement ID C02

Specified de-identified data can be extracted for clinical research.

Regulation	Paragraph	Description
FDA 21 CFR Part 312	60	...investigator is responsible for protecting the rights, safety, and welfare of the subject.
FDA 21 CFR Part 312	68	An investigator shall upon request from any properly authorized officer or employee of FDA, at reasonable times, permit such officer or employee to have access to, and copy and verify any records or reports made by the investigator pursuant to 312.62. The investigator is not required to divulge subject names unless the records of particular individuals require a more detailed study of the cases, or unless there is reason to believe that the records do not represent actual case studies, or do not represent actual results obtained.
21 CFR Part 56	111.a.7	Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
EMA eSource Reflection Paper	Topic 5a	<p>The storage of source documents should provide for their ready retrieval.</p> <p>Source documents and data should always be available when needed to authorised individuals to meet their regulatory obligations. Whilst a trial is active and after its conclusion, existing source data should be readily available to the investigator and others such as monitors, auditors and inspectors. Direct access to the system should be provided by the sponsor and/or investigator to monitors, auditors and inspectors.</p>
EMA eTMF Guideline	4.1.3c	In general, information (data/documents) shared with the sponsor/CRO or uploaded into a database or filing system that is managed by the sponsor/CRO, should only contain data of trial subjects, which has been pseudonymised.
EMA eTMF Guideline	4.1.3h	Remote access by sponsor or CRO personnel to the investigator TMF should only be possible to the documents where personal data that enable the data subjects to be directly identified (i.e. direct identifiers of trial subjects) is not present or has been pseudonymised.
EU Directive	2.1.5	All clinical trial information shall be recorded, handled, and stored in

2005 28		such a way that it can be accurately reported, interpreted and verified, while the confidentiality of records of the trial subjects remains protected.
EU GDPR	Article 20.2	In exercising his or her right to data portability pursuant to paragraph 1, the data subject shall have the right to have the personal data transmitted directly from one controller to another, where technically feasible.
EU GDPR	Article 20.3	The exercise of the right referred to in paragraph 1 of this Article shall be without prejudice to Article 17. That right shall not apply to processing necessary for the performance of a task carried out in the public interest or in the exercise of official authority vested in the controller.
EU GDPR	Article 25.1	The controller shall, both at the time of the determination of the means for processing and at the time of the processing itself, implement appropriate technical and organisational measures, such as pseudonymisation.
ICH GCP	2.11	The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).
NMPA Clinical Trial DM Guide	5.14.2	Personal privacy protection measures in the design of the database should be considered at the technical level, without affecting the integrity of the data and does not violate the principles of GCP does not include as much as possible under the conditions of the protected health information, such as: the database should not be included under Full name of those tested, but should record the full name abbreviations. In Chinese name, for example, should use the first letter of the subjects surname and first name initials.
NMPA PISS	6.2	After collecting personal information, the personal information controller should immediately perform de-identification processing and take technical and management measures to store the de-identified data separately from the information that can be used to recover the identified individuals, and ensure the follow-up individuals. Individuals are not re-identified in information processing.

Regulatory mapping for eCF Requirement ID C03

System has capability of storing data related to subject consent and should not allow data collection until the subject consent is confirmed.

Regulation	Paragraph	Description
FDA 21 CFR Part 312	62b	An investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes. The case history for each individual shall document that informed consent was obtained prior to participation in the study.
21 CFR Part 812	140.a.3	(a) Investigator records. A participating investigator shall maintain the following accurate, complete, and current records relating to the investigators participation in an investigation:... (3) Records of each subjects case history and exposure to the device. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individuals hospital chart(s), and the nurses notes.
Japanese APPI	Article 16	A personal information handling business operator shall not handle personal information without obtaining in advance a principals consent...
EU Directive 2001 20	16	The person participating in a clinical trial must consent to the scrutiny of personal information during inspection by competent authorities and properly authorised persons, provided that such personal information is treated as strictly confidential and is not made publicly available.
FDA A Risk-Based Approach to Monitoring	III.B.2.a	Verification of subjects informed consent is a critical activity that should be monitored.
FDA A Risk-Based Approach	IV.a	Verification that informed consent was obtained appropriately

to Monitoring

EU GDPR	Recital 42	Where processing is based on the data subject consent, the controller should be able to demonstrate that the data subject has given consent to the processing operation.
ICH GCP	2.9	Freely given informed consent should be obtained from every subject prior to clinical trial participation.
ICH GCP	4.8.8	Prior to a subjects participation in the trial, the written informed consent form should be signed and personally dated by the subject or by the subject's legally acceptable representative, and by the person who conducted the informed consent discussion.
NMPA PISS	5.5a	When collecting sensitive personal information, you should obtain explicit consent from the subject of your personal information. It should be ensured that the express consent of the subject of personal information is a concrete, clear and unambiguous expression of wishes that is voluntarily given on a fully informed basis.

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Regulatory mapping for eCF Requirement ID C04

System has an audit trail to include recording date/time/originator of any data creation, change, or deletion.

Regulation	Paragraph	Description
FDA 21 CFR Part 11	10e	(e) Use of secure, computer-generated, time-stamped audit trails to independently record the date and time of operator entries and actions that create, modify, or delete electronic records. Record changes shall not obscure previously recorded information. Such audit trail documentation shall be retained for a period at least as long as that required for the subject electronic records and shall be available for agency review and copying.
FDA 21 CFR Part 11 Q&A	Q19	FDA does not intend to inspect each individual mobile technology used in a clinical investigation to capture, record, and transmit data directly from study participants because access controls, audit trails, and validation that would be applied would help ensure the reliability of the data.
FDA 21 CFR Part 11 Q&A	Q20a	When data are copied or transmitted directly from the mobile technology to the sponsor's EDC system or from the mobile technology to the EHR and then to the sponsor's EDC system, the audit trail begins at the time the data enter the sponsor's EDC system.
FDA 21 CFR Part 11 Q&A	Q6a	For electronic copies in which the records are modifiable, it would be important to have audit trails in place to ensure the trustworthiness and reliability of the electronic copy.
Japanese APPI	Article 20	A personal information handling business operator shall take necessary and appropriate action for the security control of personal data including preventing the leakage, loss or damage of its handled personal data.
FDA CSUCI	D2a	It is important to keep track of all changes made to information in the electronic records that document activities related to the conduct of the trial (audit trails).
FDA CSUCI	D2b	The use of audit trails or other security measures helps to ensure that only authorized additions, deletions, or alterations of information in the electronic record have occurred and allows a means to reconstruct

significant details about study conduct and source data collection necessary to verify the quality and integrity of data.

FDA CSUCI	D2c	Computer-generated, time-stamped audit trails or other security measures can also capture information related to the creation, modification, or deletion of electronic records and may be useful to ensure compliance with the appropriate regulation.
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FDA CSUCI	D2f	Computer-generated, time-stamped electronic audits trails are the preferred method for tracking changes to electronic source documentation.
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FDA CSUCI	D2g	Audit trails or other security methods used to capture electronic record activities should describe when, by whom, and the reason changes were made to the electronic record.
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PMDA EDC Management Sheet version 2	49 and 54	<p>Outline of audit trails with regards to creation / modification of retained information</p> <ul style="list-style-type: none">- Does the system have full audit trail capability?- To clearly identify the initial data entry by user ID (account holder)- To clearly identify which data was is automatically calculated/derived- To clearly determine data loaded (through a system-to-system account or individual user account)- To clearly identify the data modifications by user ID (account holder)- To retain (i.e. not to delete) information prior to modification- To view full audit history trails (sponsor)- To view full audit history trails (medical institution) <p>Throughout the conduct and post completion of the clinical trial.</p>
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EMA eSource Reflection Paper	Topic 2d	<p>An audit trail should be maintained as part of the source documents for the original creation and subsequent modification of all source data. The maintenance of an audit trail is essential to ensure that changes to the data are traceable. Secure, computer-generated, time-stamped audit trails (or alternative methods that fulfil the audit trail requirements) should be used to independently record the date and time of operator entries and actions that create, modify, or delete electronic records. Such audit trail documentation should be retained as long as the subject electronic records. Audit trails need to be readable and changes to audit trail data should be prevented by the system. The responsible investigators, sponsors and inspectors should be able to review the audit trail. The audit trail will record changes made as a result of data queries or a clarification process. The clarification process for data entered by trial subjects should be documented and it should be clearly stated where changes to data entered by subjects will not be made.</p>
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EMA eTMF Guideline	4.1.2e	<p>The primary eTMF is a system for managing documents that should contain the controls listed below:</p> <p>an audit trail in place to identify date/time/user details for creation and/or uploading deletion of and changes to a document (explanation of the deletion or modification, if necessary);</p>
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EMA eTMF Guideline	5	Particular attention should be paid when documents are stored on electronic, magnetic, optical or other non-indelible media. In such cases suitable controls should be implemented to ensure that these documents are complete and cannot be altered without appropriate authorisation and the creation of an audit trail.
PMDA ERES (Japan)	3.1.1.2	Distinction of the creator of maintained information shall be definite. And also when modify the maintained information, previously recorded information shall be stored, and distinction of the modifier shall be definite. Audit trail shall be recorded by automatically, and recorded audit trail is desirable to be confirmed by predetermined procedure.
EU Annex 11	12.4	Management systems for data and for documents should be designed to record the identity of operators entering, changing, confirming or deleting data including date and time.
EU Annex 11	9	Consideration should be given, based on a risk assessment, to building into the system the creation of a record of all GMP-relevant changes and deletions (a system generated "audit trail"). For change or deletion of GMP-relevant data the reason should be documented. Audit trails need to be available and convertible to a generally intelligible form and regularly reviewed.
EU Clinical Trials Regulation 536 2014	58f	Any alteration to the content of the clinical trial master file shall be traceable.
EU Electronic Identification Regulation 910-2014	26.d	An advanced electronic signature shall meet the following requirements: (d) it is linked to the data signed therewith in such a way that any subsequent change in the data is detectable.
FDA EHR Guidance	V.B.3	Audit trails are available to track changes to data.
FDA EHR Guidance	V.C.1	Each electronic data element should be associated with a data originator.
FDA EHR Guidance	V.C.2.b	Modified and corrected data elements should have data element identifiers that reflect the date, time, data originator, and the reason for the change.
EU GDPR	Recital 82	In order to demonstrate compliance with this Regulation, the controller or processor should maintain records of processing activities under its responsibility.
USA HIPAA	164.312b	Implement hardware, software, and/or procedural mechanisms that record and examine activity in information systems that contain or use electronic protected health information.
USA HIPAA	164.312c1	Implement policies and procedures to protect electronic protected health information from improper alteration or destruction.

ICH GCP	4.9.0	The investigator/institution should maintain adequate and accurate source documents and trial records that include all pertinent observations on each of the site's trial subjects. Source data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry, and should be explained if necessary (e.g., via an audit trail).
ICH GCP	4.9.3	Any change or correction to a CRF should be dated, initialed, and explained (if necessary) and should not obscure the original entry (i.e. an audit trail should be maintained); this applies to both written and electronic changes or corrections (see 5.18.4(n)). Sponsors should provide guidance to investigators and/or the investigators' designated representatives on making such corrections. Sponsors should have written procedures to assure that changes or corrections in CRFs made by sponsor's designated representatives are documented, are necessary, and are endorsed by the investigator. The investigator should retain records of the changes and corrections.
ICH GCP	5.5.3c	When using electronic trial data handling and/or remote electronic trial data systems,the sponsor should: c) Ensure that the systems are designed to permit data changes in such a way that the data changes are documented and that there is no deletion of entered data (i.e.maintain an audit trail, data trail, edit trail).
ICH GCP	5.5.4	If data are transformed during processing, it should always be possible to compare the original data and observations with the processed data.
JPMA EDC Guidance	4.1.1.2a	The ability to investigate of operator, content and timing of input/modify of data.
JPMA EDC Guidance	4.1.1.2b	The ability to prevent alteration, divulgation and repudiation of fact of operation.
JPMA EDC Guidance	4.1.1.3.6c	The ability to identify of operator ID and input time of each data by log (i.e. audit trail). - Note that signature shall not be requested for every data input. - But, the operator shall be identified for every data input.
JPMA EDC Guidance	4.1.1.3c	The ability to detect any unauthorized access. (monitoring of access, alert, access logs).
JPMA EDC Supplement	1.2e	First, in case of an ePRO system using an IVRS or IWRS, data in the server is regarded as source data, as it is directly recorded PRO (original). Therefore, the data must include an input trail and, in case of correction, an edit trail.
JPMA EDC Supplement	1.2f	In case of an ePRO system using an entry device, data saved in the device is the original record created by the subject, and is thus regarded as the source data. Therefore, the Usage of Electromagnetic Records and Electronic Signatures in the Application for Drug Approval

or Licensing must be complied for the device itself. In other words, requirements for authenticity, readability and retainability must be fulfilled under precondition that the device has been validated. These requirements include recording of an audit trail in case the data saved in the device are changeable.

JPMA EDC Supplement	1.4c	Ensure that the systems are so designed as to permit data correction in such a way that the data correction are documented and that all records of correction of entered data remain undeleted as logs distinguishable to the inputter as well as to the corrector (i.e. to maintain audit trail, input trail, and edit trail);
JPMA EDC Supplement	1.5.1.1c	An audit trail can be retained automatically. Together with the entered data, the date and time of entry and the person who enters the data can be recorded. If the system is also designed to permit data correction, then the data corrections are documented and that all records of correction of entered data remain undeleted as unchangeable logs distinguishable to the inputter as well as to the corrector, automatically.
JPMA EDC Supplement	1.5.1.2a	An audit trail shall enable identification of the persons who entered the data, the entered data and the time of entry. In case of correction, the persons who corrected, the correction details and the time of correction must be identifiable.
MHRA GXP Data Integrity Guidance	6.13a	The audit trail is a form of metadata containing information associated with actions that relate to the creation, modification or deletion of GXP records. An audit trail provides for secure recording of life-cycle details such as creation, additions, deletions or alterations of information in a record, either paper or electronic, without obscuring or overwriting the original record. An audit trail facilitates the reconstruction of the history of such events relating to the record regardless of its medium, including the 'who, what, when and why' of the action.
MHRA GXP Data Integrity Guidance	6.13b	Where computerised systems are used to capture, process, report, store or archive raw data electronically, system design should always provide for the retention of audit trails to show all changes to, or deletion of data while retaining previous and original data. It should be possible to associate all data and changes to data with the persons making those changes, and changes should be dated and time stamped (time and time zone where applicable). The reason for any change, should also be recorded. The items included in the audit trail should be those of relevance to permit reconstruction of the process or activity.
NMPA Clinical Trial DM Guide	3.3.2.a	CRF data for any changes or correction should be dated and signed name and explain why (if required), and should make the original records are still visible.
NMPA Clinical Trial DM Guide	3.3.2.b	Inspection of clinical trial data track (Audit Trail), from the first data entry so that every change, delete or add, must be retained in the clinical trials database system to ensure that the data from the original

data to declare the whole process transparency. Inspection should include changing tracks the date, time, change the people, change reasons, the data value before the change, the changed data values. This inspection trajectory of system protection, does not allow any artificial modification and editing. Inspection records should be archived and trajectory queries.

NMPA PISS	10.5b	An automated audit system should be established to monitor and record personal information processing activities.
NMPA PISS	8.1e	The personal information controller should accurately record and save the circumstances of the commissioned personal information.

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Regulatory mapping for eCF Requirement ID C05

The audit trail includes the reason for changes /deletions.

Regulation	Paragraph	Description
FDA 21 CFR Part 11 Q&A	Q20b	Modified and corrected data elements should have data element identifiers that reflect the date, time, and data originator and the reason for the change. Modified and corrected data should not obscure previous entries.
Japanese APPI	Article 29.3	A personal information handling business operator shall, when having made a correction etc. on a whole or part of the contents of the retained personal data in connection with a demand ... or when having made a decision not to make a correction etc., inform a principal without delay to that effect (including, when having made a correction etc., the contents thereof).
FDA CSUCI	D2g	Audit trails or other security methods used to capture electronic record activities should describe when, by whom, and the reason changes were made to the electronic record.
EMA eTMF Guideline	4.1.2e	The primary eTMF is a system for managing documents that should contain the controls listed below: an audit trail in place to identify date/time/user details for creation and/or uploading deletion of and changes to a document (explanation of the deletion or modification, if necessary);
EU Annex 11	9	Consideration should be given, based on a risk assessment, to building into the system the creation of a record of all GMP-relevant changes and deletions (a system generated "audit trail"). For change or deletion of GMP-relevant data the reason should be documented. Audit trails need to be available and convertible to a generally intelligible form and regularly reviewed.
EU Clinical Trials Regulation 536 2014	58f	Any alteration to the content of the clinical trial master file shall be traceable.
FDA EHR Guidance	V.B.3	Audit trails are available to track changes to data.

FDA EHR Guidance	V.C.2.b	Modified and corrected data elements should have data element identifiers that reflect the date, time, data originator, and the reason for the change.
FDA and MHRA Data Integrity Discussions	P3a	Audit trails for data entry should have an automatic function to show what data element was changed, what the change was, who changed it, when and why it was changed, and not obscure the original entry and any previous changes.
EU GDPR	Article 19	The controller shall communicate any rectification or erasure of personal data or restriction of processing carried out in accordance with Articles 16, 17(1) and 18 to each recipient to whom the personal data have been disclosed.
ICH GCP	4.9.0	The investigator/institution should maintain adequate and accurate source documents and trial records that include all pertinent observations on each of the site's trial subjects. Source data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry, and should be explained if necessary (e.g., via an audit trail).
ICH GCP	4.9.3	Any change or correction to a CRF should be dated, initialed, and explained (if necessary) and should not obscure the original entry (i.e. an audit trail should be maintained); this applies to both written and electronic changes or corrections (see 5.18.4(n)). Sponsors should provide guidance to investigators and/or the investigators' designated representatives on making such corrections. Sponsors should have written procedures to assure that changes or corrections in CRFs made by sponsor's designated representatives are documented, are necessary, and are endorsed by the investigator. The investigator should retain records of the changes and corrections.
JPMA EDC Supplement	1.4c	Ensure that the systems are so designed as to permit data correction in such a way that the data correction are documented and that all records of correction of entered data remain undeleted as logs distinguishable to the inputter as well as to the corrector (i.e. to maintain audit trail, input trail, and edit trail);
NMPA Clinical Trial DM Guide	3.3.2.a	CRF data for any changes or correction should be dated and signed name and explain why (if required), and should make the original records are still visible.
NMPA Clinical Trial DM Guide	3.3.2.b	Inspection of clinical trial data track (Audit Trail), from the first data entry so that every change, delete or add, must be retained in the clinical trials database system to ensure that the data from the original data to declare the whole process transparency. Inspection should include changing tracks the date, time, change the people, change reasons, the data value before the change, the changed data values. This inspection trajectory of system protection, does not allow any artificial modification and editing. Inspection records should be archived and trajectory queries.

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Regulatory mapping for eCF Requirement ID C07

Audit trail information is readable and readily available.

Regulation	Paragraph	Description
FDA 21 CFR Part 11	10b	(b) The ability to generate accurate and complete copies of records in both human readable and electronic form suitable for inspection, review, and copying by the agency. Persons should contact the agency if there are any questions regarding the ability of the agency to perform such review and copying of the electronic records.
FDA 21 CFR Part 11	10e	(e) Use of secure, computer-generated, time-stamped audit trails to independently record the date and time of operator entries and actions that create, modify, or delete electronic records. Record changes shall not obscure previously recorded information. Such audit trail documentation shall be retained for a period at least as long as that required for the subject electronic records and shall be available for agency review and copying.
Japanese APPI	Article 29.3	A personal information handling business operator shall, when having made a correction etc. on a whole or part of the contents of the retained personal data in connection with a demand ... or when having made a decision not to make a correction etc., inform a principal without delay to that effect (including, when having made a correction etc., the contents thereof).
PMDA EDC Management Sheet version 2	66	Ensuring the readability of retained information throughout the conduct of the clinical trial.
PMDA EDC Management Sheet version 2	68	Securing of the visual readability of stored information post completion of the clinical trial.
EMA eSource Reflection Paper	Topic 2d	An audit trail should be maintained as part of the source documents for the original creation and subsequent modification of all source data. The maintenance of an audit trail is essential to ensure that changes to the data are traceable. Secure, computer-generated, time-stamped audit trails (or alternative methods that fulfil the audit trail requirements) should be used to independently record the date and time of operator entries and actions that create, modify, or delete electronic records.

Such audit trail documentation should be retained as long as the subject electronic records. Audit trails need to be readable and changes to audit trail data should be prevented by the system. The responsible investigators, sponsors and inspectors should be able to review the audit trail. The audit trail will record changes made as a result of data queries or a clarification process. The clarification process for data entered by trial subjects should be documented and it should be clearly stated where changes to data entered by subjects will not be made.

EMA eTMF Guideline	4.2b	The sponsor and/or investigator/institution should implement risk-based quality checks (QC) or review processes to ensure the TMF is being maintained up-to-date and that all essential documents are appropriately filed in the TMF. Areas to consider during QC and review include the following: - review of the audit trail (for eTMF).
EMA IRT Reflection Paper	2.2.3g	A readily accessible audit trail - audit trails should be available for all data including any alterations to the data either as a result of interacting with the system or manual interventions.
PMDA ERES (Japan)	3.1.2	Readability of electromagnetic records The contents of electromagnetic records shall be output (output to display, output to paper and copy to electronic storage media) as human readable format.
PMDA ERES (Japan)	3.1.3	Storability electromagnetic records Electromagnetic records shall be maintained with keeping its authenticity and readability.
EU Directive 2005 28	2.4.17	The sponsor and the investigator shall retain the essential documents relating to a clinical trial for at least five years after its completion. They shall retain the documents for a longer period, where so required by other applicable requirements or by an agreement between the sponsor and the investigator. Essential documents shall be archived in a way that ensures that they are readily available, upon request, to the competent authorities. The medical files of trial subjects shall be retained in accordance with national legislation and in accordance with the maximum period of time permitted by the hospital, institution or private practice.
EU Clinical Trials Regulation 536 2014	58f	Any alteration to the content of the clinical trial master file shall be traceable.
FDA and MHRA Data Integrity Discussions	P3b	It is important that audit trails can be easily accessed and reviewed during the study, as part of a dynamic system, and once the data are archived, which may be in a static format.
FDA and MHRA Data Integrity Discussions	P9a	Audit trails should be available to allow reconstruction of all changes to the study data.

EU GDPR	Article 28h	(Processor) makes available to the controller all information necessary to demonstrate compliance with the obligations laid down in this Article and allow for and contribute to audits, including inspections, conducted by the controller or another auditor mandated by the controller.
JPMA EDC Guidance	4.1.1.3.6g	The ability to confirm the audit trail on the display by the investigator.
JPMA EDC Supplement	1.4c	Ensure that the systems are so designed as to permit data correction in such a way that the data correction are documented and that all records of correction of entered data remain undeleted as logs distinguishable to the inputter as well as to the corrector (i.e. to maintain audit trail, input trail, and edit trail);
NMPA Clinical Trial DM Guide	5.13.b	Ensure data accessibility refers to the user when needed, such as login and retrieve data from, and the data in the database can be transmitted in a timely manner as needed.
NMPA PISS	7.4	Personal information controllers should provide personal information subjects with access to the following information: a) the personal information or type of information it holds about the subject; b) the source of the above personal information and the purpose for which it was used; c) The identity or type of the third party who has obtained the above personal information.

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Regulatory mapping for eCF Requirement ID C08

System does not allow new audit trail information to over-write existing (previous) information and cannot be altered without detection.

Regulation	Paragraph	Description
FDA 21 CFR Part 11	10e	(e) Use of secure, computer-generated, time-stamped audit trails to independently record the date and time of operator entries and actions that create, modify, or delete electronic records. Record changes shall not obscure previously recorded information. Such audit trail documentation shall be retained for a period at least as long as that required for the subject electronic records and shall be available for agency review and copying.
FDA 21 CFR Part 11 Q&A	Q20b	Modified and corrected data elements should have data element identifiers that reflect the date, time, and data originator and the reason for the change. Modified and corrected data should not obscure previous entries.
FDA CSUCI	D2h	Original information should not be obscured though the use of audit trails or other security measures used to capture electronic record activities.
EMA eSource Reflection Paper	Topic 2d	An audit trail should be maintained as part of the source documents for the original creation and subsequent modification of all source data. The maintenance of an audit trail is essential to ensure that changes to the data are traceable. Secure, computer-generated, time-stamped audit trails (or alternative methods that fulfil the audit trail requirements) should be used to independently record the date and time of operator entries and actions that create, modify, or delete electronic records. Such audit trail documentation should be retained as long as the subject electronic records. Audit trails need to be readable and changes to audit trail data should be prevented by the system. The responsible investigators, sponsors and inspectors should be able to review the audit trail. The audit trail will record changes made as a result of data queries or a clarification process. The clarification process for data entered by trial subjects should be documented and it should be clearly stated where changes to data entered by subjects will not be made.
EU Annex 11	9	Consideration should be given, based on a risk assessment, to building

into the system the creation of a record of all GMP-relevant changes and deletions (a system generated "audit trail"). For change or deletion of GMP-relevant data the reason should be documented. Audit trails need to be available and convertible to a generally intelligible form and regularly reviewed.

EU Clinical Trials Regulation 536 2014	58f	Any alteration to the content of the clinical trial master file shall be traceable.
FDA EHR Guidance	V.C.2.c	Modified and corrected data should not obscure previous entries.
FDA eSource Guidance	A3	The eCRF should include the capability to record who entered or generated the data and when it was entered or generated. Changes to the data must not obscure the original entry, and must record who made the change, when, and why.
ICH GCP	4.9.0	The investigator/institution should maintain adequate and accurate source documents and trial records that include all pertinent observations on each of the site's trial subjects. Source data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry, and should be explained if necessary (e.g., via an audit trail).
ICH GCP	5.5.3c	When using electronic trial data handling and/or remote electronic trial data systems, the sponsor should: c) Ensure that the systems are designed to permit data changes in such a way that the data changes are documented and that there is no deletion of entered data (i.e. maintain an audit trail, data trail, edit trail).
ICH GCP	5.5.4	If data are transformed during processing, it should always be possible to compare the original data and observations with the processed data.
JPMA EDC Guidance	4.1.1.1f	Audit trail shall be recorded automatically. (i.e. The EDC system is designed to permit data changes in such a way that the data changes are documented and that there is no deletion of entered data.)
JPMA EDC Guidance	4.1.1.1g	Audit trail shall not be modified by anyone.
JPMA EDC Guidance	4.1.1.2b	The ability to prevent alteration, divulgation and repudiation of fact of operation.
JPMA EDC Supplement	1.4c	Ensure that the systems are so designed as to permit data correction in such a way that the data correction are documented and that all records of correction of entered data remain undeleted as logs distinguishable to the inputter as well as to the corrector (i.e. to maintain audit trail, input trail, and edit trail);
JPMA EDC	1.5.1.1c	An audit trail can be retained automatically.

Supplement		Together with the entered data, the date and time of entry and the person who enters the data can be recorded. If the system is also designed to permit data correction, then the data corrections are documented and that all records of correction of entered data remain undeleted as unchangeable logs distinguishable to the inputter as well as to the corrector, automatically.
MHRA GXP Data Integrity Guidance	6.13c	Audit trails (identified by risk assessment as required) should be switched on. Users should not be able to amend or switch off the audit trail. Where a system administrator amends, or switches off the audit trail a record of that action should be retained.
NMPA Clinical Trial DM Guide	3.3.1.d	Clinical trial data management system validation include the following aspects: - Ensure data integrity, including the prevention of deleted or lost data
NMPA Clinical Trial DM Guide	3.3.2.a	CRF data for any changes or correction should be dated and signed name and explain why (if required), and should make the original records are still visible.
NMPA Clinical Trial DM Guide	3.3.2.b	Inspection of clinical trial data track (Audit Trail), from the first data entry so that every change, delete or add, must be retained in the clinical trials database system to ensure that the data from the original data to declare the whole process transparency. Inspection should include changing tracks the date, time, change the people, change reasons, the data value before the change, the changed data values. This inspection trajectory of system protection, does not allow any artificial modification and editing. Inspection records should be archived and trajectory queries.
NMPA PISS	10.5d	Unauthorized access, tampering or deletion of audit records should be prevented.

Regulatory mapping for eCF Requirement ID C10

There is a process to ensure that eCRF entries and any subsequent modifications are reviewed and approved by the investigator.

Regulation	Paragraph	Description
FDA EHR Guidance	V.C.2.d	Clinical investigators should review and electronically sign the completed eCRF for each study participant before data are archived or submitted to FDA.
FDA EHR Guidance	V.C.2.e	If modifications are made to the eCRF after the clinical investigator has already signed the eCRF, the changes should be reviewed and approved by the clinical investigator.
FDA eSource Guidance	B1a	<p>Clinical Investigator(s) Review and Electronic Signature</p> <p>To comply with the requirement to maintain accurate case histories clinical investigator(s) should review and electronically sign the completed eCRF for each subject before the data are archived or submitted to FDA. Use of electronic signatures must comply with part 11 (21 CFR part 11).</p>
FDA eSource Guidance	B2	<p>Modifications and Corrections During Clinical Investigator(s) Review of the eCRF</p> <p>To comply with the requirement to maintain accurate case histories, data elements might call for modification or correction during clinical investigator(s) review. Either the clinical investigator(s) or an originator can enter the revised data element. Modified and/or corrected data elements must have data element identifiers that reflect the date, time, originator, and reason for the change, and must not obscure previous entries.</p> <p>If changes are made to the eCRF after the clinical investigator(s) has already signed, the changes should be reviewed and electronically signed by the clinical investigator(s).</p>
FDA and MHRA Data Integrity Discussions	P9b	Sponsors and clinical investigators should ensure that all changes to the investigator's study data are documented and authorized by investigators or delegated study personnel at the site.
FDA and MHRA Data Integrity Discussions	P9c	Any changes to study data entered into the EDC system should also be authorized by the investigator.

ICH GCP	4.9.0	The investigator/institution should maintain adequate and accurate source documents and trial records that include all pertinent observations on each of the site's trial subjects. Source data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry, and should be explained if necessary (e.g., via an audit trail).
ICH GCP	4.9.1	The investigator should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.
JPMA EDC Guidance	4.1.1.3.6d	The investigator shall check and confirm the created or modified electronic CRF and put electronic or handwriting signature on it.
JPMA EDC Guidance	4.1.1.3.6f	If there are some amendments after investigator signed, the investigator shall check and confirm the modified electronic CRF and put electronic or handwriting signature on it again.
JPMA EDC Guidance	4.1.1.4e	Clearly identified signature time and intended electronic records and if electronic records are modified, electronic signature shall be executed on the modified records.
MHRA GXP Data Integrity Guidance	6.15	The approach to reviewing specific record content, such as critical data and metadata, cross-outs (paper records) and audit trails (electronic records) should meet all applicable regulatory requirements and be risk-based.
NMPA Clinical Trial DM Guide	5.6	Erroneous data in the data cleaning process will be corrected. Data sheets or data verification challenge file as a data record of the changes must be signed by the investigator.

Regulatory mapping for eCF Requirement ID C11

There is a system and/or process to ensure the investigator has control of and continuous access to their source data reported to the sponsor and the sponsor does not have exclusive control of those data.

Regulation	Paragraph	Description
EMA eSource Reflection Paper	Topic 3a	<p>The investigator should maintain the original source document or a certified copy.</p> <p>Source data should only be modified with the knowledge or approval of the investigator.</p> <p>The sponsor should not have exclusive control of a source document. The fundamentals of clinical research include that patient rights, safety and well-being are the most important considerations and the integrity of the reported data must be confirmable. To this end all data generated in a clinical trial relevant to patient care must be made available to the investigator at all times during and after the trial and all data held by the sponsor that has been generated in a clinical trial should be verifiable to a copy not held (or that has been held) by the sponsor.</p>
EMA eTMF Guideline	3.1a	<p>The investigator/institution is responsible for all essential documents generated by the investigator/institution and should therefore have control of them at all times. In cases in which the investigator is employed by an institution that is the trial sponsor, the sponsor may delegate the task for maintaining all or part of the sponsor TMF to the investigator. In this circumstance, it is possible to combine the delegated part of the sponsor TMF and investigator TMF for that investigator/institution, which avoids the duplication of documentation; however, the responsibility for the sponsor TMF remains with the sponsor. The same applies when the investigator and the sponsor are the same person. When there is co-sponsorship of a trial, there should be arrangements in place for the maintenance of the TMF based upon the responsibilities that each co- sponsor holds.</p>
EMA eTMF Guideline	4.1.3a	<p>A complete investigator TMF should be available before, during and after the trial, and accessible under the control of the investigator/institution, independent from the sponsor.</p>
EMA eTMF Guideline	4.1.3d	<p>The uploading of any investigator/institution-generated essential documents onto a sponsor/CRO-maintained eTMF system bears the risk that the investigator has no control of and no continuous access to</p>

its documents. If an eTMF is to be used for such documents, the contractual arrangements for the system and the hosting of the data should identify the investigator/institution, as owner of/responsible party for these documents.

EMA eTMF Guideline	4.1.3e	The investigator/institution is responsible for the suitability of the investigator TMF. Regardless of what arrangements are put in place for an eTMF, these should ensure that this responsibility can be fulfilled and that the investigator/institution maintains continuous access to and control of the files and their documents. When a third party eTMF is used, there should be assurance that the investigator/institution can fulfil their responsibility.
EMA eTMF Guideline	6.2	The investigator/institution should make the sponsor aware of the storage arrangements for their essential documents and conversely the sponsor should inform the investigator/institution in writing of the need for document archiving. The ultimate responsibility for the documents to be retained by the investigator/institution resides with the investigator/institution. If the investigator/institution becomes unable to be responsible for their essential documents (e.g. relocation, retirement, closure of institution, etc.) the sponsor agreement with the investigator/institution should stipulate that the sponsor is notified (preferably upfront) in writing of this change and informed to whom the responsibility will be/has been transferred. The new individual/institution responsible should be independent of the sponsor and should be free of any conflict of interest.
FDA EHR Guidance	V.C.2.a	After data are transmitted to the eCRF, the clinical investigator or delegated study personnel should be the only individuals authorized to make modifications or corrections to the data.
FDA and MHRA Data Integrity Discussions	10a	The use of a third party to prevent sponsor sole control would be undermined if the third party transfers the data to the sponsor for final distribution to investigators and the third party deletes the data.
FDA and MHRA Data Integrity Discussions	P10	The investigator should control all source data, CRFs, and other site essential documents as the sponsor should not have exclusive control of the study data.
FDA and MHRA Data Integrity Discussions	P9d	Sponsors should not be making edits in the eCRF without the investigator's authorization.
ICH GCP	4.9.4	The investigator/institution should maintain the trial documents as specified in Essential Documents for the Conduct of a Clinical Trial (see 8.) and as required by the applicable regulatory requirement(s). The investigator/institution should take measures to prevent accidental or premature destruction of these documents.
ICH GCP	8.1	ADDENDUM The sponsor and investigator/institution should maintain a record of the location(s) of their respective essential documents including source

documents. The storage system used during the trial and for archiving (irrespective of the type of media used) should provide for document identification, version history, search, and retrieval.

Essential documents for the trial should be supplemented or may be reduced where justified (in advance of trial initiation) based on the importance and relevance of the specific documents to the trial.

The sponsor should ensure that the investigator has control of and continuous access to the CRF data reported to the sponsor. The sponsor should not have exclusive control of those data.

When a copy is used to replace an original document (e.g., source documents, CRF), the copy should fulfill the requirements for certified copies.

The investigator/institution should have control of all essential documents and records generated by the investigator/institution before, during, and after the trial.

JPMA EDC Supplement	1.2a	...it is required to prepare necessary equipment (e.g. devices) and environment (e.g. internet line, telephone line) for data entry by subjects, make operational procedures for transmitting subject data to the operational database, operational procedures for providing the collected subject data to investigators and sponsors, and also procedures for data retention after completion of the clinical trial and location of storage.
JPMA EDC Supplement	1.2b	The entered data are stored in the vendor server as source documents. During this process, the vendor ensures reliability of the source documents as a trusted third party.
JPMA EDC Supplement	1.2c	During the trial, both the site and sponsor representatives can view the ePRO data in the vendor server via web as necessary.
JPMA EDC Supplement	1.5.2b	If it is necessary to evaluate safety and efficacy and/or to conduct monitoring with the data collected by an ePRO system, such data should be viewable at any time throughout the trial period.
JPMA EDC Supplement	1.5.3	Throughout the specified period of record keeping, the authenticity and readability of the electromagnetic records must be ensured.

Regulatory mapping for eCF Requirement ID C13

Controls exist such that the ability to change system settings is limited to authorized personnel.

Regulation	Paragraph	Description
FDA 21 CFR Part 11	10d	(d) Limiting system access to authorized individuals.
FDA 21 CFR Part 11	10g	(g) Use of authority checks to ensure that only authorized individuals can use the system, electronically sign a record, access the operation or computer system input or output device, alter a record, or perform the operation at hand.
FDA 21 CFR Part 11	10k	(k) Use of appropriate controls over systems documentation including: (1) Adequate controls over the distribution of, access to, and use of documentation for system operation and maintenance. (2) Revision and change control procedures to maintain an audit trail that documents time-sequenced development and modification of systems documentation.
FDA CSUCI	D2e	Should it be decided that audit trails or other appropriate security measures are needed to ensure electronic record integrity, personnel who create, modify, or delete electronic records should not be able to modify the documents or security measures used to track electronic record changes.
FDA CSUCI	D3b	The ability to change the date or time should be limited to authorized personnel, and such personnel should be notified if a system date or time discrepancy is detected.
EU Clinical Trials Regulation 536 2014	58f	Any alteration to the content of the clinical trial master file shall be traceable.
MHRA GXP Data Integrity Guidance	5.1a	At the point of use, having access to appropriately controlled/synchronised clocks for recording timed events to ensure reconstruction and traceability, knowing and specifying the time zone where this data is used across multiple sites.
NMPA Clinical Trial DM Guide	3.3.3.a	Clinical trial data management system must have a sound management system privileges. Paper-based or electronic data

management are needed to develop SOPs for access control and management. Data management system for different people with different permissions or roles that only authorized personnel are allowed to operate (record, modify, etc.), and shall take appropriate methods to monitor and prevent non-licensed person operation.

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Regulatory mapping for eCF Requirement ID C14

System allows audit trail to utilize a standard time such that the local time can be derived.

Regulation	Paragraph	Description
FDA 21 CFR Part 11	10e	(e) Use of secure, computer-generated, time-stamped audit trails to independently record the date and time of operator entries and actions that create, modify, or delete electronic records. Record changes shall not obscure previously recorded information. Such audit trail documentation shall be retained for a period at least as long as that required for the subject electronic records and shall be available for agency review and copying.
FDA CSUCI	D3e	Computerized systems are likely to be used in multi-center clinical trials and may be located in different time zones. For systems that span different time zones, it is better to implement time stamps with a clear understanding of the time zone reference used. We recommend that system documentation explain time zone references as well as zone acronyms or other naming conventions.
EMA eTMF Guideline	4.1.2k	Metadata applied to documents should be formally defined to ensure consistency across all documents. This should include the predefined document date (e.g. date of creation) and when appropriate, time, based on standard time zone, so that the files can be displayed in chronological order.
PMDA ERES (Japan)	2.6	Audit Trail means a series of operational records with accurate time stamp (date recorded by computer automatically).
EU Annex 11	12.4	Management systems for data and for documents should be designed to record the identity of operators entering, changing, confirming or deleting data including date and time.
MHRA GXP Data Integrity Guidance	5.1a	At the point of use, having access to appropriately controlled/synchronised clocks for recording timed events to ensure reconstruction and traceability, knowing and specifying the time zone where this data is used across multiple sites.

Regulatory mapping for eCF Requirement ID C16

The system has the ability to create, maintain and apply the roles, access permissions and capabilities of each user that accesses the system, such that users have access only to those system features and functions to which they have been granted access.

Regulation	Paragraph	Description
FDA 21 CFR Part 11	10d	(d) Limiting system access to authorized individuals.
FDA 21 CFR Part 11	10g	(g) Use of authority checks to ensure that only authorized individuals can use the system, electronically sign a record, access the operation or computer system input or output device, alter a record, or perform the operation at hand.
FDA 21 CFR Part 11 Q&A	Q19	FDA does not intend to inspect each individual mobile technology used in a clinical investigation to capture, record, and transmit data directly from study participants because access controls, audit trails, and validation that would be applied would help ensure the reliability of the data.
FDA 21 CFR Part 11 Q&A	Q4a	Logical and physical access controls must be employed for electronic systems that are used in clinical investigations, particularly for systems that provide access to multiple users or that reside on networks.
Japanese APPI	Article 21	A personal information handling business operator shall, in having its employees handle personal data, exercise necessary and appropriate supervision over the employees so as to seek the security control of the personal data.
FDA CSUCI	D1a	Access must be limited to authorized individuals (21 CFR 11.10(d). This requirement can be accomplished by the following recommendations. We recommend that each user of the system have an individual account.
FDA CSUCI	D1e	The system should not allow an individual to log onto the system to provide another person access to the system.
EMA eSource Reflection Paper	Topic 3b	Source documents should be protected against unauthorized access. Source documents need to be protected in order to maintain subject confidentiality. Changes or deletion by unauthorised individuals, either

accidental or deliberate, should be prevented. Authority checks should be used, as these could ensure that only authorised individuals have access to the system, or the ability to enter or make changes to data. Records of authorisation of access to the systems, with the respective levels of access clearly documented (e.g. individual user accounts) should be maintained. Audit trails should record changes to user access rights. There should be documented training on the importance of security including the need to protect and not share passwords as well as enforcement of security systems and processes. The system users should confirm that he/she accepts responsibility for data entered using their password. Security systems should prevent unauthorised access to the computer system and to the data in the electronic record. Procedures should be in place to avoid/prevent unauthorised access when a workstation is vacated. There should be timely removal of access no longer required, or no longer permitted.

EMA eSource Reflection Paper	Topic 5a	<p>The storage of source documents should provide for their ready retrieval.</p> <p>Source documents and data should always be available when needed to authorised individuals to meet their regulatory obligations. Whilst a trial is active and after its conclusion, existing source data should be readily available to the investigator and others such as monitors, auditors and inspectors. Direct access to the system should be provided by the sponsor and/or investigator to monitors, auditors and inspectors.</p>
EMA eTMF Guideline	3.1	<p>In organising the TMF, it is essential to segregate some documents that are generated and/or held by the sponsor only, from those that are generated and/or held by the investigator/institution only (e.g. subject identification code list filed in the investigator TMF only and master randomisation list filed in the sponsor TMF only).</p>
EMA eTMF Guideline	3.1b	<p>Role-based permissions should be established for activities being undertaken, such as restricted access to files/documents (e.g. randomisation codes and unblinded adverse event data).</p>
EMA eTMF Guideline	4.1	<p>The TMF should be managed securely at all times to ensure completeness and to prevent accidental or premature loss, unauthorised alteration or destruction of documents. Access to the TMF should be based on a role and permission description that is defined by the sponsor and/or investigator/institution.</p> <p>The sponsor TMF and investigator/institution TMF may contain some information that could unblind personnel who need to remain blinded during the trial conduct. This should be appropriately controlled, e.g. storage of the documentation in another system or repository and/or by a role and permission description that is defined by the sponsor and/or investigator/institution.</p>
EMA eTMF Guideline	4.1.2a	<p>The primary eTMF is a system for managing documents that should contain the controls listed below:</p> <ul style="list-style-type: none"> user accounts; secure passwords for users.

EMA eTMF Guideline	4.1.2f	The primary eTMF is a system for managing documents that should contain the controls listed below: role-based permissions for activities being undertaken, such as restricted access to files/documents (e.g. randomisation codes and unblinded adverse event data);
EMA eTMF Guideline	4.1.3h	Remote access by sponsor or CRO personnel to the investigator TMF should only be possible to the documents where personal data that enable the data subjects to be directly identified (i.e. direct identifiers of trial subjects) is not present or has been pseudonymised.
EMA eTMF Guideline	4.2a	The sponsor and/or investigator/institution should implement risk-based quality checks (QC) or review processes to ensure the TMF is being maintained up-to-date and that all essential documents are appropriately filed in the TMF. Areas to consider during QC and review include the following: - documents only accessible according to the assigned roles and permissions.
EMA eTMF Guideline	5	Particular attention should be paid when documents are stored on electronic, magnetic, optical or other non-indelible media. In such cases suitable controls should be implemented to ensure that these documents are complete and cannot be altered without appropriate authorisation and the creation of an audit trail.
EMA eTMF Guideline	6.1a	With respect to the sponsor TMF, Article 58 of the Regulation states that the sponsor shall appoint individuals within its organisation to be responsible for archives. Access to archives shall be restricted to those individuals.
EMA IRT Reflection Paper	2.2.3a	Access permissions - personnel with these access rights at the site should be qualified for these delegated activities. These permissions should be included in the project specification. It is important that the permissions be clear with respect to their ability to see what trial medication is being taken by a subject (blinded versus unblinded). Access permissions might include but not be limited to the following staff: - pharmacy staff; - principal investigator; - site research team, including any study coordinator, research nurse or sub-investigator; - contract research associate (CRA), where applicable; - sponsor staff, including project managers, clinical supplies staff.
PMDA ERES (Japan)	3.1.1.1	Rules and procedures of maintaining securities of the system are documented and practicing them appropriately.
EU Annex 11	12.3	Creation, change, and cancellation of access authorisations should be recorded.
EU Annex 11	2	There should be close cooperation between all relevant personnel

such as Process Owner, System Owner, Qualified Persons and IT. All personnel should have appropriate qualifications, level of access and defined responsibilities to carry out their assigned duties.

EU Clinical Trials Regulation 536 2014	58d	The sponsor shall appoint individuals within its organisation to be responsible for archives. Access to archives shall be restricted to those individuals.
FDA EHR Guidance	V.B.1	Policies and processes for the use of EHR systems at the clinical investigation site are in place, and there are appropriate security measures employed to protect the study data.
FDA EHR Guidance	V.B.2	Access to electronic systems is limited to authorized users.
FDA Electronic Informed Consent Q&A	Q10a	The electronic system that supports the eIC must be secure with restricted access (see 21 CFR 11.10 and 11.30) and should include methods to ensure confidentiality regarding the subjects identity, study participation, and personal information after informed consent has been obtained.
FDA and MHRA Data Integrity Discussions	P9e	Because audit trails rely on username assignment, individuals should work only under their own username and password, or other access controls, and not share these with others.
EU GDPR	Article 25.2	Controller shall implement appropriate technical and organizational measures for ensuring that, by default, only personal data which are necessary for each specific purpose are processed.
EU GDPR	Article 29	The processor and any person acting under the authority of the controller or of the processor, who has access to personal data, shall not process those data except on instructions from the controller, unless required to do so by Union or Member State law.
EU GDPR	Article 5.1c	Personal data shall be adequate, relevant and limited to what is necessary in relation to the purposes for which they are processed (data minimisation).
USA HIPAA	164.304a	Availability means the property that data or information is accessible and useable upon demand by an authorized person.
USA HIPAA	164.306a3	Protect against any reasonably anticipated uses or disclosures of such information that are not permitted or required under subpart E of this part.
USA HIPAA	164.308a3iiA	Implement procedures for the authorization and/or supervision of workforce members who work with electronic protected health information or in locations where it might be accessed.
USA HIPAA	164.514d2	(i) A covered entity must identify: (A) Those persons or classes of persons, as appropriate, in its workforce who need access to protected health information to carry out

their duties; and
 (B) For each such person or class of persons, the category or categories of protected health information to which access is needed and any conditions appropriate to such access.
 (ii) A covered entity must make reasonable efforts to limit the access of such persons or classes identified in paragraph (d)(2)(i)(A) of this section to protected health information consistent with paragraph (d)(2)(i)(B) of this section.

ICH GCP	5.5.3b	When using electronic trial data handling and/or remote electronic trial data systems, the sponsor should: b) Maintains SOPs for using these systems. ADDENDUM The SOPs should cover system setup, installation, and use. The SOPs should describe system validation and functionality testing, data collection and handling, system maintenance, system security measures, change control, data backup, recovery, contingency planning, and decommissioning. The responsibilities of the sponsor, investigator, and other parties with respect to the use of these computerized systems should be clear, and the users should be provided with training in their use.
JPMA EDC Guidance	4.1.1.1a	User management and access rights grant are conducted according to the predetermined rule appropriately.
JPMA EDC Guidance	4.1.1.3c	The ability to detect any unauthorized access. (monitoring of access, alert, access logs).
JPMA EDC Guidance	4.1.1.4a	Employ account management rule for electronic signature, and operate it properly.
JPMA EDC Supplement	1.4d	Maintain a security system for the data;
JPMA EDC Supplement	1.4f	Prepare and maintain a list of the individuals who are authorized to make data correction;
JPMA EDC Supplement	1.5.1.1a	User management and authority setting must be appropriately undertaken, as per the pre-set rules.
JPMA EDC Supplement	3.2.1c	To establish procedure to confirm that correct authority is granted to appropriate accounts.
MHRA GXP Data Integrity Guidance	5.1d	User access rights that prevent (or audit trail, if prevention is not possible) unauthorised data amendments. Use of external devices or system interfacing methods that eliminate manual data entries and human interaction with the computerised system, such as barcode scanners, ID card readers, or printers.
MHRA GXP Data Integrity Guidance	6.16	Full use should be made of access controls to ensure that people have access only to functionality that is appropriate for their job role, and that actions are attributable to a specific individual.

NMPA Clinical Trial DM Guide	3.3.1.c	Clinical trial data management system validation include the following aspects: - System access control, and user management
NMPA Clinical Trial DM Guide	3.3.1.e	Clinical trial data management system validation include the following aspects: - Prevent unauthorized data and document changes
NMPA Clinical Trial DM Guide	3.3.3.a	Clinical trial data management system must have a sound management system privileges. Paper-based or electronic data management are needed to develop SOPs for access control and management. Data management system for different people with different permissions or roles that only authorized personnel are allowed to operate (record, modify, etc.), and shall take appropriate methods to monitor and prevent non-licensed person operation.
NMPA PISS	4f	Ensuring security principles - have the security capabilities that match the security risks you face, and take adequate management measures and techniques to protect the confidentiality, integrity, and availability of your personal information.
PRC Electronic Signature Law	13a	Electronic signatures are considered reliable, when all of the following conditions are satisfied: (1) Data that create electronic signatures are owned only by the signer when they are being used for electronic signatures; (2) Data that create electronic signatures may only be controlled by the electronic signer at the time he is creating the signatures

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Regulatory mapping for eCF Requirement ID C17

There is a policy and training that instructs users not to share their access mechanisms (e.g. usernames and passwords, or access keys) or to leave their account open for others to use.

Regulation	Paragraph	Description
FDA 21 CFR Part 11	200a	<p>(a) Electronic signatures that are not based upon biometrics shall:</p> <p>(1) Employ at least two distinct identification components such as an identification code and password.</p> <p>(i) When an individual executes a series of signings during a single, continuous period of controlled system access, the first signing shall be executed using all electronic signature components; subsequent signings shall be executed using at least one electronic signature component that is only executable by, and designed to be used only by, the individual.</p> <p>(ii) When an individual executes one or more signings not performed during a single, continuous period of controlled system access, each signing shall be executed using all of the electronic signature components.</p> <p>(2) Be used only by their genuine owners;</p>
FDA 21 CFR Part 11 Q&A	Q18c	When electronic thumbprints or other biometrics are used in place of username and password combinations, controls must be designed to ensure that the biometric identifier cannot be used by anyone other than the identifier's owner.
FDA CSUCI	D1d	Individuals should work only under their own password or other access key and not share these with others.
PMDA EDC Management Sheet version 2	42	Procedures for maintaining of security: Policy / Guidance for maintaining security
PMDA EDC Management Sheet version 2	44	Procedures for maintaining of security: Written procedures for users how to use the ID/password
PMDA EDC Management Sheet version 2	45	Procedures for maintaining of security: Written procedures for users how to train users

EMA eSource Reflection Paper	Topic 3b	Source documents should be protected against unauthorized access. Source documents need to be protected in order to maintain subject confidentiality. Changes or deletion by unauthorised individuals, either accidental or deliberate, should be prevented. Authority checks should be used, as these could ensure that only authorised individuals have access to the system, or the ability to enter or make changes to data. Records of authorisation of access to the systems, with the respective levels of access clearly documented (e.g. individual user accounts) should be maintained. Audit trails should record changes to user access rights. There should be documented training on the importance of security including the need to protect and not share passwords as well as enforcement of security systems and processes. The system users should confirm that he/she accepts responsibility for data entered using their password. Security systems should prevent unauthorised access to the computer system and to the data in the electronic record. Procedures should be in place to avoid/prevent unauthorised access when a workstation is vacated. There should be timely removal of access no longer required, or no longer permitted.
EMA eTMF Guideline	4.1.2a	The primary eTMF is a system for managing documents that should contain the controls listed below: user accounts; secure passwords for users.
PMDA ERES (Japan)	4.2	Each electronic signature shall be unique to one individual and shall not be reused by, or reassigned to, anyone else.
EU Annex 11	12.1	Physical and/or logical controls should be in place to restrict access to computerised system to authorised persons. Suitable methods of preventing unauthorised entry to the system may include the use of keys, pass cards, personal codes with passwords, biometrics, restricted access to computer equipment and data storage areas.
FDA Electronic Informed Consent Q&A	Q6b	Electronic signatures based on biometrics must be designed to ensure that they cannot be used by anyone other than their genuine owners.
EU GDPR	Article 25.2	Controller shall implement appropriate technical and organizational measures for ensuring that, by default, only personal data which are necessary for each specific purpose are processed.
EU GDPR	Article 32.2	In assessing the appropriate level of security account shall be taken in particular of the risks that are presented by processing, in particular from accidental or unlawful destruction, loss, alteration, unauthorised disclosure of, or access to personal data transmitted, stored or otherwise processed.
USA HIPAA	164.308a5i	Implement a security awareness and training program for all members of its workforce (including management).
USA HIPAA	164.308a5iiD	Procedures for creating, changing, and safeguarding passwords.

JPMA EDC Guidance	4.1.1.1c	Operation shall be adequate and compliance shall be ensured by training. (i.e. Prevent from spoofing, stealing password and so on.)
JPMA EDC Guidance	4.1.1.2c	The ability to prevent unauthorized access. (take a measure of malware and security hole, management and prevent of leaking of ID and password, user management).
JPMA EDC Supplement	1.4d	Maintain a security system for the data;
NMPA Clinical Trial DM Guide	3.3.3.c	The electronic management system, user can only work with their own password, the password can not be shared, nor let other people access to login
NMPA PISS	10.4e	Personal information security professional training and assessment should be carried out on relevant personnel in personal information processing positions on a regular basis (at least once a year) or in the event of major changes in the privacy policy to ensure that relevant personnel are proficient in privacy policies and related procedures.
PRC Electronic Signature Law	13a	Electronic signatures are considered reliable, when all of the following conditions are satisfied: (1) Data that create electronic signatures are owned only by the signer when they are being used for electronic signatures; (2) Data that create electronic signatures may only be controlled by the electronic signer at the time he is creating the signatures
PRC Electronic Signature Law	15	The signer of electronic signatures shall keep custody of the data that create the electronic signatures. If the electronic signer learns that the data that created the electronic signatures are already deciphered or might be deciphered, he shall inform every involved party in a timely manner and terminate the use of the data.

Regulatory mapping for eCF Requirement ID C18

The monitor, auditor and inspector can within reasonable timeframe obtain direct access to trial subjects records in order to perform their regulatory duties.

Regulation	Paragraph	Description
FDA 21 CFR Part 11 Q&A	Q8	FDA may request to review and copy records in a human readable form using electronic system hardware.
FDA 21 CFR Part 312	58a	FDA inspection. A sponsor shall upon request from any properly authorized officer or employee of the Food and Drug Administration, at reasonable times, permit such officer or employee to have access to and copy and verify any records and reports relating to a clinical investigation conducted under this part.
FDA 21 CFR Part 312	68	An investigator shall upon request from any properly authorized officer or employee of FDA, at reasonable times, permit such officer or employee to have access to, and copy and verify any records or reports made by the investigator pursuant to 312.62. The investigator is not required to divulge subject names unless the records of particular individuals require a more detailed study of the cases, or unless there is reason to believe that the records do not represent actual case studies, or do not represent actual results obtained.
21 CFR Part 812	145b	Records inspection. A sponsor, IRB, or investigator, or any other person acting on behalf of such a person with respect to an investigation, shall permit authorized FDA employees, at reasonable times and in a reasonable manner, to inspect and copy all records relating to an investigation.
21 CFR Part 812	145c	Records identifying subjects. An investigator shall permit authorized FDA employees to inspect and copy records that identify subjects, upon notice that FDA has reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the investigator to the sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading.
Japanese APPI	Article 40.1	The Personal Information Protection Commission may ... require a personal information handling business operator ... to submit necessary information or material relating to the handling of personal information ..., or have its officials enter a business office or other

necessary place of a personal information handling business operator etc., inquire about the handling of personal information etc., or inspect a book, document and other property.

EMA eSource Reflection Paper	6.3.2	The monitor, auditor and inspector should have direct access to trial subjects entire electronic health records whilst the trial site staff should ensure that the medical records of patients who are not trial subjects should not be accessible.
EMA eTMF Guideline	2	The TMF should provide for document identification, version history, search and retrieval; also, as stated in both Directive 2005/28/EC (Article 17) and the Regulation (Articles 57 and 58) it shall be archived in a way that ensures that it is readily available and directly accessible upon request, to the competent authorities of the Member States.
EMA eTMF Guideline	3.2c	The clinical trial contract/agreement and other documents and procedures agreed between all parties should outline the arrangements for the TMF in some detail, such as: - how the TMF would be made available to the competent authorities; - arrangements for oversight of the TMF performed by the sponsor and how this would be achieved (e.g. audit reports and/or monitoring).
EMA eTMF Guideline	4.1.1	At all times the storage area for the TMF documents (such as paper or electronic media archives and server rooms) should be appropriate to maintain the documents in a manner that they remain complete and legible throughout the trial conduct and the required period of retention and can be made available to the competent authorities of the Member States, upon request.
EMA eTMF Guideline	4.2c	In addition, the sponsor should ensure the TMF is readily available and directly accessible to the competent authority, e.g. for inspection purposes.
EMA Q&A eTMF 1	b	Inspectors/auditors should have direct access to the e-TMF and the documents held in the e-TMF (the live system, not a copy) to allow direct searching.
EU Clinical Trials Regulation 536 2014	57	The clinical trial master file shall at all times contain the essential documents relating to that clinical trial which allow verification of the conduct of a clinical trial and the quality of the data generated, taking into account all characteristics of the clinical trial, including in particular whether the clinical trial is a low-intervention clinical trial. It shall be readily available, and directly accessible upon request, to the Member States.
EU Clinical Trials Regulation 536 2014	58b	The content of the clinical trial master file shall be archived in a way that ensures that it is readily available and accessible, upon request, to the competent authorities.
FDA EHR Guidance	V.2	Sponsors should also ensure that study monitors have suitable access to all relevant subject information pertaining to a clinical investigation, as appropriate.

FDA EHR Guidance	VI.1	All relevant information in the EHR pertaining to the clinical investigation must be made available to FDA for review upon request.
FDA Electronic Informed Consent Q&A	Q16	FDA regulations require that FDA be granted access to records and reports made by the investigator, including site-specific versions of the eIC, the materials submitted to IRBs for review and approval, all amendments to the site-specific eICs, and all subject-specific signed eICs.
FDA eSource Guidance	A2c	Transcription of Data From Paper or Electronic Sources to the eCRF Data elements can be transcribed into the eCRF from paper or electronic source documents. The authorized person transcribing the data from the source documents is regarded as the data originator. For these data elements, the electronic or paper documents from which the data elements are transcribed are the source. These data must be maintained by the clinical investigator(s) and available to an FDA inspector if requested (e.g., an original or certified copy of a laboratory report, instrument printout, progress notes of the physician, the study subjects hospital chart(s), nurses notes).
FDA eSource Guidance	A2d	Direct Transmission of Data From the Electronic Health Record to the eCRF Data elements originating in an EHR can be transmitted directly into the eCRF automatically. Unlike a direct transmission to an eCRF from instruments or medical devices, EHRs can use intervening processes (e.g., algorithms for the selection of the appropriate data elements). For this reason the EHR is the source, and the pertinent data for the subjects in the clinical study should be made available for review during an FDA inspection. The ability of sponsors and/or monitors to access health records of study subjects in clinical information systems relevant to the clinical investigation should not differ from their ability to access health records recorded on paper.
EU GDPR	Article 28h	(Processor) makes available to the controller all information necessary to demonstrate compliance with the obligations laid down in this Article and allow for and contribute to audits, including inspections, conducted by the controller or another auditor mandated by the controller.
USA HIPAA	164.512d1	A covered entity may disclose protected health information to a health oversight agency for oversight activities authorized by law...
ICH GCP	4.9.7	Upon request of the monitor, auditor, IRB/IEC, or regulatory authority, the investigator/institution should make available for direct access all requested trial related records.
ICH GCP	5.1.2	The sponsor is responsible for securing agreement from all involved parties to ensure direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by domestic and foreign regulatory authorities.

JPMA EDC Guidance	4.1.1.3.5	In the institutes, authority and investigators are able to check the data of CRF at anytime within the retention period.
NMPA PISS	7.1c	Separate roles should be set for the roles of security managers, data operators, and auditors.

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Regulatory mapping for eCF Requirement ID C19

System limits the number of log-in attempts and records unsuccessful attempts.

Regulation	Paragraph	Description
Japanese APPI	Article 20	A personal information handling business operator shall take necessary and appropriate action for the security control of personal data including preventing the leakage, loss or damage of its handled personal data.
FDA CSUCI	D1c	The system should be designed to limit the number of log-in attempts and to record unauthorized access log-in attempts.
EMA eSource Reflection Paper	Topic 3b	Source documents should be protected against unauthorized access. Source documents need to be protected in order to maintain subject confidentiality. Changes or deletion by unauthorized individuals, either accidental or deliberate, should be prevented. Authority checks should be used, as these could ensure that only authorized individuals have access to the system, or the ability to enter or make changes to data. Records of authorization of access to the systems, with the respective levels of access clearly documented (e.g. individual user accounts) should be maintained. Audit trails should record changes to user access rights. There should be documented training on the importance of security including the need to protect and not share passwords as well as enforcement of security systems and processes. The system users should confirm that he/she accepts responsibility for data entered using their password. Security systems should prevent unauthorized access to the computer system and to the data in the electronic record. Procedures should be in place to avoid/prevent unauthorized access when a workstation is vacated. There should be timely removal of access no longer required, or no longer permitted.
EU GDPR	Article 33.5	The controller shall document any personal data breaches, comprising the facts relating to the personal data breach, its effects and the remedial action taken. That documentation shall enable the supervisory authority to verify compliance with this Article.
USA HIPAA	164.308a5iiC	Procedures for monitoring log-in attempts and reporting discrepancies.
JPMA EDC Guidance	4.1.1.2c	The ability to prevent unauthorized access. (take a measure of malware and security hole, management and prevent of leaking of ID

and password, user management).

JPMA EDC
Supplement

1.4d

Maintain a security system for the data;

JPMA EDC
Supplement

1.5.1.2b

The system must be designed to prevent and/or detect unauthorized access.
For example, the system has a function that demands an access code in case of loss of a device, or a specific equipment or program to download data from the device, etc.

NMPA PISS

10.3

Personal information controllers should establish appropriate data security capabilities and implement necessary management and technical measures to prevent leakage, damage, and loss of personal information in accordance with the requirements of relevant national standards.

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Regulatory mapping for eCF Requirement ID C20

System records and notifies a system administrator of unauthorized access log-in attempts.

Regulation	Paragraph	Description
FDA 21 CFR Part 11	300d	(d) Use of transaction safeguards to prevent unauthorized use of passwords and/or identification codes, and to detect and report in an immediate and urgent manner any attempts at their unauthorized use to the system security unit, and, as appropriate, to organizational management.
Japanese APPI	Article 20	A personal information handling business operator shall take necessary and appropriate action for the security control of personal data including preventing the leakage, loss or damage of its handled personal data.
FDA CSUCI	D1c	The system should be designed to limit the number of log-in attempts and to record unauthorized access log-in attempts.
EMA eSource Reflection Paper	Topic 3b	Source documents should be protected against unauthorized access. Source documents need to be protected in order to maintain subject confidentiality. Changes or deletion by unauthorised individuals, either accidental or deliberate, should be prevented. Authority checks should be used, as these could ensure that only authorised individuals have access to the system, or the ability to enter or make changes to data. Records of authorisation of access to the systems, with the respective levels of access clearly documented (e.g. individual user accounts) should be maintained. Audit trails should record changes to user access rights. There should be documented training on the importance of security including the need to protect and not share passwords as well as enforcement of security systems and processes. The system users should confirm that he/she accepts responsibility for data entered using their password. Security systems should prevent unauthorised access to the computer system and to the data in the electronic record. Procedures should be in place to avoid/prevent unauthorised access when a workstation is vacated. There should be timely removal of access no longer required, or no longer permitted.
EU Annex 11	12.1	Physical and/or logical controls should be in place to restrict access to computerised system to authorised persons. Suitable methods of preventing unauthorised entry to the system may include the use of

keys, pass cards, personal codes with passwords, biometrics, restricted access to computer equipment and data storage areas.

FDA EHR Guidance	V.B.2	Access to electronic systems is limited to authorized users.
EU GDPR	Article 33.5	The controller shall document any personal data breaches, comprising the facts relating to the personal data breach, its effects and the remedial action taken. That documentation shall enable the supervisory authority to verify compliance with this Article.
USA HIPAA	164.308a5iiC	Procedures for monitoring log-in attempts and reporting discrepancies.
JPMA EDC Guidance	4.1.1.2c	The ability to prevent unauthorized access. (take a measure of malware and security hole, management and prevent of leaking of ID and password, user management).
JPMA EDC Guidance	4.1.1.2d	The ability to detect any unauthorized access. (monitoring of access, alert, access logs).
JPMA EDC Supplement	1.4d	Maintain a security system for the data;
JPMA EDC Supplement	1.5.1.2b	The system must be designed to prevent and/or detect unauthorized access. For example, the system has a function that demands an access code in case of loss of a device, or a specific equipment or program to download data from the device, etc.
NMPA Clinical Trial DM Guide	3.3.3.a	Clinical trial data management system must have a sound management system privileges. Paper-based or electronic data management are needed to develop SOPs for access control and management. Data management system for different people with different permissions or roles that only authorized personnel are allowed to operate (record, modify, etc.), and shall take appropriate methods to monitor and prevent non-licensed person operation.
NMPA PISS	10.3	Personal information controllers should establish appropriate data security capabilities and implement necessary management and technical measures to prevent leakage, damage, and loss of personal information in accordance with the requirements of relevant national standards.

Regulatory mapping for eCF Requirement ID C21

The system enforces user authentication mechanisms that follow current information security best practices.

Regulation	Paragraph	Description
FDA 21 CFR Part 11	100a	(a) Each electronic signature shall be unique to one individual and shall not be reused by, or reassigned to, anyone else.
FDA 21 CFR Part 11	100b	(b) Before an organization establishes, assigns, certifies, or otherwise sanctions an individual's electronic signature, or any element of such electronic signature, the organization shall verify the identity of the individual.
FDA 21 CFR Part 11	10j	(j) The establishment of, and adherence to, written policies that hold individuals accountable and responsible for actions initiated under their electronic signatures, in order to deter record and signature falsification.
FDA 21 CFR Part 11	300b	(b) Ensuring that identification code and password issuances are periodically checked, recalled, or revised (e.g., to cover such events as password aging).
FDA CSUCI	D1f	We also recommend that passwords or other access keys be changed at established intervals commensurate with a documented risk assessment.
PMDA EDC Management Sheet version 2	41	Measures for maintaining security: Personal authentication - ID/password - One-time password - Biometrics authentication (fingerprint, retina, vein) - Other ()
PMDA EDC Management Sheet version 2	43	Procedures for maintaining of security: Written procedures of requesting user registration, granting ID/password, reviewing users, removing the registered users
JPMA EDC Guidance	4.1.1.2c	The ability to prevent unauthorized access. (take a measure of malware and security hole, management and prevent of leaking of ID and password, user management).

JPMA EDC Supplement	1.4d	Maintain a security system for the data;
JPMA EDC Supplement	1.5.1.2b	The system must be designed to prevent and/or detect unauthorized access. For example, the system has a function that demands an access code in case of loss of a device, or a specific equipment or program to download data from the device, etc.
NMPA Clinical Trial DM Guide	3.3.3.d	The electronic management system, password should be changed regularly

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Regulatory mapping for eCF Requirement ID C22

System feature to allow automatic logoff or other access lock (such as password protected screen saver) after a set period of time of inactivity.

Regulation	Paragraph	Description
FDA CSUCI	D1g	When someone leaves a workstation, the person should log off the system. Alternatively, an automatic log off may be appropriate for long idle periods. For short periods of inactivity, we recommend that a type of automatic protection be installed against unauthorized data entry (e.g., an automatic screen saver can prevent data entry until a password is entered).
EMA eSource Reflection Paper	Topic 3b	Source documents should be protected against unauthorized access. Source documents need to be protected in order to maintain subject confidentiality. Changes or deletion by unauthorised individuals, either accidental or deliberate, should be prevented. Authority checks should be used, as these could ensure that only authorised individuals have access to the system, or the ability to enter or make changes to data. Records of authorisation of access to the systems, with the respective levels of access clearly documented (e.g. individual user accounts) should be maintained. Audit trails should record changes to user access rights. There should be documented training on the importance of security including the need to protect and not share passwords as well as enforcement of security systems and processes. The system users should confirm that he/she accepts responsibility for data entered using their password. Security systems should prevent unauthorised access to the computer system and to the data in the electronic record. Procedures should be in place to avoid/prevent unauthorised access when a workstation is vacated. There should be timely removal of access no longer required, or no longer permitted.
JPMA EDC Guidance	4.1.1.2c	The ability to prevent unauthorized access. (take a measure of malware and security hole, management and prevent of leaking of ID and password, user management).
JPMA EDC Supplement	1.4d	Maintain a security system for the data;
NMPA Clinical Trial DM Guide	3.3.3.b	The electronic management system, the system should have a personal account for each user, system requirements before you start

data manipulation login account, exit the system after completion

NMPA Clinical
Trial DM Guide

3.3.3.e

The electronic management system, leave your workstation should terminate the connection to the host computer is idle for a long time to implement self-disconnect after short pause work, there should be automatic protection procedures to prevent unauthorized data manipulation, such as the use of the screen before entering the password protection.

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Regulatory mapping for eCF Requirement ID C23

The system must have the ability to provide a history of all individuals who have access to the system and their access privileges over time.

Regulation	Paragraph	Description
FDA CSUCI	E4	You should maintain a cumulative record that indicates, for any point in time, the names of authorized personnel, their titles, and a description of their access privileges. That record should be kept in the study documentation, accessible for use by appropriate study personnel and for inspection by FDA investigators.
PMDA EDC Management Sheet version 2	47	List of persons authorized to access the system (i.e. list of persons authorized to create and modify the data): - Trial being conducted: - Upon completion of the trial (to be submitted at the time of inspection)
EMA eSource Reflection Paper	Topic 3b	Source documents should be protected against unauthorized access. Source documents need to be protected in order to maintain subject confidentiality. Changes or deletion by unauthorised individuals, either accidental or deliberate, should be prevented. Authority checks should be used, as these could ensure that only authorised individuals have access to the system, or the ability to enter or make changes to data. Records of authorisation of access to the systems, with the respective levels of access clearly documented (e.g. individual user accounts) should be maintained. Audit trails should record changes to user access rights. There should be documented training on the importance of security including the need to protect and not share passwords as well as enforcement of security systems and processes. The system users should confirm that he/she accepts responsibility for data entered using their password. Security systems should prevent unauthorised access to the computer system and to the data in the electronic record. Procedures should be in place to avoid/prevent unauthorised access when a workstation is vacated. There should be timely removal of access no longer required, or no longer permitted.
PMDA ERES (Japan)	5	Persons who uses electromagnetic records and electronic signatures for materials and raw-materials of applications for approval or licensing of drugs, and for registration of conformity certification bodies shall prepare documents described persons in charge, managers, organizations, equipments and training for using electromagnetic

records and electronic signatures.

EU Annex 11	12.3	Creation, change, and cancellation of access authorisations should be recorded.
FDA EHR Guidance	V.B.2	Access to electronic systems is limited to authorized users.
FDA eSource Guidance	D	<p>Data Access</p> <p>Sponsors, CROs, data safety monitoring boards, and other authorized personnel can view the data elements in the eCRF before and after the clinical investigator(s) has electronically signed the completed eCRF. We encourage viewing the data to allow early detection of study-related problems (e.g., safety concerns, protocol deviations) and problems with conducting the study (e.g., missing data, data discrepancies).</p> <p>The sponsor should have a list (e.g., in a data management plan) of the individuals with authorized access to the eCRF. Only those individuals who have documented training and authorization should have access to the eCRF data. Individuals with authorized access should be assigned their own identification (log-on) codes and passwords. Log-on access should be disabled if the individual discontinues involvement during the study.</p>
EU GDPR	Article 36.3a	<p>When consulting the supervisory authority pursuant to paragraph 1, the controller shall provide the supervisory authority with:</p> <p>(a) where applicable, the respective responsibilities of the controller, joint controllers and processors involved in the processing, in particular for processing within a group of undertakings.</p>
USA HIPAA	164.308a3iiA	Implement procedures for the authorization and/or supervision of workforce members who work with electronic protected health information or in locations where it might be accessed.
ICH GCP	5.5.3e	<p>When using electronic trial data handling and/or remote electronic trial data systems, the sponsor should:</p> <p>e) Maintain a list of the individuals who are authorized to make data changes (see 4.1.5 and 4.9.3).</p>
JPMA EDC Guidance	4.1.1.3.6a	The account list which mentions personnel access rights shall be created and operated instead of handwriting signature list.
JPMA EDC Supplement	1.4f	Prepare and maintain a list of the individuals who are authorized to make data correction;
NMPA PISS	7.1d	If it is necessary to authorize a specific person to handle personal information because of the need of work, it shall be examined and approved by the person responsible for personal information protection or the personal information protection agency, and recorded in the book.

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Regulatory mapping for eCF Requirement ID C24

System has the ability to produce a human-readable copy of data (which includes associated audit trails and any decoded data).

Regulation	Paragraph	Description
FDA 21 CFR Part 11	10b	(b) The ability to generate accurate and complete copies of records in both human readable and electronic form suitable for inspection, review, and copying by the agency. Persons should contact the agency if there are any questions regarding the ability of the agency to perform such review and copying of the electronic records.
FDA CSUCI	C3	When source data are transmitted from one system to another (e.g., from a personal data assistant to a sponsors server), or entered directly into a remote computerized system (e.g., data are entered into a remote server via a computer terminal that is located at the clinical site), or an electrocardiogram at the clinical site is transmitted to the sponsors computerized system, a copy of the data should be maintained at another location, typically at the clinical site but possibly at some other designated site.
FDA CSUCI	C4	Copies should be made contemporaneously with data entry and should be preserved in an appropriate format, such as XML, PDF or paper formats.
PMDA EDC Management Sheet version 2	68	Securing of the visual readability of stored information post completion of the clinical trial.
EMA eSource Reflection Paper	Topic 2b	Source data should be Accurate, Legible, Contemporaneous, Original, Attributable, Complete and Consistent. Legible: Readable at the input and output stage in a form meaningful to an independent reviewer i.e. a human being should be able to read it, not encrypted, coded or in programmed language.
EMA eTMF Guideline	2	The TMF should provide for document identification, version history, search and retrieval; also, as stated in both Directive 2005/28/EC (Article 17) and the Regulation (Articles 57 and 58) it shall be archived in a way that ensures that it is readily available and directly accessible upon request, to the competent authorities of the Member States.

EMA eTMF Guideline	4.1.1	At all times the storage area for the TMF documents (such as paper or electronic media archives and server rooms) should be appropriate to maintain the documents in a manner that they remain complete and legible throughout the trial conduct and the required period of retention and can be made available to the competent authorities of the Member States, upon request.
EMA Q&A eTMF 1	a	The e-TMF should allow review in an efficient manner, analagous to that possible with paper TMFs. Such a review should not take longer to access than for a paper TMF. (Efficient, straightforward navigation and opening of documents permitting searching and browsing (analogous to leafing through a paper file).
PMDA ERES (Japan)	3.1.2	Readability of electromagnetic records The contents of electromagnetic records shall be output (output to display, output to paper and copy to electronic storage media) as human readable format.
PMDA ERES (Japan)	3.1.3.2	When maintained electromagnetic records will be migrated into other electronic storage media or method, migrated electromagnetic records shall be established its authenticity, readability and storability.
EU Annex 11	8.1	It should be possible to obtain clear printed copies of electronically stored data.
EU Clinical Trials Regulation 536 2014	58e	The media used to archive the content of the clinical trial master file shall be such that the content remains complete and legible throughout the period referred to in the first paragraph.
ICH GCP	1.63	A copy (irrespective of the type of media used) of the original record that has been verified (i.e., by a dated signature or by generation through a validated process) to have the same information, including data that describe the context, content, and structure, as the original.
JPMA EDC Guidance	4.1.1.3e	The electronic CRF copy which is maintained by investigators shall meet following requirements. - The electronic CRF copy is exported directly or converted automatically (which shall be qualified in advance) from the original data in the server. - The electronic CRF copy shall be comparable to the original. - The electronic CRF copy shall be identified. - Be able to identify the time point of copy from the original.
JPMA EDC Guidance	4.1.2	1) The ability to generate output for display and printouts of every input/modified data and audit trail (including electronic signature) for human readable format at anytime. 2) Readability means that not only human readable format but also legible and easy to read. Poor display functionality such as users are obliged to trace many tables according to some kind of key code is not met with readability requirements. All information shall be integrated when users display or print out.

JPMA EDC Guidance	4.2.2	Clinical data captured can be displayed on screen or printed on paper as forms or inventory for each clinical case.
JPMA EDC Supplement	1.5.2a	All the data entered into an ePRO system and audit trail should be able to output in a human-readable format (e.g. showing on a display device, printing on paper, copying to electromagnetic recording media). The output should be easy to read and handle.
NMPA Clinical Trial DM Guide	5.13.d	<p>The following table illustrates the different types of clinical trial data and common archive format.</p> <ul style="list-style-type: none"> - CSV: Comma delimited ASCII text file, you can use a text editor, word processor and Excel spreadsheet software to edit. - XML: In ASCII technology, different systems to facilitate the conversion of structured information. - SAS Version 5 transport files: SAS offers an open source format. Typically used to submit clinical trial data. - Adobe PDF: Widely used text output formats.
NMPA Clinical Trial DM Guide	5.13.e	For the use of electronic data test, clinical trial data management system vendor shall provide a copy of the clinical research center all the electronic case report form as a PDF file format to record.

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Regulatory mapping for eCF Requirement ID C25

Copies of electronic records must be certified copies if they are being used for regulatory purposes

Regulation	Paragraph	Description
FDA 21 CFR Part 11 Q&A	Q6b	The copy of the original record should be verified as having all of the same attributes and information as the original record and certified as indicated by a dated signature.
FDA 21 CFR Part 11 Q&A	Q7	Sponsors and other regulated entities should designate which electronic document is the original and should certify the electronic copies by generating the copies through a validated process.
EMA eSource Reflection Paper	6.3.3	Whenever copies of electronic health records are provided for the purpose of monitoring/ auditing/inspecting the monitor/auditor/inspector should be able to verify that this copy is a complete and accurate copy of the electronic health record.
EMA eSource Reflection Paper	Topic 4	<p>It is a fundamental requirement that a source document and data can be copied and that there is a practical method of copying that is complete and accurate, including relevant metadata. When required, it should be possible to print the source document/data for review, audit or inspection purposes.</p> <p>Accurate and complete copies for certification should include the meaning of the data (e.g. date formats, context, layout, electronic signature and authorisations), as well as the full audit trail. The investigator site should have the ability of reviewing the data and generate copies. Where certified copies are made the process for certification should be described, including the process for ensuring that the copy is complete and accurate and for identifying the certifying party and their authority for making that copy. The process of making a certified copy needs to be validated.</p>
EMA eTMF Guideline	5.1	A certified copy is a paper or electronic copy of the original document that has been verified (e.g. by a dated signature) or has been generated through a validated process to produce an exact copy having all the same information, including data that describe the context, content and structure, as the original. The ICH GCP guideline requires that copies (irrespective of the media used) in the eTMF that irreversibly replace originals should be certified copies of the original. Any transfer or conversion (e.g. digitisation or printing), which does not

fulfill the criteria for a certified copy, is not suitable to replace an original file.

EMA Q&A eTMF
1 c

Documents held on an e-TMF should be evidently authentic, complete and legible copies of the original documents.

EMA RBM in CT 1.1

The key elements of the quality system include:... documentation system that preserves and allows for the retrieval of any information/documentation (quality records/essential documents) to show actions taken, decisions made and results

EMA RBM in CT 1.4

The key elements of the quality system include:... quality assurance including internal and external audits performed by independent auditors

ICH GCP 1.63

A copy (irrespective of the type of media used) of the original record that has been verified (i.e., by a dated signature or by generation through a validated process) to have the same information, including data that describe the context, content, and structure, as the original.

ICH GCP 8.1

ADDENDUM

The sponsor and investigator/institution should maintain a record of the location(s) of their respective essential documents including source documents. The storage system used during the trial and for archiving (irrespective of the type of media used) should provide for document identification, version history, search, and retrieval.

Essential documents for the trial should be supplemented or may be reduced where justified (in advance of trial initiation) based on the importance and relevance of the specific documents to the trial.

The sponsor should ensure that the investigator has control of and continuous access to the CRF data reported to the sponsor. The sponsor should not have exclusive control of those data.

When a copy is used to replace an original document (e.g., source documents, CRF), the copy should fulfill the requirements for certified copies.

The investigator/institution should have control of all essential documents and records generated by the investigator/institution before, during, and after the trial.

JPMA EDC
Guidance 4.1.3.2.A1

In case of data (original) transfer, the data shall be exported directly or converted automatically (which shall be qualified in advance) and keeping their contents and meaning.

MHRA GXP
Data Integrity
Guidance 6.11.2

A copy (irrespective of the type of media used) of the original record that has been verified (i.e. by a dated signature or by generation through a validated process) to have the same information, including data that describe the context, content, and structure, as the original.

Regulatory mapping for eCF Requirement ID C26

There are sufficient system and/or process controls for backup and recovery procedures.

Regulation	Paragraph	Description
FDA CSUCI	F4a	When electronic formats are the only ones used to create and preserve electronic records, sufficient backup and recovery procedures should be designed to protect against data loss.
FDA CSUCI	F4b	Records should regularly be backed up in a procedure that would prevent a catastrophic loss and ensure the quality and integrity of the data. Records should be stored at a secure location specified in the SOP. Storage should typically be offsite or in a building separate from the original records.
FDA CSUCI	F4c	We recommend that you maintain backup and recovery logs to facilitate an assessment of the nature and scope of data loss resulting from a system failure.
FDA CSUCI	S09	- Data backup, recovery, and contingency plans
EMA eSource Reflection Paper	Topic 5b	Source documents and data should be protected from destruction. Source data should be protected from destruction, either accidental or deliberate. Regular backups should be made. Suitable archiving systems should be in place to safeguard the data integrity for the periods established by the regulatory requirements including those in any of the regions where the data may be used for regulatory submissions, and not just those of the country where the data are generated. Checks of accessibility to archived data, irrespective of format, including relevant metadata, should be undertaken to confirm that the data are enduring, continue to be available, readable and understandable by a human being.
EMA eTMF Guideline	4.1.2c	The primary eTMF is a system for managing documents that should contain the controls listed below: regular backup;
EMA eTMF Guideline	4.1.2d	The primary eTMF is a system for managing documents that should contain the controls listed below: periodic test retrieval or restores to confirm the on-going availability and integrity of the data;

EMA IRT Reflection Paper	2.2.3d	Disaster recovery system - there should be back-up systems in place such that if there is a server break-down the IRT is still able to keep running. There will be occasions when the system is down and the provider should have prepared for these such that manual interventions can be made, documented and the system updated when it is fully operational again.
PMDA ERES (Japan)	3.1.1.3	The procedure of backup of electromagnetic records is documented and practicing appropriately.
PMDA ERES (Japan)	3.1.3	Storability electromagnetic records Electromagnetic records shall be maintained with keeping its authenticity and readability.
EU Annex 11	7.2	Regular back-ups of all relevant data should be done. Integrity and accuracy of backup data and the ability to restore the data should be checked during validation and monitored periodically.
EU Clinical Trials Regulation 536 2014	58b	The content of the clinical trial master file shall be archived in a way that ensures that it is readily available and accessible, upon request, to the competent authorities.
EU GDPR	Article 32.1b	The ability to ensure the ongoing confidentiality, integrity, availability and resilience of processing systems and services.
EU GDPR	Article 32.1c	The ability to restore the availability and access to personal data in a timely manner in the event of a physical or technical incident.
EU GDPR	Article 32.1d	A process for regularly testing, assessing and evaluating the effectiveness of technical and organisational measures for ensuring the security of the processing.
EU GDPR	Article 32.2	In assessing the appropriate level of security account shall be taken in particular of the risks that are presented by processing, in particular from accidental or unlawful destruction, loss, alteration, unauthorised disclosure of, or access to personal data transmitted, stored or otherwise processed.
EU GDPR	Article 5.1e	Personal data shall be processed in a manner that ensures appropriate security of the personal data, including protection against unauthorised or unlawful processing and against accidental loss, destruction or damage, using appropriate technical or organisational measures (integrity and confidentiality).
USA HIPAA	164.308a7iiB	Disaster recovery plan (Required). Establish (and implement as needed) procedures to restore any loss of data.
ICH GCP	4.9.4	The investigator/institution should maintain the trial documents as specified in Essential Documents for the Conduct of a Clinical Trial (see 8.) and as required by the applicable regulatory requirement(s). The investigator/institution should take measures to prevent accidental or premature destruction of these documents.

ICH GCP	5.5.3b	<p>When using electronic trial data handling and/or remote electronic trial data systems, the sponsor should:</p> <p>b) Maintains SOPs for using these systems.</p> <p>ADDENDUM</p> <p>The SOPs should cover system setup, installation, and use. The SOPs should describe system validation and functionality testing, data collection and handling, system maintenance, system security measures, change control, data backup, recovery, contingency planning, and decommissioning. The responsibilities of the sponsor, investigator, and other parties with respect to the use of these computerized systems should be clear, and the users should be provided with training in their use.</p>
ICH GCP	5.5.3f	<p>When using electronic trial data handling and/or remote electronic trial data systems, the sponsor should:</p> <p>f) Maintain adequate backup of the data.</p>
JPMA EDC Guidance	4.1.1.5	<p>Backup of CRF data and EDC system (including users list, access rights information, and so on) is performed appropriately.</p> <p>a) According to the documented procedures, latest electronic CRF data, audit trail and electronic signatures are backup periodically. In case of emergency, CRF data shall be recovered in accordance with predetermined procedures. In this case the original data set shall be uniquely identified.</p> <p>b) In terms of recognizing that the recovered data is original, recovering procedures shall be tested and qualified in advance.</p> <p>c) In case of H/W or S/W incidents, the environments shall be recovered in accordance with predetermined procedures.</p>
JPMA EDC Supplement	1.4e	Maintain the adequate backup of the data;
JPMA EDC Supplement	1.5.1.4a	Based on a documented procedure, the latest data should be backed up on a regular schedule. In case of an unexpected situation, the data should be restored through a predetermined procedure.
MHRA GXP Data Integrity Guidance	6.17.2	<p>Backup and recovery processes should be validated and periodically tested. Each back up should be verified to ensure that it has functioned correctly e.g. by confirming that the data size transferred matches that of the original record.</p> <p>The backup strategies for the data owners should be documented.</p>
MHRA GXP Data Integrity Guidance	6.17a	Data retention may be for archiving (protected data for long-term storage) or backup (data for the purposes of disaster recovery).
NMPA Clinical Trial DM Guide	3.3.1.f	<p>Clinical trial data management system validation include the following aspects:</p> <ul style="list-style-type: none"> - Disaster Recovery Plan / Backup
NMPA Clinical	5.12.a	Data management throughout the study process, the database should

Trial DM Guide

be backed up. Usually in addition a separate computer for backup, and according to the progress of work weekly backup file synchronization update. Final data set will be backed up on CD-ROM form, when necessary, the dataset is not locked disc can also be backed up. When the database irreparable damage occurs, you should use the most recent backup to restore the database and adds the corresponding data entry.

NMPA PISS

10.3

Personal information controllers should establish appropriate data security capabilities and implement necessary management and technical measures to prevent leakage, damage, and loss of personal information in accordance with the requirements of relevant national standards.

NMPA PISS

10.5d

Unauthorized access, tampering or deletion of audit records should be prevented.

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Regulatory mapping for eCF Requirement ID C27

Documentation of the backup and recovery process can be produced for inspection by a monitor, auditor or inspector.

Regulation	Paragraph	Description
FDA CSUCI	F4b	Records should regularly be backed up in a procedure that would prevent a catastrophic loss and ensure the quality and integrity of the data. Records should be stored at a secure location specified in the SOP. Storage should typically be offsite or in a building separate from the original records.
PMDA EDC Management Sheet version 2	59 and 61	Procedures of operation for data backup and recovery: Written procedure for management of data backup and recovery Throughout the conduct and post completion of the clinical trial.
EMA RBM in CT	1.4	The key elements of the quality system include:... quality assurance including internal and external audits performed by independent auditors
PMDA ERES (Japan)	3.1.1.3	The procedure of backup of electromagnetic records is documented and practicing appropriately.
PMDA ERES (Japan)	3.1.3	Storability electromagnetic records Electromagnetic records shall be maintained with keeping its authenticity and readability.
EU Annex 11	7.2	Regular back-ups of all relevant data should be done. Integrity and accuracy of backup data and the ability to restore the data should be checked during validation and monitored periodically.
EU GDPR	Article 32.1b	The ability to ensure the ongoing confidentiality, integrity, availability and resilience of processing systems and services.
EU GDPR	Article 32.1c	The ability to restore the availability and access to personal data in a timely manner in the event of a physical or technical incident.
EU GDPR	Article 32.3	Adherence to an approved code of conduct as referred to in Article 40 or an approved certification mechanism as referred to in Article 42 may be used as an element by which to demonstrate compliance with the requirements set out in paragraph 1 of this Article.

ICH GCP	4.9.4	The investigator/institution should maintain the trial documents as specified in Essential Documents for the Conduct of a Clinical Trial (see 8.) and as required by the applicable regulatory requirement(s). The investigator/institution should take measures to prevent accidental or premature destruction of these documents.
ICH GCP	5.5.3f	When using electronic trial data handling and/or remote electronic trial data systems, the sponsor should: f) Maintain adequate backup of the data.
JPMA EDC Supplement	1.4e	Maintain the adequate backup of the data;
JPMA EDC Supplement	1.5.1.4a	Based on a documented procedure, the latest data should be backed up on a regular schedule. In case of an unexpected situation, the data should be restored through a predetermined procedure.
NMPA PISS	10.3	Personal information controllers should establish appropriate data security capabilities and implement necessary management and technical measures to prevent leakage, damage, and loss of personal information in accordance with the requirements of relevant national standards.

Copyright eClinical Forum

Regulatory mapping for eCF Requirement ID C28

Process and/or system controls ensure that regulated data used for clinical research, including source data and metadata are enduring, continue to be available, readable and understandable and are retained in an archive for the legal period.

Regulation	Paragraph	Description
FDA 21 CFR Part 11	10c	(c) Protection of records to enable their accurate and ready retrieval throughout the records retention period.
FDA 21 CFR Part 11	10e	(e) Use of secure, computer-generated, time-stamped audit trails to independently record the date and time of operator entries and actions that create, modify, or delete electronic records. Record changes shall not obscure previously recorded information. Such audit trail documentation shall be retained for a period at least as long as that required for the subject electronic records and shall be available for agency review and copying.
FDA 21 CFR Part 312	62c	An investigator shall retain records required to be maintained under this part for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified
Japanese APPI	Article 19	A personal information handling business operator shall strive to keep personal data accurate and up to date within the scope necessary to achieve a utilization purpose, and to delete the personal data without delay when such utilization has become unnecessary.
FDA CSUCI	C2	Under 21 CFR 312.62, 511.1(b)(7)(ii) and 812.140, the clinical investigator must retain records required to be maintained under part 312, 511.1(b), and part 812, for a period of time specified in these regulations. This requirement applies to the retention of the original source document, or a copy of the source document.
PMDA EDC Management Sheet version 2	51	Written procedure for securing the authenticity of retained information: Written procedure for modifying information retained in the EDC System
PMDA EDC	73	Ensuring the storage stability during the retention period:

Management Sheet version 2		Written procedure of electromagnetic records after the completion of trial
EMA eSource Reflection Paper	Topic 2a	<p>Source data should be Accurate, Legible, Contemporaneous, Original, Attributable, Complete and Consistent.</p> <p>Accurate: The use of such instruments/systems should ensure that the data are at least as accurate as those recorded by paper means. The validity of the data capture process is fundamental to ensuring that high-quality data are produced as part of a trial. The process needs to ensure that all data required are captured and that data are captured in a consistent manner. The coding process which consists in matching text or data collected on the CRF to terms in a standard dictionary, thesaurus or tables (e.g. units, scales, etc.) should be controlled. The process of data transfer between systems should be validated.</p>
EMA eSource Reflection Paper	Topic 5b	<p>Source documents and data should be protected from destruction. Source data should be protected from destruction, either accidental or deliberate. Regular backups should be made. Suitable archiving systems should be in place to safeguard the data integrity for the periods established by the regulatory requirements including those in any of the regions where the data may be used for regulatory submissions, and not just those of the country where the data are generated. Checks of accessibility to archived data, irrespective of format, including relevant metadata, should be undertaken to confirm that the data are enduring, continue to be available, readable and understandable by a human being.</p>
EMA eTMF Guideline	2	<p>The TMF should provide for document identification, version history, search and retrieval; also, as stated in both Directive 2005/28/EC (Article 17) and the Regulation (Articles 57 and 58) it shall be archived in a way that ensures that it is readily available and directly accessible upon request, to the competent authorities of the Member States.</p>
EMA eTMF Guideline	3.2d	<p>The clinical trial contract/agreement and other documents and procedures agreed between all parties should outline the arrangements for the TMF in some detail, such as:</p> <ul style="list-style-type: none"> - retention times; - arrangements regarding the archiving of and access to data/documents held in centralised systems (such as central training documents and central e-mail repository).
EMA eTMF Guideline	3.2e	<p>The clinical trial contract/agreement and other documents and procedures agreed between all parties should outline the arrangements for the TMF in some detail, such as:</p> <ul style="list-style-type: none"> - procedures in case of an involved party closing down its business for any reason.
EMA eTMF Guideline	3.5.1	<p>Documents demonstrating software validation may be retained by a CRO when the activity has been contracted by the sponsor, but the sponsor should ensure continued access to these documents in the contractual arrangements with the CRO for the required archiving period. Documents relating to the trial-specific software configuration</p>

are part of the TMF and it should be determined whether these are maintained/archived by the sponsor or CRO providing this service. Some documents from good manufacturing practice activities should also be defined as part of the TMF, for example, when these relate to the assembly and packaging of the investigational medicinal product (IMP) and confirm, as applicable, compliance with the randomisation schedule and blinding of the trial.

EMA eTMF Guideline	4.1.1	At all times the storage area for the TMF documents (such as paper or electronic media archives and server rooms) should be appropriate to maintain the documents in a manner that they remain complete and legible throughout the trial conduct and the required period of retention and can be made available to the competent authorities of the Member States, upon request.
EMA eTMF Guideline	4.1.2b	The primary eTMF is a system for managing documents that should contain the controls listed below: user accounts; a system in place locking/protecting individual documents or the entire eTMF (e.g. at time of archiving) to prevent changes to documents.
EMA eTMF Guideline	4.1.2g	The primary eTMF is a system for managing documents that should contain the controls listed below: user accounts; the suitability of the system for archiving purposes should be appropriate.
EMA eTMF Guideline	4.1.3g	All agreements should include provisions for the situation that any of the parties mentioned above are going out of business and how the integrity and accessibility of the complete investigator TMF will be maintained throughout the required archiving period.
EMA Q&A eTMF 1	d	The e-TMF system should have validated methods for preventing any changes being made to the TMF documents, this includes the process of transferring from original media to the electronic medium.
PMDA ERES (Japan)	3.1.1	Authenticity of electromagnetic records Electromagnetic records are complete, accurate and reliable, and also responsibilities of its creation, modification and deletion are definite.
PMDA ERES (Japan)	3.1.3	Storability electromagnetic records Electromagnetic records shall be maintained with keeping its authenticity and readability.
EU Annex 11	17	Data may be archived. This data should be checked for accessibility, readability and integrity. If relevant changes are to be made to the system (e.g. computer equipment or programs), then the ability to retrieve the data should be ensured and tested.
EU Directive 2005 28	2.4.17	The sponsor and the investigator shall retain the essential documents relating to a clinical trial for at least five years after its completion. They shall retain the documents for a longer period, where so required by

other applicable requirements or by an agreement between the sponsor and the investigator. Essential documents shall be archived in a way that ensures that they are readily available, upon request, to the competent authorities. The medical files of trial subjects shall be retained in accordance with national legislation and in accordance with the maximum period of time permitted by the hospital, institution or private practice.

EU Directive 2005 28	2.4.20	The media used to store essential documents shall be such that those documents remain complete and legible throughout the required period of retention and can be made available to the competent authorities upon request. Any alteration to records shall be traceable.
EU Clinical Trials Regulation 536 2014	57	The clinical trial master file shall at all times contain the essential documents relating to that clinical trial which allow verification of the conduct of a clinical trial and the quality of the data generated, taking into account all characteristics of the clinical trial, including in particular whether the clinical trial is a low-intervention clinical trial. It shall be readily available, and directly accessible upon request, to the Member States.
EU Clinical Trials Regulation 536 2014	58a	Unless other Union law requires archiving for a longer period, the sponsor and the investigator shall archive the content of the clinical trial master file for at least 25 years after the end of the clinical trial. However, the medical files of subjects shall be archived in accordance with national law.
EU Clinical Trials Regulation 536 2014	58b	The content of the clinical trial master file shall be archived in a way that ensures that it is readily available and accessible, upon request, to the competent authorities.
EU Clinical Trials Regulation 536 2014	58e	The media used to archive the content of the clinical trial master file shall be such that the content remains complete and legible throughout the period referred to in the first paragraph.
FDA EHR Guidance	V.B.4	Records are available and retained for FDA inspection for as long as the records are required by applicable regulations.
FDA EHR Guidance	VI.2	Clinical investigators must retain all records.
FDA EHR Guidance	VI.3	Investigator or sponsor must maintain all records.
FDA Electronic Informed Consent Q&A	Q15	The eIC process should incorporate procedures to ensure that electronic documents can be archived appropriately and that all versions of the IRB-approved eIC can be retrieved easily.
FDA eSource Guidance	A2c	Transcription of Data From Paper or Electronic Sources to the eCRF Data elements can be transcribed into the eCRF from paper or electronic source documents. The authorized person transcribing the data from the source documents is regarded as the data originator. For

these data elements, the electronic or paper documents from which the data elements are transcribed are the source. These data must be maintained by the clinical investigator(s) and available to an FDA inspector if requested (e.g., an original or certified copy of a laboratory report, instrument printout, progress notes of the physician, the study subjects hospital chart(s), nurses notes).

FDA and MHRA
Data Integrity
Discussions

P13

The sponsor has flexibility in where these essential documents should be retained but the location for long-term retention should be defined in the quality system and should be appropriate to the type of file (i.e., dynamic file or flat file). The retention times required by regulation necessitates the need for managed archival of electronic files.

FDA and MHRA
Data Integrity
Discussions

P14a

There should be quality assurance and quality control mechanisms at each stage of data handling.

EU GDPR

Article 32.1b

The ability to ensure the ongoing confidentiality, integrity, availability and resilience of processing systems and services.

EU GDPR

Article 32.1c

The ability to restore the availability and access to personal data in a timely manner in the event of a physical or technical incident.

EU GDPR

Article 32.1d

A process for regularly testing, assessing and evaluating the effectiveness of technical and organisational measures for ensuring the security of the processing.

USA HIPAA

164.304a

Availability means the property that data or information is accessible and useable upon demand by an authorized person.

USA HIPAA

164.308a8

Perform a periodic technical and nontechnical evaluation, based initially upon the standards implemented under this rule and, subsequently, in response to environmental or operational changes affecting the security of electronic protected health information, that establishes the extent to which a covered entity's or business associate's security policies and procedures meet the requirements of this subpart.

ICH GCP

4.9.0

The investigator/institution should maintain adequate and accurate source documents and trial records that include all pertinent observations on each of the site's trial subjects. Source data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry, and should be explained if necessary (e.g., via an audit trail).

ICH GCP

4.9.4

The investigator/institution should maintain the trial documents as specified in Essential Documents for the Conduct of a Clinical Trial (see 8.) and as required by the applicable regulatory requirement(s). The investigator/institution should take measures to prevent accidental or premature destruction of these documents.

ICH GCP	4.9.5	Essential documents should be retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents should be retained for a longer period however if required by the applicable regulatory requirements or by an agreement with the sponsor. It is the responsibility of the sponsor to inform the investigator/institution as to when these documents no longer need to be retained (see 5.5.12).
ICH GCP	5.18.4k	Verifying that source documents and other trial records are accurate, complete, kept up-to-date and maintained.
ICH GCP	8.1	<p>ADDENDUM</p> <p>The sponsor and investigator/institution should maintain a record of the location(s) of their respective essential documents including source documents. The storage system used during the trial and for archiving (irrespective of the type of media used) should provide for document identification, version history, search, and retrieval.</p> <p>Essential documents for the trial should be supplemented or may be reduced where justified (in advance of trial initiation) based on the importance and relevance of the specific documents to the trial.</p> <p>The sponsor should ensure that the investigator has control of and continuous access to the CRF data reported to the sponsor. The sponsor should not have exclusive control of those data.</p> <p>When a copy is used to replace an original document (e.g., source documents, CRF), the copy should fulfill the requirements for certified copies.</p> <p>The investigator/institution should have control of all essential documents and records generated by the investigator/institution before, during, and after the trial.</p>
JPMA EDC Guidance	4.1.1.3.5	In the institutes, authority and investigators are able to check the data of CRF at anytime within the retention period.
JPMA EDC Guidance	4.1.1.6.4	After new EDC system has gone live, if you discard previous EDC system, related records such as validation deliverables shall be maintained and ensure adequacy of all documents produced by previous EDC system.
JPMA EDC Guidance	4.1.2	<p>1) The ability to generate output for display and printouts of every input/modified data and audit trail (including electronic signature) for human readable format at anytime.</p> <p>2) Readability means that not only human readable format but also legible and easy to read. Poor display functionality such as users are obliged to trace many tables according to some kind of key code is not met with readability requirements. All information shall be integrated when users display or print out.</p>
JPMA EDC Supplement	1.2a	...it is required to prepare necessary equipment (e.g. devices) and environment (e.g. internet line, telephone line) for data entry by

subjects, make operational procedures for transmitting subject data to the operational database, operational procedures for providing the collected subject data to investigators. and sponsors, and also procedures for data retention after completion of the clinical trial and location of storage.

JPMA EDC
Supplement

1.2d

After the completion of the trial, the source documents on the vendor server are transferred to a CD-R or other general media, such as a PDF file or other format that can address the requirements of readability and retainability, through a process required for ensuring authenticity, and are stored at the site.

JPMA EDC
Supplement

1.4h

It must also be noted that, the ePRO must be durable enough to be kept for their retention period specified in Article 26 of the GCP, The sponsor shall appropriately retain the records, since ePRO refers to data generated in conducting the clinical trial.

JPMA EDC
Supplement

1.5.2c

During the transfer of data with the relevant audit trail to recording media for archiving after the completion of the trial, the readability should be maintained at the same level as in the ePRO system, so that such data is easily accessible throughout the specified period of record keeping.

JPMA EDC
Supplement

1.5.3

Throughout the specified period of record keeping, the authenticity and readability of the electromagnetic records must be ensured.

MHRA GXP
Data Integrity
Guidance

6.17.1

Archived records may be the original record or a 'true copy' and should be protected so they cannot be altered or deleted without detection and protected against any accidental damage such as fire or pest. Archive arrangements must be designed to permit recovery and readability of the data and metadata throughout the required retention period. In the case of archiving of electronic data, this process should be validated, and in the case of legacy systems the ability to review data periodically verified (i.e. to confirm the continued support of legacy computerised systems). Where hybrid records are stored, references between physical and electronic records must be maintained such that full verification of events is possible throughout the retention period.

MHRA GXP
Data Integrity
Guidance

6.2

In the case of basic electronic equipment that does not store electronic data, or provides only a printed data output (e.g. balances or pH meters), then the printout constitutes the raw data. Where the basic electronic equipment does store electronic data permanently and only holds a certain volume before overwriting; this data should be periodically reviewed and where necessary reconciled against paper records and extracted as electronic data where this is supported by the equipment itself.

NMPA Clinical
Trial DM Guide

5.13.a

Ensure data security is to prevent the data may be subject to physical damage or damaged. Conducting clinical trials in the process, all the collected raw data (such as CRF and electronic data) stored in a safe place, such as a controlled room to ensure that the appropriate temperature, humidity, fire safety measures have improved, fireproof

lock document cabinet. The original document is traced to the original data audit part of the path should be like an electronic audit trail of any changes to the database or backup recording done the same strict protection. Recommended data kept for at least 10 years. Data were entered into the database content and time input data in the database and the history of the amendment requires all intact. Ensure data accessibility refers to the user when needed, such as login and retrieve data from, and the data in the database can be transmitted in a timely manner as needed.

NMPA Clinical Trial DM Guide	5.13.c	In clinical trials completed, the response during the test documents to be archived.
NMPA PISS	6.1a	The retention period of personal information should be the minimum time necessary to achieve the purpose.

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Regulatory mapping for eCF Requirement ID C29

There are sufficient process controls for the system covering Business Continuity.

Regulation	Paragraph	Description
Japanese APPI	Article 20	A personal information handling business operator shall take necessary and appropriate action for the security control of personal data including preventing the leakage, loss or damage of its handled personal data.
FDA CSUCI	S09	- Data backup, recovery, and contingency plans
FDA CSUCI	S10	- Alternative recording methods (in the case of system unavailability)
EMA eTMF Guideline	4.1.3g	All agreements should include provisions for the situation that any of the parties mentioned above are going out of business and how the integrity and accessibility of the complete investigator TMF will be maintained throughout the required archiving period.
EMA IRT Reflection Paper	2.2.3d	Disaster recovery system - there should be back-up systems in place such that if there is a server break-down the IRT is still able to keep running. There will be occasions when the system is down and the provider should have prepared for these such that manual interventions can be made, documented and the system updated when it is fully operational again.
EU Annex 11	16	For the availability of computerised systems supporting critical processes, provisions should be made to ensure continuity of support for those processes in the event of a system breakdown (e.g. a manual or alternative system). The time required to bring the alternative arrangements into use should be based on risk and appropriate for a particular system and the business process it supports. These arrangements should be adequately documented and tested.
EU Annex 11	7.1	Data should be secured by both physical and electronic means against damage. Stored data should be checked for accessibility, readability and accuracy. Access to data should be ensured throughout the retention period.
EU GDPR	Article 32.1b	The ability to ensure the ongoing confidentiality, integrity, availability and resilience of processing systems and services.

EU GDPR	Article 32.1c	The ability to restore the availability and access to personal data in a timely manner in the event of a physical or technical incident.
EU GDPR	Article 32.1d	A process for regularly testing, assessing and evaluating the effectiveness of technical and organisational measures for ensuring the security of the processing.
EU GDPR	Article 32.2	In assessing the appropriate level of security account shall be taken in particular of the risks that are presented by processing, in particular from accidental or unlawful destruction, loss, alteration, unauthorised disclosure of, or access to personal data transmitted, stored or otherwise processed.
EU GDPR	Article 5.1e	Personal data shall be processed in a manner that ensures appropriate security of the personal data, including protection against unauthorised or unlawful processing and against accidental loss, destruction or damage, using appropriate technical or organisational measures (integrity and confidentiality).
USA HIPAA	164.308a8	Perform a periodic technical and nontechnical evaluation, based initially upon the standards implemented under this rule and, subsequently, in response to environmental or operational changes affecting the security of electronic protected health information, that establishes the extent to which a covered entity's or business associate's security policies and procedures meet the requirements of this subpart.
ICH GCP	5.5.3b	When using electronic trial data handling and/or remote electronic trial data systems, the sponsor should: b) Maintains SOPs for using these systems. ADDENDUM The SOPs should cover system setup, installation, and use. The SOPs should describe system validation and functionality testing, data collection and handling, system maintenance, system security measures, change control, data backup, recovery, contingency planning, and decommissioning. The responsibilities of the sponsor, investigator, and other parties with respect to the use of these computerized systems should be clear, and the users should be provided with training in their use.
JPMA EDC Supplement	1.5.1.4b	In case of hardware or software failure, the operating environment should be restored through a predetermined procedure.
NMPA PISS	10.3	Personal information controllers should establish appropriate data security capabilities and implement necessary management and technical measures to prevent leakage, damage, and loss of personal information in accordance with the requirements of relevant national standards.

Regulatory mapping for eCF Requirement ID C30

There are sufficient process controls based on industry standards, covering Disaster Recovery Procedures.

Regulation	Paragraph	Description
Japanese APPI	Article 20	A personal information handling business operator shall take necessary and appropriate action for the security control of personal data including preventing the leakage, loss or damage of its handled personal data.
EMA eSource Reflection Paper	Topic 5b	Source documents and data should be protected from destruction. Source data should be protected from destruction, either accidental or deliberate. Regular backups should be made. Suitable archiving systems should be in place to safeguard the data integrity for the periods established by the regulatory requirements including those in any of the regions where the data may be used for regulatory submissions, and not just those of the country where the data are generated. Checks of accessibility to archived data, irrespective of format, including relevant metadata, should be undertaken to confirm that the data are enduring, continue to be available, readable and understandable by a human being.
EMA IRT Reflection Paper	2.2.3d	Disaster recovery system - there should be back-up systems in place such that if there is a server break-down the IRT is still able to keep running. There will be occasions when the system is down and the provider should have prepared for these such that manual interventions can be made, documented and the system updated when it is fully operational again.
EU GDPR	Article 32.1b	The ability to ensure the ongoing confidentiality, integrity, availability and resilience of processing systems and services.
EU GDPR	Article 32.1c	The ability to restore the availability and access to personal data in a timely manner in the event of a physical or technical incident.
EU GDPR	Article 32.1d	A process for regularly testing, assessing and evaluating the effectiveness of technical and organisational measures for ensuring the security of the processing.
EU GDPR	Article 32.2	In assessing the appropriate level of security account shall be taken in

particular of the risks that are presented by processing, in particular from accidental or unlawful destruction, loss, alteration, unauthorised disclosure of, or access to personal data transmitted, stored or otherwise processed.

EU GDPR	Article 5.1e	Personal data shall be processed in a manner that ensures appropriate security of the personal data, including protection against unauthorised or unlawful processing and against accidental loss, destruction or damage, using appropriate technical or organisational measures (integrity and confidentiality).
USA HIPAA	164.308a7iiB	Disaster recovery plan (Required). Establish (and implement as needed) procedures to restore any loss of data.
ICH GCP	4.9.4	The investigator/institution should maintain the trial documents as specified in Essential Documents for the Conduct of a Clinical Trial (see 8.) and as required by the applicable regulatory requirement(s). The investigator/institution should take measures to prevent accidental or premature destruction of these documents.
ICH GCP	5.5.3b	When using electronic trial data handling and/or remote electronic trial data systems, the sponsor should: b) Maintains SOPs for using these systems. ADDENDUM The SOPs should cover system setup, installation, and use. The SOPs should describe system validation and functionality testing, data collection and handling, system maintenance, system security measures, change control, data backup, recovery, contingency planning, and decommissioning. The responsibilities of the sponsor, investigator, and other parties with respect to the use of these computerized systems should be clear, and the users should be provided with training in their use.
JPMA EDC Supplement	1.5.1.4b	In case of hardware or software failure, the operating environment should be restored through a predetermined procedure.
MHRA GXP Data Integrity Guidance	6.17b	Data and document retention arrangements should ensure the protection of records from deliberate or inadvertent alteration or loss. Secure controls must be in place to ensure the data integrity of the record throughout the retention period and should be validated where appropriate (see also data transfer/migration).
NMPA Clinical Trial DM Guide	3.3.1.f	Clinical trial data management system validation include the following aspects: - Disaster Recovery Plan / Backup
NMPA PISS	10.3	Personal information controllers should establish appropriate data security capabilities and implement necessary management and technical measures to prevent leakage, damage, and loss of personal information in accordance with the requirements of relevant national standards.

Regulatory mapping for eCF Requirement ID C31

There is a process to demonstrate that individuals who develop, maintain, or use the system have appropriate education, training, and experience necessary to perform their assigned task.

Regulation	Paragraph	Description
FDA 21 CFR Part 11	10i	(i) Determination that persons who develop, maintain, or use electronic record/electronic signature systems have the education, training, and experience to perform their assigned tasks.
FDA 21 CFR Part 11 Q&A	Q23a	Sponsors, clinical investigators, study personnel, and study participants must be adequately trained on the use of any mobile technology they will use in a clinical investigation.
FDA CSUCI	E2	Staff should be kept thoroughly aware of system security measures and the importance of limiting access to authorized personnel.
FDA CSUCI	G1	Those who use computerized systems must determine that individuals (e.g., employees, contractors) who develop, maintain, or use computerized systems have the education, training and experience necessary to perform their assigned tasks (21 CFR 11.10(i)).
FDA CSUCI	G2	Training should be provided to individuals in the specific operations with regard to computerized systems that they are to perform
FDA CSUCI	G3	Training should be conducted by qualified individuals on a continuing basis, as needed, to ensure familiarity with the computerized system and with any changes to the system during the course of the study.
FDA CSUCI	G4	We recommend that computer education, training, and experience be documented.
FDA CSUCI	S11	- Computer user training
PMDA EDC Management Sheet version 2	95 and 101	Management Method: Training Describe the training for the person who administers/maintains electromagnetic records. Training for end users is described in the above section of <i>Education and training on securing of security</i> Throughout the conduct and post completion of the clinical trial.

EMA eSource Reflection Paper	Topic 2c	<p>Source data should be Accurate, Legible, Contemporaneous, Original, Attributable, Complete and Consistent.</p> <p>Completeness and consistency: can be assisted by the use of features such as drop-down lists, online edits, check boxes and branching of questions or data entry fields based on entries. The individual (investigator site staff, study subjects, caregivers or others) capturing the data need to have documented training in the correct use of the instrument and the electronic data capture document. In addition, when considering data from an environment where analysis, tests, scans, imaging, evaluations, etc. are performed in support of clinical trials, it should be possible to fully reconstruct the activities performed.</p>
EMA eSource Reflection Paper	Topic 3b	<p>Source documents should be protected against unauthorized access. Source documents need to be protected in order to maintain subject confidentiality. Changes or deletion by unauthorised individuals, either accidental or deliberate, should be prevented. Authority checks should be used, as these could ensure that only authorised individuals have access to the system, or the ability to enter or make changes to data. Records of authorisation of access to the systems, with the respective levels of access clearly documented (e.g. individual user accounts) should be maintained. Audit trails should record changes to user access rights. There should be documented training on the importance of security including the need to protect and not share passwords as well as enforcement of security systems and processes. The system users should confirm that he/she accepts responsibility for data entered using their password. Security systems should prevent unauthorised access to the computer system and to the data in the electronic record. Procedures should be in place to avoid/prevent unauthorised access when a workstation is vacated. There should be timely removal of access no longer required, or no longer permitted.</p>
EMA eTMF Guideline	3.2g	<p>When a CRO is used for the management of the eTMF and/or for the digitisation/transfer of TMF documents, appropriate pre-qualification checks should be undertaken prior to contracting the CRO. It should be verified during the clinical trial that the CROs quality management measures are complied with.</p>
EMA eTMF Guideline	4.1.2i	<p>All staff members involved in the conduct of the trial and using the system should receive appropriate training.</p>
EMA eTMF Guideline	6.1b	<p>The appointment and appropriate training of these individuals should be documented. These individuals should be employed within the organisation of the sponsor or the organisation contracted by the sponsor.</p>
EMA IRT Reflection Paper	2.2.2c	<p>The quality system encompassing the IRT system should include:</p> <ul style="list-style-type: none"> - Training records for all those involved in the development and day to day running of the system. This should include help desk personnel.
EMA RBM in CT	1.2	<p>The key elements of the quality system include:... appropriate training of sponsor personnel as well as of the personnel in affiliates, at the Contract Research Organisations (CROs), vendors or other service</p>

providers and at trial sites

PMDA ERES (Japan)	5	Persons who uses electromagnetic records and electronic signatures for materials and raw-materials of applications for approval or licensing of drugs, and for registration of conformity certification bodies shall prepare documents described persons in charge, managers, organizations, equipments and training for using electromagnetic records and electronic signatures.
EU Annex 11	2	There should be close cooperation between all relevant personnel such as Process Owner, System Owner, Qualified Persons and IT. All personnel should have appropriate qualifications, level of access and defined responsibilities to carry out their assigned duties.
FDA Electronic Informed Consent Q&A	Q2	If the investigator delegates this responsibility, the responsibility should be delegated to an individual qualified by education, training, and experience to perform this activity.
FDA eSource Guidance	D	<p>Data Access</p> <p>Sponsors, CROs, data safety monitoring boards, and other authorized personnel can view the data elements in the eCRF before and after the clinical investigator(s) has electronically signed the completed eCRF. We encourage viewing the data to allow early detection of study-related problems (e.g., safety concerns, protocol deviations) and problems with conducting the study (e.g., missing data, data discrepancies).</p> <p>The sponsor should have a list (e.g., in a data management plan) of the individuals with authorized access to the eCRF. Only those individuals who have documented training and authorization should have access to the eCRF data. Individuals with authorized access should be assigned their own identification (log-on) codes and passwords. Log-on access should be disabled if the individual discontinues involvement during the study.</p>
EU GDPR	Article 41.2b	Established procedures which allow it to assess the eligibility of controllers and processors concerned to apply the code, to monitor their compliance with its provisions and to periodically review its operation.
USA HIPAA	164.308a5i	Implement a security awareness and training program for all members of its workforce (including management).
ICH GCP	5.5.3b	<p>When using electronic trial data handling and/or remote electronic trial data systems, the sponsor should:</p> <p>b) Maintains SOPs for using these systems.</p> <p>ADDENDUM</p> <p>The SOPs should cover system setup, installation, and use. The SOPs should describe system validation and functionality testing, data collection and handling, system maintenance, system security measures, change control, data backup, recovery, contingency planning, and decommissioning. The responsibilities of the sponsor, investigator, and other parties with respect to the use of these</p>

		computerized systems should be clear, and the users should be provided with training in their use.
JPMA EDC Guidance	4.1.1.1c	Operation shall be adequate and compliance shall be ensured by training. (i.e. Prevent from spoofing, stealing password and so on.)
JPMA EDC Guidance	4.1.1.4b	Training record of every related people shall be maintained.
JPMA EDC Supplement	1.5.1.1b	Appropriate training must be provided to ensure appropriate usage and compliance. Since the users of an ePRO system are subjects, it is essential to provide them with understandable manuals and pre-trial trainings using equipment related to the ePRO system in order to collect intended data and improve quality of the trial data. It must be noted that, basic handling procedures of equipment and management of passwords and IDs must be included in the training program. It is also desirable to establish a help desk in advance to minimize loss of data reliability due to missing data that may be caused by device failure, forgotten access codes etc., and subsequent transcription from paper media.
JPMA EDC Supplement	3.2.1d	To establish rules for users to be granted with the authority of electronic signatures, and the timing of authorization and other relevant rules (e.g. after education, training) must be established in advance.
JPMA EDC Supplement	3.2.5	Relevant education and/or training should be provided to all related persons, and recorded.
MHRA GXP Data Integrity Guidance	5.1h	Sufficient training in data integrity principles provided to all appropriate staff (including senior management).
NMPA Clinical Trial DM Guide	2.2	Responsible for the management of clinical trial data must go through GCP, relevant laws and regulations, the relevant standard operating procedures (SOP, Standard Operating Procedure), and data management professional training, job requirements to ensure that it has appropriate qualifications.
NMPA Clinical Trial DM Guide	3.3.1.h	Clinical trial data management system validation include the following aspects: - User Training
NMPA Clinical Trial DM Guide	3.3.1.j	Clinical trial data management software end users, the need for local installation and commissioning, testing and training of personnel records.
NMPA Clinical Trial DM Guide	6.1.1.1	All clinical researchers should have qualified and trained. Develop quality control procedures, such as: - Security: clinical researchers have been trained, and in accordance with rights management procedures. - Equipment: clinical researchers follow procedures to ensure safe and proper equipment and data storage.

- Data privacy: Ensuring compliance with procedures to protect the privacy of the subjects.
- Quality Audit: clinical researchers conducted an internal audit of the data.
- Storage and archiving: Ensuring data and files stored in the archive.

NMPA PISS

10.4e

Personal information security professional training and assessment should be carried out on relevant personnel in personal information processing positions on a regular basis (at least once a year) or in the event of major changes in the privacy policy to ensure that relevant personnel are proficient in privacy policies and related procedures.

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Regulatory mapping for eCF Requirement ID C32

There is a process to demonstrate that the development, hosting and deployment of the computerised system follows good software lifecycle practices such that it is sufficiently validated based on risk.

Regulation	Paragraph	Description
FDA 21 CFR Part 11	10a	(a) Validation of systems to ensure accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered records.
FDA 21 CFR Part 11	10f	(f) Use of operational system checks to enforce permitted sequencing of steps and events, as appropriate.
FDA 21 CFR Part 11	10h	(h) Use of device (e.g., terminal) checks to determine, as appropriate, the validity of the source of data input or operational instruction.
FDA 21 CFR Part 11	10k	(k) Use of appropriate controls over systems documentation including: (1) Adequate controls over the distribution of, access to, and use of documentation for system operation and maintenance. (2) Revision and change control procedures to maintain an audit trail that documents time-sequenced development and modification of systems documentation.
FDA 21 CFR Part 11 Q&A	Q1	Consistent with the policy announced in the 2003 part 11 guidance, sponsors and other regulated entities should use a risk-based approach for validating electronic systems owned or managed by sponsors and other regulated entities. Validation is critical to ensure that the electronic system is correctly performing its intended function. Validation may include, but is not limited to, demonstrating correct installation of the electronic system and testing of the system to ensure that it functions in the manner intended.
FDA 21 CFR Part 11 Q&A	Q15	It is ultimately the responsibility of the sponsor or other regulated entity to ensure that the outsourced electronic service is validated as appropriate.
FDA 21 CFR Part 11 Q&A	Q19	FDA does not intend to inspect each individual mobile technology used in a clinical investigation to capture, record, and transmit data directly from study participants because access controls, audit trails, and validation that would be applied would help ensure the reliability of the data.

FDA CSUCI	A3	The computerized systems should be designed: (1) to satisfy the processes assigned to these systems for use in the specific study protocol (e.g., record data in metric units, blind the study), and (2) to prevent errors in data creation, modification, maintenance, archiving, retrieval, or transmission (e.g., inadvertently unblinding a study).
FDA CSUCI	F5a	The integrity of the data and the integrity of the protocols should be maintained when making changes to the computerized system, such as software upgrades, including security and performance patches, equipment, or component replacement, or new instrumentation.
FDA CSUCI	F5b	The effects of any changes to the system should be evaluated and some should be validated depending on risk. Changes that exceed previously established operational limits or design specifications should be validated. Finally, all changes to the system should be documented.
FDA CSUCI	S02	- System setup/installation (including the description and specific use of software, hardware, and physical environment and the relationship)
FDA CSUCI	S03	- System operating manual
FDA CSUCI	S04	- Validation and functionality testing
FDA CSUCI	S06	- System maintenance (including system decommissioning)
FDA CSUCI	S08	- Change control
PMDA EDC Management Sheet version 2	36	Procedure of validating trial-specific setup: Written procedure of validating trial-specific setup
EMA eSource Reflection Paper	Topic 1	An instrument used to capture source data should ensure that the data are captured as specified within the protocol. The instrument should be created in a controlled manner to ensure that it conforms to the protocol and is validated. In addition, appropriate change control as part of ongoing validation is needed, in cases where protocol amendments require changes to the instrument. Records of system validation including requirements, design, installation, access and security, testing (e.g. user acceptance testing, installation, operational and performance testing), training and controlled release for use should be maintained.
EMA eTMF Guideline	3.5.1	Documents demonstrating software validation may be retained by a CRO when the activity has been contracted by the sponsor, but the sponsor should ensure continued access to these documents in the contractual arrangements with the CRO for the required archiving period. Documents relating to the trial-specific software configuration are part of the TMF and it should be determined whether these are maintained/archived by the sponsor or CRO providing this service. Some documents from good manufacturing practice activities should also be defined as part of the TMF, for example, when these relate to

the assembly and packaging of the investigational medicinal product (IMP) and confirm, as applicable, compliance with the randomisation schedule and blinding of the trial.

EMA eTMF
Guideline

4.1.2h

The eTMF systems should be validated to demonstrate that the functionality is fit for purpose, with formal procedures in place to manage this process.

EMA IRT
Reflection Paper

2.2.1

The validation of the IRT system should be in line with the expectations of Annex 11, Volume 4 of Good Manufacturing Practice, and Medicinal Products for Human and Veterinary Use, hereafter called Annex 11. The principles of Good Automated Manufacturing Practice (GAMP) should be considered.

EMA IRT
Reflection Paper

2.2.1a

With regards to the validation, as a minimum, the following should be in place:

- Regardless of what clinical research activities are undertaken by the IRT, the sponsors should assure themselves that the IRT provider has adequately validated the system. This system should be subject to a robust change control procedure. The expectations would be the same for any in-house system.
- A user requirements specification (URS) or equivalent should be produced and approved by the sponsor. Any subsequent validation documents produced by the provider should be mapped back to the URS. This should be down to the level of mapping individual test scripts back to the requirement tested.
- Client user acceptance testing (UAT) should always be offered to sponsors. This is an opportunity for the sponsor to test the system and this should be undertaken, preferably with test scripts written by the sponsor.
- All incidents affecting functionality should be fixed prior to release and this should be documented appropriately. It is acceptable for some bug fixes to be remedied at a later stage if they do not affect the initial calls into the system, for example an end of study visit (with the exception of early withdrawals); however, it is expected that a plan for fixing such incidents should be in place prior to the system going live. There should be clear traceability of the testing of these fixes right back to the URS.
- It is recommended that key steps should be subject to review and sign off by an independent department (QA), which could be at the IRT provider or outsourced.
- There should be a formal sign off of the system prior to use.

EMA QA GCP
Matters 8

4

- That GCP inspections can take place at the vendor in case the vendor is performing services for the sponsor, when the sponsor has relied fully or partly on the vendor to perform the qualification activities and when it was established during the inspection of the sponsor that part of the documentation can only be verified by inspection of the vendor.
- That any qualification documentation prepared by the vendor in relation to the system should be available for inspection.

EMA QA GCP Matters 9	2	Sponsors and vendors should be aware that if the electronic systems are used for generating/handling relevant clinical trial data or to maintain control and oversight of clinical trial processes, documentation regarding the qualification process and any other relevant documentation on the electronic system maintained at the sponsor level, as well as on the vendor level, and it is the sponsor's responsibility to ensure that these documents are available for inspections by Member States GCP inspectors.
EMA RBM in CT	1.3	The key elements of the quality system include:... validation of computerised systems
EMA RBM in CT	1.4	The key elements of the quality system include:... quality assurance including internal and external audits performed by independent auditors
EMA RBM in CT	3d	Risk management tools: can be paper based or built with the use of information technology. The tools can allow detection, identification, prediction, tracking, analysing with the generation of metrics. Broadly the tools support the risk management system and the decision making.
PMDA ERES (Japan)	3.1	Following items shall be established by electromagnetic records system and its operating procedures. In this case, ensuring the system reliability by computerized system validation of the electromagnetic records system is premised.
EU Annex 11	1	Risk management should be applied throughout the lifecycle of the computerised system taking into account patient safety, data integrity and product quality. As part of a risk management system, decisions on the extent of validation and data integrity controls should be based on a justified and documented risk assessment of the computerised system.
EU Annex 11	10	Any changes to a computerised system including system configurations should only be made in a controlled manner in accordance with a defined procedure.
EU Annex 11	4.1	The validation documentation and reports should cover the relevant steps of the life cycle. Manufacturers should be able to justify their standards, protocols, acceptance criteria, procedures and records based on their risk assessment.
EU Annex 11	4.2	Validation documentation should include change control records (if applicable) and reports on any deviations observed during the validation process.
EU Annex 11	4.3	An up to date listing of all relevant systems and their GMP functionality (inventory) should be available. For critical systems an up to date system description detailing the physical and logical arrangements, data flows and interfaces with other systems or processes, any hardware and software pre-requisites, and

security measures should be available.

EU Annex 11	4.4	User Requirements Specifications should describe the required functions of the computerised system and be based on documented risk assessment and GMP impact. User requirements should be traceable throughout the life-cycle.
EU Annex 11	4.5	The regulated user should take all reasonable steps, to ensure that the system has been developed in accordance with an appropriate quality management system. The supplier should be assessed appropriately.
EU Annex 11	4.6	For the validation of bespoke or customised computerised systems there should be a process in place that ensures the formal assessment and reporting of quality and performance measures for all the life-cycle stages of the system.
EU Annex 11	4.7	Evidence of appropriate test methods and test scenarios should be demonstrated. Particularly, system (process) parameter limits, data limits and error handling should be considered. Automated testing tools and test environments should have documented assessments for their adequacy.
EU Annex 11	6	For critical data entered manually, there should be an additional check on the accuracy of the data. This check may be done by a second operator or by validated electronic means. The criticality and the potential consequences of erroneous or incorrectly entered data to a system should be covered by risk management.
FDA and MHRA Data Integrity Discussions	P11a	The sponsor may choose what validation model to follow; however, all validation documentation (for both the core software and the study-specific configuration) demonstrating that the eSystem is validated should be retained and available for inspection.
FDA and MHRA Data Integrity Discussions	P14b	SOPs should cover the setup, installation, and use of eSystems. The SOPs should also describe eSystem validation and functionality testing, data collection and handling, system maintenance, system security measures, change control, data backup, recovery, contingency planning, and decommissioning.
FDA Mobile Medical Applications	F2	<p>FDA believes all manufacturers of medical device software should have in place an adequate quality management system that helps ensure that their products consistently meet applicable requirements and specifications and can support the software throughout its total life cycle.</p> <p>Adequate quality management systems incorporate appropriate risk management strategies, good design practices, adequate verification and validation, and appropriate methods to correct and prevent risks to patients and adverse events that may arise from the use of the product.</p>
EU GDPR	Article 32.2	In assessing the appropriate level of security account shall be taken in particular of the risks that are presented by processing, in particular

from accidental or unlawful destruction, loss, alteration, unauthorised disclosure of, or access to personal data transmitted, stored or otherwise processed.

EU GDPR	Article 5.1e	Personal data shall be processed in a manner that ensures appropriate security of the personal data, including protection against unauthorised or unlawful processing and against accidental loss, destruction or damage, using appropriate technical or organisational measures (integrity and confidentiality).
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ICH GCP	1.65	A process of establishing and documenting that the specified requirements of a computerized system can be consistently fulfilled from design until decommissioning of the system or transition to a new system. The approach to validation should be based on a risk assessment that takes into consideration the intended use of the system and the potential of the system to affect human subject protection and reliability of trial results.
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ICH GCP	5.5.3a	<p>When using electronic trial data handling and/or remote electronic trial data systems, the sponsor should:</p> <p>a) Ensure and document that the electronic data processing system(s) conforms to the sponsors established requirements for completeness, accuracy, reliability, and consistent intended performance (i.e. validation).</p> <p>ADDENDUM</p> <p>The sponsor should base their approach to validation of such systems on a risk assessment that takes into consideration the intended use of the system and the potential of the system to affect human subject protection and reliability of trial results.</p>
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ICH GCP	5.5.3b	<p>When using electronic trial data handling and/or remote electronic trial data systems, the sponsor should:</p> <p>b) Maintains SOPs for using these systems.</p> <p>ADDENDUM</p> <p>The SOPs should cover system setup, installation, and use. The SOPs should describe system validation and functionality testing, data collection and handling, system maintenance, system security measures, change control, data backup, recovery, contingency planning, and decommissioning. The responsibilities of the sponsor, investigator, and other parties with respect to the use of these computerized systems should be clear, and the users should be provided with training in their use.</p>
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ICH GCP	5.5.3h	<p>ADDENDUM</p> <p>(h) Ensure the integrity of the data including any data that describe the context, content, and structure. This is particularly important when making changes to the computerized systems, such as software upgrades or migration of data.</p>
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JPMA EDC Guidance	4.1.1.6.1	<p>The revised system shall be ensured its quality by CSV in accordance with CSV policy. The revising means followings,</p> <p>- EDC systems version up. (Program change such as functionality</p>
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addition, modification and elimination to the system, and environment change.)

- Revising input form of electronic CRF. (In case of protocol amendments or bug fix.)
- Program addition, modification and elimination due to automatically query output.

JPMA EDC
Guidance

4.1.1.6.2

In case of data migration due to revising of EDC system, the original data shall be exported directly or converted automatically (which shall be qualified in advance) and keeping their contents and meaning. And also readability of data (including audit trail) is ensured.

- Validation deliverables shall be maintained that ensure the data is converted or exported according to the qualified procedures and the data is in consistency with original data.

JPMA EDC
Guidance

4.1.1.6.3

In case of revising of related records such as validation deliverables, change control procedures shall be predetermined, and creation or change history of validation deliverables shall be maintained and traceable in chronological order.

JPMA EDC
Guidance

4.1.1.6.4

After new EDC system has gone live, if you discard previous EDC system, related records such as validation deliverables shall be maintained and ensure adequacy of all documents produced by previous EDC system.

JPMA EDC
Guidance

4.1.3.2.B1

In case of not maintain EDC system after data transfer, necessary records should be maintained.

- In case of not maintain EDC system after data transferred to permanent electronic CRF, validation deliverables such as system requirements specification deliverables, design specification deliverables and qualification deliverables are to be maintained for inspection.

JPMA EDC
Guidance

4.1.3.2.B2

Readability shall be ensured if the EDC software is migrated for new computer system.

- After data transfer, if you intend to preserve EDC software and re-install it in any occasion, readability shall be ensured on the new computer environment.

JPMA EDC
Supplement

1.4a

Ensure and document that the electronic data processing systems fulfill the sponsors established requirements for completeness, accuracy, reliability and consistent intended performance (i.e. validation);

JPMA EDC
Supplement

1.5.1.5a

Revision of an ePRO system includes upgrading of the system version, modification of the data entry screen, and addition, correction, deletion of programmed automatic queries, etc. In any case, reliability of the system must be ensured through CSV.

JPMA EDC
Supplement

1.5.1.5c

Procedures for the revision and change control of validation documents and other documents must also be established in advance, thus enabling a chronological and traceable history of the creation and revision of validation documents and other documents to be retained.

MHRA GXP Data Integrity Guidance	6.19	Computerised systems should comply with regulatory requirements and associated guidance. These should be validated for their intended purpose which requires an understanding of the computerised system's function within a process. For this reason, the acceptance of vendor- supplied validation data in isolation of system configuration and users intended use is not acceptable. In isolation from the intended process or end-user IT infrastructure, vendor testing is likely to be limited to functional verification only and may not fulfil the requirements for performance qualification.
MHRA GXP Data Integrity Guidance	6.8	Data migration is the process of moving stored data from one durable storage location to another.
NMPA Clinical Trial DM Guide	3.3.1.a	Reliability refers to a system under specified conditions, within the specified time, the ability to achieve the required functionality. Clinical trial data management system must be based on risk considerations validation to ensure data integrity, security and credibility, and to reduce the problems due to system or process arising from the possibility of error.
NMPA Clinical Trial DM Guide	3.3.1.b	Clinical trial data management system validation include the following aspects: - Proof system to meet the specific purpose of use
NMPA Clinical Trial DM Guide	3.3.1.g	Clinical trial data management system validation include the following aspects: - System maintenance and change control
NMPA Clinical Trial DM Guide	3.3.1.i	Data management software development software manufacturers have their rigorous design, serious verification, and rigorous testing.
NMPA Clinical Trial DM Guide	6.1.1.3	Computer system life cycle process and quality control If using a computer system, must meet the test and let staff needs. In every step of the life cycle of the system are required to perform quality control to ensure that all requirements are documented, tested and met. For example: - Requirements: To ensure system operation and maintenance covers all users as well as technical, commercial and regulatory requirements. - System verification process: ensure compliance with the procedures defined verification and record complete and accurate. - Change control: system life cycle process all changes are subject to evaluation and testing.
NMPA Clinical Trial DM Guide	6.1.1.4	Quality Control of the design, such as CRF design, database design and the establishment of the logical test, are generally multi-process quality control method for use. Process provides product quality control in the production process quality status at every stage to ensure the quality of each stage are reliable.

Regulatory mapping for eCF Requirement ID C35

There are sufficient system and/or process controls to prevent or mitigate effects of viruses, worms, or other harmful software code.

Regulation	Paragraph	Description
FDA 21 CFR Part 11 Q&A	Q4b	There should also be external security safeguards in place to prevent, detect, and mitigate effects of computer viruses, worms, and other potentially harmful software code on study data and software (e.g., firewalls, antivirus and anti-spy software).
Japanese APPI	Article 20	A personal information handling business operator shall take necessary and appropriate action for the security control of personal data including preventing the leakage, loss or damage of its handled personal data.
FDA CSUCI	E5	We also recommend that controls be implemented to prevent, detect, and mitigate effects of computer viruses, worms, or other potentially harmful software code on study data and software.
PMDA ERES (Japan)	3.1.1.1	Rules and procedures of maintaining securities of the system are documented and practicing them appropriately.
EU GDPR	Article 32.2	In assessing the appropriate level of security account shall be taken in particular of the risks that are presented by processing, in particular from accidental or unlawful destruction, loss, alteration, unauthorised disclosure of, or access to personal data transmitted, stored or otherwise processed.
USA HIPAA	164.308a5iiB	Procedures for guarding against, detecting, and reporting malicious software.
JPMA EDC Guidance	4.1.1.2c	The ability to prevent unauthorized access. (take a measure of malware and security hole, management and prevent of leaking of ID and password, user management).
JPMA EDC Supplement	1.4d	Maintain a security system for the data;
NMPA Clinical Trial DM Guide	5.12.b	Related computer must have the corresponding effective antivirus settings, including firewall, kill virus software.

Personal information controllers should establish appropriate data security capabilities and implement necessary management and technical measures to prevent leakage, damage, and loss of personal information in accordance with the requirements of relevant national standards.

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Regulatory mapping for eCF Requirement ID C36

There are sufficient system and/or process controls over data transfers from/to other systems, including validation of data mapping and transfer, security of data in transit, and confirmation of receipt.

Regulation	Paragraph	Description
FDA 21 CFR Part 11	30	Persons who use open systems to create, modify, maintain, or transmit electronic records shall employ procedures and controls designed to ensure the authenticity, integrity, and, as appropriate, the confidentiality of electronic records from the point of their creation to the point of their receipt. Such procedures and controls shall include those identified in 11.10, as appropriate, and additional measures such as document encryption and use of appropriate digital signature standards to ensure, as necessary under the circumstances, record authenticity, integrity, and confidentiality.
FDA 21 CFR Part 11 Q&A	Q2	During inspection, FDA will focus on any source data that are transferred to another data format or system to ensure that checks are in place and that critical data are not altered in value or meaning during the migration process. FDA will also review standard operating procedures and support mechanisms in place, such as training, technical support, and auditing to ensure that the system is functioning and is being used in the manner intended.
FDA 21 CFR Part 11 Q&A	Q22a	If the data are transmitted wirelessly from the mobile technology to the sponsor's EDC system in a clinical investigation, the data must be encrypted at rest and in transit to prevent access by intervening or malicious parties.
FDA 21 CFR Part 11 Q&A	Q22b	In addition to having encryption and basic user access controls in place, sponsors should consider implementing additional security safeguards as follows: <ul style="list-style-type: none"> - Remote wiping and remote disabling - Disable function for installing and using file-sharing applications - Firewalls - Procedures and processes to delete all stored health information before discarding or reusing the mobile device
Japanese APPI	Article 23.2	A personal information handling business operator, in regard to personal data provided to a third party ... may,... when pursuant to rules of the Personal Information Protection Commission it has in

advance informed a principal of those matters set forth in the following or put them into a state where a principal can easily know, and notified them to the Personal Information Protection Commission, provide the said personal data to a third party ...

- (i) to set a third-party provision as a utilization purpose
- (ii) the categories of personal data provided to a third party
- (iii) a method of a third-party provision

Japanese APPI Article 24

A personal information handling business operator ... shall, in case of providing personal data to a third party ... in a foreign country ... in advance obtain a principals consent to the effect that he or she approves the provision to a third party in a foreign country.

Japanese APPI Article 26.1

A personal information handling business operator shall, when receiving the provision of personal data from a third party, confirm those matters set forth in the following pursuant to rules of the Personal Information Protection Commission.

- (i) the name or appellation and address of the third party and, for a corporate body, the name of its representative (for a non-corporate body having appointed a representative or administrator, the said representative or administrator)
- (ii) circumstances under which the said personal data was acquired by the said third party

PMDA EDC Management Sheet version 2 40

Measures for maintaining security:

- SSL (Secure Socket Layer)
- VPN (Virtual Private Network)
- Other ()

EMA eSource Reflection Paper Topic 2a

Source data should be Accurate, Legible, Contemporaneous, Original, Attributable, Complete and Consistent.

Accurate: The use of such instruments/systems should ensure that the data are at least as accurate as those recorded by paper means. The validity of the data capture process is fundamental to ensuring that high-quality data are produced as part of a trial. The process needs to ensure that all data required are captured and that data are captured in a consistent manner. The coding process which consists in matching text or data collected on the CRF to terms in a standard dictionary, thesaurus or tables (e.g. units, scales, etc.) should be controlled. The process of data transfer between systems should be validated.

EMA eTMF Guideline 4.1.2j

When different TMF systems are linked to facilitate the trial conduct, e.g. when the CRO eTMF system uploads documents into the sponsor eTMF system (possibly by an intermediate system), the process for transferring documents should be robust and should be validated to prevent any loss.

EMA eTMF Guideline 5.4

The use of eTMFs and electronic archiving may require the digitisation of paper documents or the transfer of electronic documents to generate electronic copies of the documents. The process of digitisation or transfer should be validated to ensure that no information is lost or altered.

EMA Q&A eTMF 1	d	The e-TMF system should have validated methods for preventing any changes being made to the TMF documents, this includes the process of transferring from original media to the electronic medium.
EMA Q&A eTMF 1	e	The process for transferring original TMF documents to e-TMF (or other media) should be robust and have been validated to prevent failure of transfer the entire content of the original TMF without loss (i.e. there should be a demonstrable 1:1 mapping between the content of the original TMF and the e-TMF).
PMDA ERES (Japan)	3.1.3.2	When maintained electromagnetic records will be migrated into other electronic storage media or method, migrated electromagnetic records shall be established its authenticity, readability and storability.
PMDA ERES (Japan)	3.3	Using open system Persons who use open systems to create, modify, maintain, retrieve or transmit electromagnetic records shall meet requirements identified in 3.1, additionally shall employ appropriate controls to ensure integrity and confidentiality of electromagnetic records from the point of their creation to the point of their receipt. Such controls shall include such as document encryption and use of appropriate digital signature. Also, persons who use electronic signature shall meet requirements identified in 4.
EU Annex 11	4.8	If data are transferred to another data format or system, validation should include checks that data are not altered in value and/or meaning during this migration process.
FDA and MHRA Data Integrity Discussions	P11b	When integrating data in the study database, electronic transfer methods should be used rather than any manual entry via CRFs. Electronic data transfer requires careful controls to ensure no data loss or alteration, the correct data are allocated to correct fields in the new environment, and the fields are compatible (e.g., data type, length, and formats).
EU GDPR	Article 34.3a	Data affected by the personal data breach, in particular those that render data unintelligible such as encryption.
EU GDPR	Article 5.1e	Personal data shall be processed in a manner that ensures appropriate security of the personal data, including protection against unauthorised or unlawful processing and against accidental loss, destruction or damage, using appropriate technical or organisational measures (integrity and confidentiality).
USA HIPAA	164.502e1i	A covered entity may disclose protected health information to a business associate and may allow a business associate to create, receive, maintain, or transmit protected health information on its behalf, if the covered entity obtains satisfactory assurance that the business associate will appropriately safeguard the information. A covered entity is not required to obtain such satisfactory assurances from a business associate that is a subcontractor.

ICH GCP	5.5.3h	<p>ADDENDUM</p> <p>(h) Ensure the integrity of the data including any data that describe the context, content, and structure. This is particularly important when making changes to the computerized systems, such as software upgrades or migration of data.</p>
JPMA EDC Guidance	4.1.1.1h	<p>If sponsor would like to capture certain electronic data in institute via electronic media, sponsor shall make clear the scope of responsibilities of quality assurance provision of transferring electronic data in a contract, and shall ensure its quality by checking of data.</p>
JPMA EDC Guidance	4.1.1.1i	<p>Sponsor shall check compliance of quality management agreement at institutes.</p> <ul style="list-style-type: none"> - Sponsor shall check quality of provided data.
JPMA EDC Guidance	4.1.1.6.2	<p>In case of data migration due to revising of EDC system, the original data shall be exported directly or converted automatically (which shall be qualified in advance) and keeping their contents and meaning. And also readability of data (including audit trail) is ensured.</p> <ul style="list-style-type: none"> - Validation deliverables shall be maintained that ensure the data is converted or exported according to the qualified procedures and the data is in consistency with original data.
JPMA EDC Guidance	4.1.3.2.A23	<p>2) Appropriate document format for permanent electronic CRF</p> <ul style="list-style-type: none"> - Document format can be using throughout the records retention period. (i.e. open format such as PDF, XML, SGML are preferable) - Officially admit document format for long term retention. (i.e. ISO) - Searchable format. <p>3) Appropriate electronic media for permanent electronic CRF</p> <ul style="list-style-type: none"> - Enough warranty periods for not data missing throughout the records retention period. - Method for checking quality of data on the electronic media periodically. - Not be able to amend and delete. (i.e. optical disk)
JPMA EDC Guidance	4.1.3.2.B2	<p>Readability shall be ensured if the EDC software is migrated for new computer system.</p> <ul style="list-style-type: none"> - After data transfer, if you intend to preserve EDC software and re-install it in any occasion, readability shall be ensured on the new computer environment.
JPMA EDC Guidance	4.2	<p>If sponsors get clinical data directly from central laboratories not via institutes, and import them into sponsors server or EDC server, sponsors should have primary responsibility to assure identity of the data and data reported from central laboratories to institutes. In consequence, sponsors need to make measures to assure identity of data reported to institutes and data which sponsor imported directly from central laboratories by contracts with central laboratories. There are some cases that analysis results are included in electronic case report form or not, but in both case authenticity , readability and storability are should be guaranteed...</p>

JPMA EDC Guidance	4.2.1.1.a	<p>Make articles that central laboratories should comply with by contract documents to ensure scope of responsibilities for quality of transferred electronic data and reliability of data.</p> <ol style="list-style-type: none"> 1. Central laboratories shall assure accuracy of analysis results and ensure that laboratory reports to institutes correspond with electronic data sent to sponsors. 2. Arrange procedures of handling electronic data and scope of responsibilities in central laboratories.
JPMA EDC Guidance	4.2.1.1.c	Create operation in advance procedures for data acceptance/acceptance confirmation, and data import/import confirmation at sponsors side.
JPMA EDC Guidance	4.2.1.1.d	Reliability, repeatability and security should be assured in methods of data import.
JPMA EDC Guidance	4.2.1.1.e	Records should be maintained to make sure that operations of both sponsors and central laboratories are done as procedures
JPMA EDC Guidance	4.2.1.2	Confirm laboratory reports regarding as source documents stored in institutes are correspond with electronic data transferred to sponsors.
JPMA EDC Supplement	1.2a	...it is required to prepare necessary equipment (e.g. devices) and environment (e.g. internet line, telephone line) for data entry by subjects, make operational procedures for transmitting subject data to the operational database, operational procedures for providing the collected subject data to investigators. and sponsors, and also procedures for data retention after completion of the clinical trial and location of storage.
JPMA EDC Supplement	1.2g	Encryption or other security methods must be implemented in data transmission to the server via an open system. Since the data stored in the device lacks durability, it is necessary to transfer the data to a durable ePRO server at an early stage, by a verified procedure.
JPMA EDC Supplement	1.5.1.5b	If data migration is needed after the revision of an ePRO system, validation documents must prove that the data conversion or export has been performed through a verified procedure, and the updated data are identical to the source data before the conversion or export.
JPMA EDC Supplement	1.5.4	When an open system is used for the creation, change, maintenance, storage, retrieval and/or transmission of electromagnetic records in an ePRO system, appropriate measures must be taken and added in addition to the requirements indicated from 1.5.1 through 1.5.3, in order to ensure the authenticity and confidentiality of electromagnetic records from their creation to receipt.
JPMA EDC Supplement	2.2	The sponsor must test its transfer and conversion processes of electronic data, and ensure that there are no problems with the operating procedures and data identicalness before and after the transfer or conversion of data.

NMPA PISS	8.2a	Conduct personal information security impact assessment in advance and take effective measures to protect the subject of personal information based on the assessment results.
NMPA PISS	8.2d	Accurately record and preserve the sharing and transfer of personal information, including the date, size, purpose of sharing, transfer, and basic information of the recipient of the data.
NMPA PISS	8.7	Where personal information collected and generated during the operation of the People's Republic of China is provided overseas, the personal information controller shall conduct safety assessment in accordance with the methods and relevant standards formulated by the State Administration of Credit and the relevant departments of the State Council, and meet the requirements.

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Regulatory mapping for eCF Requirement ID C37

When third parties are used to provide GxP-related services, formal agreements must exist and include clear statements of the roles and responsibilities of the third party.

Regulation	Paragraph	Description
FDA 21 CFR Part 11 Q&A	B	When these electronic services are used to process data for FDA-regulated clinical investigations, sponsors and other regulated entities should consider whether there are adequate controls in place to ensure the reliability and confidentiality of the data.
FDA 21 CFR Part 11 Q&A	Q12	Sponsors and other regulated entities should obtain service agreements with the electronic service vendor.
Japanese APPI	Article 25	A personal information handling business operator shall, when having provided personal data to a third party ... keep a record pursuant to rules of the Personal Information Protection Commission on the date of the personal data provision, the name or appellation of the third party, and other matters prescribed by rules of the Personal Information Protection Commission.
PMDA EDC Management Sheet version 2	25 to 27	Outsourcing contract (Construction/operation of the EDC System, operation of Help Desk, etc.: <ul style="list-style-type: none"> - Name of vendor/contracted resource - Scope of outsourced services - Date/period of Contract, etc.
EMA eTMF Guideline	3.2a	The sponsor may choose to outsource duties and functions of the sponsor to a CRO. The sponsor remains responsible for the trial and will need to maintain oversight. Therefore, access to the CRO-maintained part of the sponsor TMF (e.g. by remote access to an eTMF) or at least regular access to relevant documents from it will be necessary to fulfil these responsibilities effectively. In conducting contracted duties and functions, the CRO will be generating documentation that should reside in the TMF. The clinical trial contract/agreement and other documents and procedures agreed between all parties should outline the arrangements for the TMF in some detail.
EMA eTMF Guideline	3.2f	If multiple CROs are involved, the sponsor should clearly define expectations regarding the creation, management, exchange or remote

access and retention of documentation amongst CROs. Specific requirements may be put in place when CRO interaction is required. The sponsor should provide CROs access to sponsor essential documents of the TMF that are required by the CRO to execute their delegated duties and functions.

EMA eTMF Guideline	3.3	The investigator/institution may choose to delegate duties and functions related to the conduct of the trial to a third party (e.g. site management organisation or external archive).
EMA eTMF Guideline	3.5.1	Documents demonstrating software validation may be retained by a CRO when the activity has been contracted by the sponsor, but the sponsor should ensure continued access to these documents in the contractual arrangements with the CRO for the required archiving period. Documents relating to the trial-specific software configuration are part of the TMF and it should be determined whether these are maintained/archived by the sponsor or CRO providing this service. Some documents from good manufacturing practice activities should also be defined as part of the TMF, for example, when these relate to the assembly and packaging of the investigational medicinal product (IMP) and confirm, as applicable, compliance with the randomisation schedule and blinding of the trial.
EMA QA GCP Matters 8	1	Any trial-related tasks and functions that are delegated to a third party should be specified in a written contract and made clear between the sponsor, third party and when relevant, with the investigator.
EMA QA GCP Matters 8	2	Due diligence should be exercised from the sponsor to ensure that the distribution of tasks is clearly documented and agreed by the vendor, and that each party has the control and access to the data and information that their legal responsibilities require.
EMA QA GCP Matters 8	3	It is sometimes not stated that the sponsor should have access to conduct audits at the vendor site and that the vendor site could be subject to inspections (by national and international authorities) and shall accept these. In addition, it needs to be specified that vendors shall provide necessary documentation (e.g. qualification documentation prepared by the vendor in relation to the system) when requested during a GCP audit or inspection process.
EMA QA GCP Matters 9	3	A sponsor should amend any contract with vendors to ensure availability of qualification documentation.
EU Annex 11	3.1	When third parties (e.g. suppliers, service providers) are used e.g. to provide, install, configure, integrate, validate, maintain (e.g. via remote access), modify or retain a computerised system or related service or for data processing, formal agreements must exist between the manufacturer and any third parties, and these agreements should include clear statements of the responsibilities of the third party. IT-departments should be considered analogous.
FDA and MHRA	P12	The contracts should include details on maintaining sponsor access to

Data Integrity Discussions		and management of essential documents and central records (e.g., software validation records) and retaining the data to ensure full dynamic data are available.
EU GDPR	Article 28	Processing by a processor shall be governed by a contract or other legal act under Union or Member State law, that is binding on the processor with regard to the controller and that sets out the subject-matter and duration of the processing, the nature and purpose of the processing, the type of personal data and categories of data subjects and the obligations and rights of the controller.
EU GDPR	Article 30	Each controller and, where applicable, the controller representative, shall maintain a record of processing activities under its responsibility.
USA HIPAA	164.504e2iiD	...ensure that any subcontractors that create, receive, maintain, or transmit protected health information on behalf of the business associate agree to the same restrictions and conditions that apply to the business associate with respect to such information;
ICH GCP	4.2.5	The investigator is responsible for supervising any individual or party to whom the investigator delegates trial-related duties and functions conducted at the trial site.
ICH GCP	4.2.6	If the investigator/institution retains the services of any individual or party to perform trial-related duties and functions, the investigator/institution should ensure this individual or party is qualified to perform those trial-related duties and functions and should implement procedures to ensure the integrity of the trial-related duties and functions performed and any data generated.
ICH GCP	5.2.2	Any trial-related duty and function that is transferred to and assumed by a CRO should be specified in writing. ADDENDUM The sponsor should ensure oversight of any trial-related duties and functions carried out on its behalf, including trial-related duties and functions that are subcontracted to another party by the sponsors contracted CRO(s).
ICH GCP	5.5.3b	When using electronic trial data handling and/or remote electronic trial data systems, the sponsor should: b) Maintains SOPs for using these systems. ADDENDUM The SOPs should cover system setup, installation, and use. The SOPs should describe system validation and functionality testing, data collection and handling, system maintenance, system security measures, change control, data backup, recovery, contingency planning, and decommissioning. The responsibilities of the sponsor, investigator, and other parties with respect to the use of these computerized systems should be clear, and the users should be provided with training in their use.
JPMA EDC	4.1	Sponsor has the responsibility of ensuring the quality of entrusted

Guidance		business for vendors and CROs.
JPMA EDC Guidance	4.1.1.1h	If sponsor would like to capture certain electronic data in institute via electronic media, sponsor shall make clear the scope of responsibilities of quality assurance provision of transferring electronic data in a contract, and shall ensure its quality by checking of data.
JPMA EDC Guidance	4.2.1.1.a	<p>Make articles that central laboratories should comply with by contract documents to ensure scope of responsibilities for quality of transferred electronic data and reliability of data.</p> <ol style="list-style-type: none"> 1. Central laboratories shall assure accuracy of analysis results and ensure that laboratory reports to institutes correspond with electronic data sent to sponsors. 2. Arrange procedures of handling electronic data and scope of responsibilities in central laboratories.
MHRA GXP Data Integrity Guidance	6.20	The responsibilities of the contract giver and acceptor should be defined in a technical agreement or contract. This should ensure timely access to data (including metadata and audit trails) to the data owner and national competent authorities upon request. Contracts with providers should define responsibilities for archiving and continued readability of the data throughout the retention period (see archive).
NMPA Clinical Trial DM Guide	2.1.5	Upon election, the sponsor will be entered into a valid contract with the CRO, required in the contract specifying the responsibilities, rights and interests. Trial sponsors when necessary, conduct relevant training for CRO to ensure that the services provided meet its sponsor quality standards. In clinical trials, data management process, trial sponsors are required to carry out the activities for the CRO immediate and effective management, communication and verification, to ensure compliance with mutually agreed process requirements. The quality management plan sponsor must include CRO quality management information, and must be clear processes and desired outcomes.
NMPA PISS	8.2e	<p>When personal information controllers need to share and transfer, they should pay full attention to risks. Sharing or transferring personal information, other than due to acquisition, merger, or restructuring, shall comply with the following requirements:</p> <p>...</p> <p>e) bear the corresponding responsibility for damage caused by sharing or transferring personal information to the legitimate rights and interests of the individual's information subject</p>

Regulatory mapping for eCF Requirement ID C39

Signed electronic records shall contain information associated with the signing that clearly indicates all of the following:

- The name of the signer
- The date and time when the signature was executed
- The meaning (such as creation, confirmation or approval)
- Electronic signatures are permanently linked to their respective record

Regulation	Paragraph	Description
FDA 21 CFR Part 11	50a	(a) Signed electronic records shall contain information associated with the signing that clearly indicates all of the following: (1) The printed name of the signer; (2) The date and time when the signature was executed; and (3) The meaning (such as review, approval, responsibility, or authorship) associated with the signature.
FDA 21 CFR Part 11	70	Electronic signatures and handwritten signatures executed to electronic records shall be linked to their respective electronic records to ensure that the signatures cannot be excised, copied, or otherwise transferred to falsify an electronic record by ordinary means.
FDA 21 CFR Part 11 Q&A	Q18d	When identification of data originators relies on usernames and unique passwords, controls must be employed to ensure the security and the integrity of the authorized usernames and passwords (see 21 CFR 11.10(d)).
FDA 21 CFR Part 11 Q&A	Q23b	To be considered equivalent to full handwritten signatures, electronic signatures must comply with all applicable requirements under part 11.
FDA 21 CFR Part 11 Q&A	Q24	When a document is electronically signed, the electronic signature must be accompanied by a computer-generated, time-stamped audit trail.
PMDA EDC Management Sheet version 2	83	Information included in electronic signature: - Name of signer - Date and time of signature - Meaning of signature (creation, confirmation, approval, etc.)
PMDA EDC	85	Describe the validation mechanism(s) ensuring and preserving

Management Sheet version 2		eSignatures authenticity.
PMDA ERES (Japan)	4.3	Signed materials by electromagnetic records shall contain information associated with the signing that clearly indicates all of the following: <ul style="list-style-type: none"> - The printed name of the signer - The date and time when the signature was executed - The meaning (such as creation, confirmation or approval) associated with the signature.
PMDA ERES (Japan)	4.4	Electronic signatures executed to electromagnetic records shall be linked to their respective electromagnetic records to refrain from injustice operation that the signatures cannot be excised, copied, etc. by ordinary means.
EU Annex 11	14	Electronic records may be signed electronically. Electronic signatures are expected to: <ol style="list-style-type: none"> a. have the same impact as hand-written signatures within the boundaries of the company, b. be permanently linked to their respective record, c. include the time and date that they were applied.
EU Electronic Identification Regulation 910-2014	25	Legal effects of electronic signatures <ol style="list-style-type: none"> 1. An electronic signature shall not be denied legal effect and admissibility as evidence in legal proceedings solely on the grounds that it is in an electronic form or that it does not meet the requirements for qualified electronic signatures. 2. A qualified electronic signature shall have the equivalent legal effect of a handwritten signature. 3. A qualified electronic signature based on a qualified certificate issued in one Member State shall be recognised as a qualified electronic signature in all other Member States.
EU Electronic Identification Regulation 910-2014	26	An advanced electronic signature shall meet the following requirements: <ol style="list-style-type: none"> (a) it is uniquely linked to the signatory; (b) it is capable of identifying the signatory; (c) it is created using electronic signature creation data that the signatory can, with a high level of confidence, use under his sole control; and (d) it is linked to the data signed therewith in such a way that any subsequent change in the data is detectable.
FDA EHR Guidance	V.C.2.f	Use of electronic signatures for records that are subject to 21 CFR part 11 must comply with relevant requirements in that regulation (see 21 CFR 11.2).
FDA Electronic Informed Consent Q&A	Q6a	In order to be considered equivalent to full handwritten signatures, electronic signatures must comply with all applicable requirements under 21 CFR part 11.
JPMA EDC	4.1.1.3.6e	The signature (including handwriting signature) and CRF is linked

Guidance		properly.
JPMA EDC Guidance	4.1.1.4c	The EDC system shall clearly specify the signature time, intended data and meaning of signature. And ensure that the signatures cannot be excised or copied. Signed electronic records shall contain information such as signer, the date and time when the signature was executed and meaning of signature.
JPMA EDC Guidance	4.1.1.4d	When using handwriting signature, ensure that the link between intended electronic records and handwriting signature is certainty.
JPMA EDC Guidance	4.1.1.4e	Clearly identified signature time and intended electronic records and if electronic records are modified, electronic signature shall be executed on the modified records.
JPMA EDC Supplement	3.2.3	An electromagnetic record with an electronic signature shall contain explicit information on all of the following items: <ul style="list-style-type: none"> - First and last name of the signer, - Date and time of when the signature was executed, and - Roles of the signature (e.g. creation, confirmation, approval) The same information must be included in each copy of the eCRF.
MHRA GXP Data Integrity Guidance	6.14	The use of electronic signatures should be appropriately controlled with consideration given to: <ul style="list-style-type: none"> - How the signature is attributable to an individual. - How the act of 'signing' is recorded within the system so that it cannot be altered or manipulated without invalidating the signature or status of the entry. - How the record of the signature will be associated with the entry made and how this can be verified. - The security of the electronic signature i.e. so that it can only be applied by the 'owner' of that signature.
PRC Electronic Signature Law	13b	Electronic signatures are considered reliable, when all of the following conditions are satisfied: (3) Any alteration made to the electronic signatures after the signing is discernible; (4) Any alteration made to the contents and format of the electronic data is discernible.
PRC Electronic Signature Law	5.2	Data that can guarantee a complete, unaltered status of the contents once they come into being. The completeness of electronic data will not be affected by the adding of endorsements or altered forms that take place in the process of the interchange, preservation, and presentation of the data.

Regulatory mapping for eCF Requirement ID C40

There is a process to ensure that in case of data breach, the Sponsor and/or Investigator shall notify the relevant Data Protection supervisory authority.

Regulation	Paragraph	Description
FDA Electronic Informed Consent Q&A	Q10b	If the entity holding the subjects personal information is a covered entity under the Health Insurance Portability and Accountability Act of 1996 (HIPAA) or acting as a business associate of a HIPAA-covered entity, the requirements in the HIPAA Privacy, Security, and Breach Notification Rules apply.
EU GDPR	Article 33.1	In case of data breach, the controller shall not later than 72 hours after having become aware of it, notify the personal data breach to the supervisory authority.
USA HIPAA	164.408a	A covered entity shall, following the discovery of a breach of unsecured protected health information ... notify the Secretary.
NMPA PISS	9.2	<p>Notification of safety incidents</p> <p>Requirements for personal information controllers include:</p> <p>a) The relevant information of the incident should be promptly notified to the affected personal information subject by email, letter, telephone, push notification, etc. When it is difficult to inform the personal information subject one by one, it is necessary to adopt a reasonable and effective way to issue warning information related to the public;</p> <p>b) The content of the notice should include but is not limited to:</p> <ol style="list-style-type: none"> 1) the content and impact of security incidents; 2) Disposal measures taken or to be taken; 3) Advice on the prevention and risk reduction of personal information subjects; 4) Remedial measures provided for the subject of personal information; 5) Contact information of the person in charge of personal information protection and the work organization of personal information protection.

Regulatory mapping for eCF Requirement ID C41

The alignment of a trial-specific eSystem(s) with each protocol amendment should be evaluated and the system updated as needed

Regulation	Paragraph	Description
FDA CSUCI	A3	The computerized systems should be designed: (1) to satisfy the processes assigned to these systems for use in the specific study protocol (e.g., record data in metric units, blind the study), and (2) to prevent errors in data creation, modification, maintenance, archiving, retrieval, or transmission (e.g., inadvertently unblinding a study).
FDA CSUCI	F5b	The effects of any changes to the system should be evaluated and some should be validated depending on risk. Changes that exceed previously established operational limits or design specifications should be validated. Finally, all changes to the system should be documented.
FDA CSUCI	S08	- Change control
EMA eSource Reflection Paper	Topic 1	An instrument used to capture source data should ensure that the data are captured as specified within the protocol. The instrument should be created in a controlled manner to ensure that it conforms to the protocol and is validated. In addition, appropriate change control as part of ongoing validation is needed, in cases where protocol amendments require changes to the instrument. Records of system validation including requirements, design, installation, access and security, testing (e.g. user acceptance testing, installation, operational and performance testing), training and controlled release for use should be maintained.
EU Annex 11	10	Any changes to a computerised system including system configurations should only be made in a controlled manner in accordance with a defined procedure.
EU Annex 11	4.2	Validation documentation should include change control records (if applicable) and reports on any deviations observed during the validation process.
FDA and MHRA Data Integrity Discussions	P10a	A key issue often identified during inspections is that sponsors, CROs, and other third parties do not have adequate controls in place to ensure that the eSystems approved for release in the study (e.g.,

eCRF, ePRO, and IRT) are consistent with the currently approved protocol (initial or subsequently amended).

FDA and MHRA
Data Integrity
Discussions

P14b

SOPs should cover the setup, installation, and use of eSystems. The SOPs should also describe eSystem validation and functionality testing, data collection and handling, system maintenance, system security measures, change control, data backup, recovery, contingency planning, and decommissioning.

ICH GCP

5.5.3b

When using electronic trial data handling and/or remote electronic trial data systems, the sponsor should:

b) Maintains SOPs for using these systems.

ADDENDUM

The SOPs should cover system setup, installation, and use. The SOPs should describe system validation and functionality testing, data collection and handling, system maintenance, system security measures, change control, data backup, recovery, contingency planning, and decommissioning. The responsibilities of the sponsor, investigator, and other parties with respect to the use of these computerized systems should be clear, and the users should be provided with training in their use.

JPMA EDC
Guidance

4.1.1.6.1

The revised system shall be ensured its quality by CSV in accordance with CSV policy. The revising means followings,

- EDC systems version up. (Program change such as functionality addition, modification and elimination to the system, and environment change.)
- Revising input form of electronic CRF. (In case of protocol amendments or bug fix.)
- Program addition, modification and elimination due to automatically query output.

JPMA EDC
Guidance

4.1.1.6.3

In case of revising of related records such as validation deliverables, change control procedures shall be predetermined, and creation or change history of validation deliverables shall be maintained and traceable in chronological order.

JPMA EDC
Supplement

1.5.1.5a

Revision of an ePRO system includes upgrading of the system version, modification of the data entry screen, and addition, correction, deletion of programmed automatic queries, etc. In any case, reliability of the system must be ensured through CSV.

NMPA Clinical
Trial DM Guide

6.1.1.3

Computer system life cycle process and quality control

If using a computer system, must meet the test and let staff needs. In every step of the life cycle of the system are required to perform quality control to ensure that all requirements are documented, tested and met. For example:

- Requirements: To ensure system operation and maintenance covers all users as well as technical, commercial and regulatory requirements.
- System verification process: ensure compliance with the procedures defined verification and record complete and accurate.
- Change control: system life cycle process all changes are subject to

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Regulatory mapping for eCF Requirement ID C42

A change to the core system should be evaluated to determine if it affects trial-specific configurations.

Updates should be made as needed.

Regulation	Paragraph	Description
FDA 21 CFR Part 11	10a	(a) Validation of systems to ensure accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered records.
FDA CSUCI	F5a	The integrity of the data and the integrity of the protocols should be maintained when making changes to the computerized system, such as software upgrades, including security and performance patches, equipment, or component replacement, or new instrumentation.
FDA CSUCI	F5b	The effects of any changes to the system should be evaluated and some should be validated depending on risk. Changes that exceed previously established operational limits or design specifications should be validated. Finally, all changes to the system should be documented.
PMDA EDC Management Sheet version 2	36	Procedure of validating trial-specific setup: Written procedure of validating trial-specific setup
EMA eTMF Guideline	3.2b	The clinical trial contract/agreement and other documents and procedures agreed between all parties should outline the arrangements for the TMF in some detail, such as: - when an eTMF is being used, the details of the system and change control management;
PMDA ERES (Japan)	3.1	Following items shall be established by electromagnetic records system and its operating procedures. In this case, ensuring the system reliability by computerized system validation of the electromagnetic records system is premised.
EU Annex 11	10	Any changes to a computerised system including system configurations should only be made in a controlled manner in accordance with a defined procedure.
EU Annex 11	4.2	Validation documentation should include change control records (if applicable) and reports on any deviations observed during the

validation process.

FDA and MHRA
Data Integrity
Discussions

P14b

SOPs should cover the setup, installation, and use of eSystems. The SOPs should also describe eSystem validation and functionality testing, data collection and handling, system maintenance, system security measures, change control, data backup, recovery, contingency planning, and decommissioning.

ICH GCP

5.5.3b

When using electronic trial data handling and/or remote electronic trial data systems, the sponsor should:

b) Maintains SOPs for using these systems.

ADDENDUM

The SOPs should cover system setup, installation, and use. The SOPs should describe system validation and functionality testing, data collection and handling, system maintenance, system security measures, change control, data backup, recovery, contingency planning, and decommissioning. The responsibilities of the sponsor, investigator, and other parties with respect to the use of these computerized systems should be clear, and the users should be provided with training in their use.

ICH GCP

5.5.3h

ADDENDUM

(h) Ensure the integrity of the data including any data that describe the context, content, and structure. This is particularly important when making changes to the computerized systems, such as software upgrades or migration of data.

JPMA EDC
Guidance

4.1.1.6.1

The revised system shall be ensured its quality by CSV in accordance with CSV policy. The revising means followings,

- EDC systems version up. (Program change such as functionality addition, modification and elimination to the system, and environment change.)
- Revising input form of electronic CRF. (In case of protocol amendments or bug fix.)
- Program addition, modification and elimination due to automatically query output.

JPMA EDC
Supplement

1.5.1.5a

Revision of an ePRO system includes upgrading of the system version, modification of the data entry screen, and addition, correction, deletion of programmed automatic queries, etc. In any case, reliability of the system must be ensured through CSV.

NMPA Clinical
Trial DM Guide

6.1.1.3

Computer system life cycle process and quality control

If using a computer system, must meet the test and let staff needs. In every step of the life cycle of the system are required to perform quality control to ensure that all requirements are documented, tested and met. For example:

- Requirements: To ensure system operation and maintenance covers all users as well as technical, commercial and regulatory requirements.
- System verification process: ensure compliance with the procedures defined verification and record complete and accurate.
- Change control: system life cycle process all changes are subject to

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Regulatory mapping for eCF Requirement ID C43

There should be a process to periodically affirm the continued suitability of a deployed computerized system taking into account changes in risk, users, roles and protocol.

Regulation	Paragraph	Description
FDA CSUCI	F5a	The integrity of the data and the integrity of the protocols should be maintained when making changes to the computerized system, such as software upgrades, including security and performance patches, equipment, or component replacement, or new instrumentation.
FDA CSUCI	F5b	The effects of any changes to the system should be evaluated and some should be validated depending on risk. Changes that exceed previously established operational limits or design specifications should be validated. Finally, all changes to the system should be documented.
EMA eSource Reflection Paper	Topic 1	An instrument used to capture source data should ensure that the data are captured as specified within the protocol. The instrument should be created in a controlled manner to ensure that it conforms to the protocol and is validated. In addition, appropriate change control as part of ongoing validation is needed, in cases where protocol amendments require changes to the instrument. Records of system validation including requirements, design, installation, access and security, testing (e.g. user acceptance testing, installation, operational and performance testing), training and controlled release for use should be maintained.
EU Annex 11	11	Computerised systems should be periodically evaluated to confirm that they remain in a valid state and are compliant with GMP. Such evaluations should include, where appropriate, the current range of functionality, deviation records, incidents, problems, upgrade history, performance, reliability, security and validation status reports.
FDA Electronic Informed Consent Q&A	Q2b	OHRP encourages investigators to apply a risk-based approach to the consideration of subject identity.
EU GDPR	Article 32.1d	A process for regularly testing, assessing and evaluating the effectiveness of technical and organisational measures for ensuring the security of the processing.

Regulatory mapping for eCF Requirement ID C44

For eTMF, the audit trail additionally captures accessing of records.

Regulation	Paragraph	Description
EMA eTMF Guideline	4.1.3f	In this situation there should be procedures and controls in place that demonstrate at all times when versions of documents were made available to the investigator/institution and when these documents were accessed (e.g. through an audit trail) and implemented by the investigator/institution.

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