

Audit Report

Version 0.1, dated **XX/XX/20XX**

Audit type: Data Management Audit

Audit performed by: **XXX**, Auditor, SUNNIKAN Consulting

Audit requested by: **XXX**

Audited Systems : **XXX**

Company audited : **XXX**

Adresse : **XXX**

Audit dates : **XX/XX/20XX**

XXX

Lead Auditor
Sunnikan Consulting

Date

XXX

Auditor
Sunnikan Consulting

Date

**AV : à mettre à jour avec : Italie - Decree March 31, 2008 - Definition of minimum
requisites for contract research organizations (CROs) in the sector of clinical trials of
medicinal products. (Décret indiqué par l'Afssaps lors d'un groupe de travail Afssaps du
25 juin 2009)**

Table des matières

1	Audit context	3
2	Audit Methodology.....	3
2.1	Audit Objectives.....	3
2.2	Audit Agenda.....	3
3	Classification of the audit findings	4
4	Executive summary	5
6	The service provider	6
7	Data Management.....	6
7.1	Regulations and references.....	6
7.2	Data Protection	7
7.3	Data Management Procedures.....	7
7.4	Resources devoted to Data Management.....	7
7.5	Case Report Form Prototype Design	8
7.6	Paper CRF production	8
7.7	eCRF.....	8
7.8	Data Management Plan.....	9
7.9	In-house Data Management System	10
7.10	Annotated CRF	10
7.11	Database Design.....	10
7.12	Database Hosting.....	11
7.13	Computerized System Business Continuity Plan	11
7.14	Data Entry Design.....	11
7.15	Clinical Trial Change Control.....	11
7.16	Data Receipt.....	12
7.17	Data Review Before Data Entry.....	12
7.18	Data Entry.....	13
7.19	Data Translation.....	14
7.20	Data Coding.....	14
7.21	Data Query Management.....	16
7.22	Audit Trail.....	16
7.23	Electronic data from third party.....	17
7.24	Database on-line Quality Controls	17
7.25	Reconciliation with SAE database	18
7.26	Blind Review.....	18
7.27	Database closure / lock	18
7.28	Database unblinding.....	18
7.29	Data Export.....	19
7.30	Data Management Report.....	19
7.31	Specific Aspects of "Remote Data Entry" Systems (e-CRF, IWRS)	20
7.32	Data management Computerized System Validation	22
7.33	Validation of the computerized system "SSS"	30
7.34	Additional Documentation for systems non-developed in-house.....	37
7.35	Specific Documentation for the validation of the clinical databases management system.....	37
7.36	Specific Documentation for the validation of a clinical data entry system.....	42
7.37	Specific Documentation for validation of the electronic data collection system ("Remote Data Entry").....	43
7.38	Change Management.....	44
7.39	Security.....	45
8	Curriculum Vitae de l'Auditeur	46

1 Audit context

Within the framework of its obligations in terms of research and clinical development, LABO PHARMA wanted to achieve a quality audit of activities / of qualification / a follow-up audit of the provider YYY.

- Audit requested by? within the framework of ...
- Previous Audits: when and by whom, findings?
- Possible Inspection: when, who and findings?
- Major changes since the last audit: standards, organization, staff...

- ☐ The sub-contractor is working for the Sponsor since
- ☐ The sub-contractor has never experienced working for the Sponsor
- ☐ The Services provided are...
- ☐ The Contract Research Organization is audited previously.
- ☐ The Contract Research Organization has never been audited by the Sponsor.
- ☐ The corrective actions are addressed.
- ☐ There is a recent major change (acquisition / takeover)...
- ☐ These changes affected: staff, location, procedures...

2 Audit Methodology

2.1 Audit Objectives

The aim of the audit of the system XXX is to assess:

- the compliance of the quality system with the applicable references,
- the adequacy of the quality system elements with the clinical project,
- the compliance of XXX with the applicable procedures,
- the adequacy of the various elements of the XXX process with the expected goal

The audit is conducted according to the main applicable standards:

- ICH Good Clinical Practices (CPMP/ICH/135/95),
- Regulations applicable in France, including French Good Clinical Practices (Décision du 24 novembre 2006)

2.2 Audit Agenda

The audit, performed by J, SUNNIKAN Consulting, took place in YYY offices on Date.

2.2.1 Opening meeting

An opening meeting was held in the presence of:

- Status, name and duties
-

2.2.2 Audit

On the basis of the project YYYY, the audit has achieved the following evaluations:

- organization of the department,
- training,
- system / XXX of the process.

The CRO audit consisted of a review of:

- the CRO organization
- the personnel qualification
- the computerised systems
- the Quality documentation for the processes xxx and yyyy
- the facilities
- the services provided (xxx, yyyy)

Interviews, site visits and documentation review are performed during the audit.

2.2.3 Closing meeting

A closing meeting took place to present and discuss the audit findings in the presence of:

- Status, name and duties
-

2.2.4 Audit report

The improvement suggestions included in this report are only advices. They are not based on a prior assessment of costs / timelines / quality objectives of the CRO. They do not represent by themselves the appropriate actions plan and should be considered within the global context.

3 Classification of the audit findings

In this report, the audit findings are classified according to the following classification:

- **"Critical Non conformity":**
 - Conditions, practices or processes that adversely affect the rights, safety or well being of the subjects and/or the quality and integrity of data. Critical observations are considered totally unacceptable. Observations classified as critical may include a pattern of deviations classified as major, bad quality of the data and/or absence of source documents. Fraud belongs to this group.
- **"Major Non conformity":**
 - Conditions, practices or processes that might adversely affect the rights, safety or well-being of the subjects and/or the quality and integrity of data. Major observations are serious deficiencies and are direct violations of GCP principles. Observations classified as major, may include a pattern of deviations and/or numerous minor observations"
- **"Minor Non conformity ":**
 - Conditions, practices or processes that would not be expected to adversely affect the rights, safety or well being of the subjects and/or the quality and integrity of data. Many minor observations might indicate a bad quality and the sum might be equal to a major finding with its consequences.
- **"Critical Non conformity":**
 - Suggestions for improvement.

4 Executive summary

LABO PHARMA is a pharmaceutical company

YYY is a Contract Research Organization specialized in clinical research / Center Phase I, located in ...

An audit was requested by LABO PHARMA and performed by [redacted], SUNNIKAN Consulting.

SUNNIKAN Consulting is requested by LABO PHARMA to conduct the audit system XXX.

The audit is performed by [redacted] on the [redacted] Date.

The objective of the audit is to assess the compliance of the quality system elements regarding [redacted] compared to the applicable requirements, the compliance of actions regarding [redacted] compared to the elements of quality system, compliance of [redacted] compared to applicable procedures, the adequacy of the different elements of the process of XXX compared to the intended goal.

Overall, it was noted that

According to this audit, the subcontractor quality system is considered to be compliant with the applicable regulations, provided that the action plan related to the following findings are in place:

The main findings concern the following:

6 The service provider

- ☐ The sub-contractor is a service provider in the following fields:
- ☐ The sub-contractor exists since
- ☐ The sub-contractor is located in
- ☐ The main activities of the sub-contractor are:
 -
- ☐ The "business volume".
- ☐ The organization of the Contract Research Organization is described in a organizational chart dated
- ☐ The chart is updated.
- ☐ The chart is not updated.
- ☐ If applicable, the Contract Research Organization authorization is present and adequate.
- ☐ The number of persons working for the Contract Research Organization is...
- ☐ The staff turnover rate is (past three years)

Finding #1.	Improvement suggestion

7 Data Management

7.1 Regulations and references

- "Décision du 24 novembre 2006 fixant les règles de bonnes pratiques cliniques pour les recherches biomédicales portant sur des médicaments à usage humain"
- "Décision du 5 janvier 2006 portant homologation d'une méthodologie de référence pour les traitements de données personnelles opérés dans le cadre des recherches biomédicales (méthodologie de référence MR-001)"
- "Norme ISO 27002:2005 : Technologies de l'information - Techniques de sécurité - Code de bonne pratique pour la gestion de la sécurité de l'information"
- Note for guidance on Good Clinical Practice, CPMP/ICH/135/95, E6, post-Step 4, September 1997
- Good Clinical Data Management Practices, Published April 2011, Society For Clinical Data Management (SCDM)"
- Guideline for Standard Operating Procedures for Good Statistical Practice in Clinical Research, versions 1-6, June 1999 – July 2001, Statisticians in the Pharmaceutical Industry (PSI)
- GAMP (Good Automated Practices), a risk-based approach to compliant GxP computerized systems, version 5, April 2008, ISPE
- Computerised systems validation in Clinical Research, a practical guide, 2nd edition, February 2004, CR-CSV Working Party
- FDA Guidance for Industry - Computerized Systems used in Clinical Investigations, May 2007
- Guidance for Industry - Part 11, Electronic Records; Electronic Signatures — Scope and Application, FDA, August 2003
- 21 CFR Part 11 "Electronic Records; Electronic Signatures ; Final Rule, Federal Register, 4–1–03 Edition"

7.2 Data Protection

- ☐ The "Conformity Assessment to the official methodology" ("Engagement de conformité à la méthodologie de référence publié par la CNIL") regarding Data Protection is available and signed.
- ☐ The "Conformity Assessment to the official methodology" ("Engagement de conformité à la méthodologie de référence publié par la CNIL") regarding Data Protection is not available.
- ☐ The assessment is regularly checked and documented.
- ☐ The assessment is not regularly checked.
- ☐ For each clinical trial a check is performed to confirm that the assessment is applicable and this check is documented.
- ☐ For each clinical trial a check is not performed to confirm that the assessment is applicable.

7.3 Data Management Procedures

- ☐ The data management processes are described in procedures and/or other quality documents.
- ☐ Some processes are not fully described in a procedure although the operational steps are known and apply by the staff.

7.4 Resources devoted to Data Management

- ☐ The human resources dedicated to the Data management System are sufficient and adapted.

Specify the resources

- ☐ The human resources dedicated to Data management System are not sufficient and not adapted.
- ☐ The manner provided in case of Data Manager Change during the project can ensure the project continuity (deadlines and quality).

- ☐ The used data management softwares are the followings:

- Data entry: ...
- Data management: ...
- Other (specify)

- ☐ These systems are validated (see "computer system validation" part):

-

- ☐ There is no validated software for data entry / data management / electronic-CRF / IVRS / IWRS.

-

- ☐ The staff is trained in the use of systems.
- ☐ The staff is not trained in the use of systems.

- ☐ There is no validated software for data entry / data management / electronic-CRF / IVRS / IWRS.

7.5 Case Report Form **Prototype** Design

Commenté [LH1]: draft?

☐ The management of the CRF design is described in the procedure "", version __, dated __.

☐ The management of the CRF design is not described in a procedure...

☐ The CRF is designed from:

- ☐ the Protocol
- ☐ a list of specifications ("sponsor specifications")
- ☐ internal standards
- ☐ sponsor standards.

☐ The CRF is validated internally (before submission tot the sponsor).

The validation covers the following:

- ☐ check the consistency with the Protocol
- ☐ medical validation
- ☐ other (specify)

☐ These validation is documented.

☐ The CRF is approved by the Sponsor. This approbation is documented.

☐ The CRF is not approved by the Sponsor.

☐ If applicable, how to integrate sponsor comments help ensure a comprehensive consideration of these comments. This step is documented with justification of the comments commentaires eventually rejected.

☐ If there are amendments to the Clinical Trial Protocol, the CRF is updated. The updated version is validated.

☐ There is no CRF History Form.

☐ The versions of the CRF are correctly identified.

7.6 Paper CRF **production**

7.7 eCRF

7.7.1 eCRF design

The procedure describing the eCRF design is available.

The core is validated

There are documented specifications:

- validated CRF prototype (paper CRF)
- database structure = CRF annotated
- User profiles and access rights
- Data consistency checks:
 - online
 - off line
- services:

- availability of the eCRF
- maintenance
- training
- hotline
- any indicators...,
- eCRF user guidelines

These specifications are validated by the sponsor

The documents used for eCRF design (study protocol) are version controlled and documented

The eCRF design is compliant with the "règles de creation des cahiers d'observation"

The study specificities (language, indication, Investigational medicinal product) are taken into account

A checklist is available for the QC

7.8 Data Management Plan

☐ The Data Management Plan handling (written, approval, update processes, etc.) is described in the procedure " _ ", version __, dated __.

☐ The Data Management Plan handling (written, approval, update processes, etc.) is not addressed in a procedure.

☐ The Data Management Plan is updated during the study.

☐ The Data Management Plan history is documented in the " _ ".

☐ The Data Management Plan history is not documented.

☐ The Data Management Plan is internally validated (before the submission to the sponsor).

☐ The Data Management Plan is not internally validated (before the submission to the sponsor).

☐ The Data Management Plan approval is documented.

☐ The Data Management Plan approval is not documented.

☐ The Data Management Plan covers the following topics:

- ☐ roles and responsibilities and specially specification of the person who has approval authority for the database
- ☐ a "data flow chart" describing the data circuit of the study.
- ☐ level of monitoring carried out on the CRFs before transmission to the data management
- ☐ database design and documentation
- ☐ details of coding systems to be used
- ☐ conventions for the naming of variables and tables
- ☐ requirements for derived data fields (e.g. totals, averages, means, medians, etc.)
- ☐ specific details of automatic data validation/plausibility checks (i.e. checks of the data consistency using study-specific computer programs)
- ☐ handling of case report forms
- ☐ handling of missing data, giving due attention to the primary outcome and safety data
- ☐ procedure for query resolution, i.e. the generation and logging of queries
- ☐ documentation of all stages of data management (data circuit, data entry, coding...)

- ☐ details of quality control checks, taking account of which efficacy and safety data are critical
- ☐ details of the software and hardware being used
- ☐ details of any electronically transferred data
- ☐ interim data management status reports (for internal use, particularly in large, long term studies)

☐ The Data Management Plan does not address the following topics:

-

7.9 In-house Data Management System

7.10 Annotated CRF

7.11 Database Design

Study-specific programming:

"best practices include identifying all intended uses of study-specific programming and testing each logic condition in the programming based on a validation plan. Algorithms for variable derivations occurring within the database must be validated"

Page 13 of 20 chapter "Database validation, Programming and standards "

"Data cleaning or validation:

Data cleaning or validation is a collection of activities used to assure the validity and accuracy of the data. Activities for data cleaning may include manual review of the data or computer checks designed to identify inaccurate or invalid data using ranges, completeness, protocol violations and consistency checks, or aggregate descriptive statistics that reveal unusual patterns in the data.

Page 7 of 12 chapter "Data entry and data processing" (Good Clinical Data Management Practices, Published July 2009, Society For Clinical Data Management (SCDM))

☐ The database design is addressed in a document (procedure, Data Management Plan?)

☐ The database design is not addressed in a document.

☐ The database design includes the following steps:

- ☐ utilization of standard data architectures (e.g., data structure libraries available, standards published by the CDISC)
- ☐ database testing and validation
 - ☐ Testing: entering test or "dummy" data, or loading test data transfer files, or ...
 - ☐ Testing performed on all data
 - ☐ edit checks programming and their validation
- ☐ database change control management
- ☐ database access rights management
- ☐ documentation of the process

☐ The database design does not include the following steps:

-

-
- ☐ The database specifications are addressed in a document that provides at a minimum the following information for each variable:
 - Name and label
 - Dataset label, panel, or other logical group to which the data belongs
 - Type (e.g., numeric, character, decimal, date)
 - Length
 - Definitions for all coded values included in code lists
 - Algorithms for variables derived or calculated within the database
- ☐ The database specifications are not addressed in a document.
- ☐ The database can be exported in a SAS format.

7.12 Database Hosting

Hosting specificities (security, backup...) appropriate

7.13 Computerized System Business Continuity Plan

- Backup and restoration system
- Plan de Reprise Informatique

7.14 Data Entry Design

7.14.1 Data Entry Screens

- ☐ The data entry screens design is addressed in a procedure ...
- ☐ The data entry screens design is not addressed in a procedure ...
- ☐ The procedure addresses the following topics:
 - ☐ production of an annotated CRF to document the tables, variable item names, forms, visits and any other object, codelists...)
 - ☐ checking of data entry screens conformity with the CRF:
 - ☐ Direct checking (manual validation)
 - ☐ documentation of data entry tests using the first completed CRFs
 - ☐ management of data entry screens design non-conformities (identified during the test)
 - ☐ handling of data entry screens modification (e.g. in case of protocol amendment),
 - ☐ set-up of automatic controls supporting the data entry (e.g. automatic control on the format)
 - ☐ automatic controls validation and documentation.
- ☐ The procedure does not address the following topics:
 -

7.14.2 Data Entry Roles and Access Rights

7.15 Clinical Trial Change Control

- ☐ Le processus de maîtrise des modifications du système de data management est décrit dans la procédure...
- ☐ Le système de maîtrise des modifications du système de data management n'est pas décrit dans une procédure.

☐ Le système de maîtrise des modifications prévoit :

- ☐ un suivi des modifications et de leur traitement
- ☐ une analyse d'impact, documentée, incluant une analyse de risque si approprié, des demandes avant réalisation des modifications :
 - ☐ impact sur la base de données
 - ☐ impact sur les données
 - ☐ impact sur la documentation (du système, de l'étude)
 - ☐ impact sur les utilisateurs...
- ☐ une documentation de cette analyse d'impact
- ☐ la réalisation d'opérations de validation appropriées.*

7.16 Data Receipt

"6. DATABASE

... 4. For every database, there should be a **detailed data trail** allowing an external auditor to follow the progress of each data point from the original case report form, and any other original sources used, to the final electronic database. Items that should be considered in this process are:

- internal logging and tracking of case report forms and other original source data
- documentation of query handling procedures (internally and with the investigator)..." (Guideline for Standard Operating Procedures for Good Statistical Practice in Clinical Research, versions 1-6, June 1999 – July 2001, Statisticians in the Pharmaceutical Industry (PSI))

☐ The handling of CRFs, queries and other data received by the data management department is addressed in a procedure...

☐ The handling of CRFs, queries and other data received by the data management department is not addressed in a procedure...

☐ The procedure addresses the following topics:

- ☐ CRFs check at receipt (partial or total)
- ☐ documentation of the check
- ☐ Actions taken in case of issues
- ☐ Acknowledgements of receipt returned to the sender
- ☐ CRFs / queries / other data tracking tools
- ☐ CRFs storage
- ☐ CRFs transfer between departments

☐ The procedure does not address the following topics:

-

☐ The storage of the CRFs is acceptable.

☐ The storage of the CRFs is not acceptable.

7.17 Data Review Before Data Entry

☐ A CRF review is performed before data entry for medical review / translation / other reason :

☐ The CRF review is described in a procedure xxx

☐ The CRF review is not described in a procedure.

☐ Manual Queries are generated after CRF review and these queries are tracked.

☐ Manual Queries are generated after CRF review but these queries are not tracked.

7.18 Data Entry

"6. DATABASE ... 6 Techniques should exist to ensure that the electronic database provides a complete and accurate representation of the raw data. (See also point 3 of this GSOP.) These techniques may consist of the following: - double data entry Note that double data entry is the normal practice, but it may not necessarily be used. There should be an indication of how data comparisons will be made and who will make the decisions in the case of discrepancies. - programmed inclusion of electronic raw data - manual checking of the database performed after double (or single) data entry Consideration should be given to the percentage and/or number of fields to be checked, the tolerable error rate, who will perform the manual checks and what action will be taken if the acceptable error rate is not achieved. - manual or automatic coding of data in case report forms and the methods of checking the resulting data in the database - documentation of methods of database validation and procedures for correction of errors." (Guideline for Standard Operating Procedures for Good Statistical Practice in Clinical Research, versions 1-6, June 1999 – July 2001, Statisticians in the Pharmaceutical Industry (PSI)) "Chapter Data Entry and Data Processing ... Data Entry The data entry process should address the data-quality needs of the trial. Commonly used data-entry processes include the following: 1. Independent double data entry with a third person: two people enter the same data independently and a third person resolves any discrepancies between first and second entry; 2. Double data entry with blind verification: two people enter the data independently and any discrepancies are resolved during second entry; 3. Double entry with interactive verification: the second entry operator resolves discrepancies between first and second entry and is aware of the first entered values; 4. Single entry with a manual review; and 5. Single entry with no manual review..." (Good Clinical Data Management Practices, Published July 2008, Society For Clinical Data Management (SCDM))

- ☐ Data entry is addressed in a procedure...
- ☐ Data entry is not addressed in a procedure...
- ☐ The procedure covers the following steps:
 - Data entry processes (double, single, etc.)
 - Data entry manual production / update and its validation
 - Data entry training and its documentation

- Data entry system access rights management
- ☐ The procedure does not cover the following steps:
 -
- ☐ The data entry process is independent double data entry with a third person (two independent files, two independent operators, a third person to resolves discrepancies).
- ☐ The data entry process is independent double data entry with blind verification (two people enter the data independently and any discrepancies are resolved during the second entry)
- ☐ The data entry process is double data entry with interactive verification (the second entry operator resolves discrepancies between first and second entry and is aware of the first entered values)
- ☐ The double data entry is effective and documented through:
 - ☐ Data Entry Operators training,
 - ☐ data comparison methodology
 - ☐ discrepancies management
- ☐ The double data entry is not documented appropriately.
- ☐ The data entry process is single data entry (with or without manual review / full or partial check)
- ☐ The single data entry is effective and documented through:
 - ☐ Data Entry Operators training,
 - ☐ data check methodology
 - ☐ entry errors management
- ☐ The single data entry is not documented appropriately.
- ☐ A data entry manual is prepared for each clinical study.
- ☐ No data entry manual is prepared.
- ☐ The management of specific data (comments, lab results, normal values etc.) is addressed in a procedure / manual.
- ☐ The management of specific data (comments, lab results, normal values etc.) is not addressed in a procedure / manual.

7.19 Data Translation

- ☐ The management of the translation is addressed in a procedure.
- ☐ The management of the translation is not addressed in a procedure.
- ☐ The translations are validated and the validation is appropriately documented through...

7.20 Data Coding

"Medical Coding:

If textual or free text data are collected and reported, they usually must be coded before they can be aggregated and used in summary analyses. Medical history, adverse events, procedures, and medications are usually coded with standard dictionaries. The coding process consists of matching text collected on the CRF to terms in a standard dictionary. Frequently, items that appear on a CRF cannot be matched, or coded without clarification from the site. For example, ulcers require a

location (gastric, duodenal, mouth, foot, etc.) to be coded." (Good Clinical Data Management Practices, Published July 2008, Society For Clinical Data Management (SCDM))

"Dictionary Selection:

One common use of a dictionary is to code adverse events. Recognizing that pharmaceutical and biotech companies are increasingly conducting global trials and submitting marketing applications to multiple regulatory agencies, an initiative to establish a global dictionary was undertaken by the International Conference on Harmonisation (ICH), resulting in **MedDRA**. **This dictionary is especially useful in the coding of clinical trial data and the electronic transmission of adverse event reporting.** The Food and Drug Administration is currently using MedDRA in its Adverse Events Reporting Systems (AERS). **It is planned that MedDRA will eventually replace the multiple coding dictionaries in use, such as COSTART and WHO-ART, as well as proprietary variations of those dictionaries that have been developed by the sponsors of clinical trials...**

Medications used by study participants prior to or concurrently with study materials are also commonly coded to facilitate the reporting and analysis of possible drug interactions. A variety of dictionaries or medication references provide information about prescription, generic, over-the-counter (OTC) medications, and herbal supplements. The references used for coding in a particular study should be selected based upon the scope of medications included, how recently the reference has been updated, the frequency of updates to include the release of new medications, and the coding information available in the dictionary. Such coding information may include generic terms, active ingredients, indications, or Anatomical Therapeutic Chemical (ATC) classification. **WHODRUG is commonly used for coding medications.**

Other CRF data may be coded using established medical or clinical references (e.g., medical history body classifications, medication route of administration, adverse event severity and relationships) or in-house determined code lists (e.g., gender, action taken). These same code lists should be utilized across similar studies and projects to ensure consistent analysis and reporting of coded data." (Good Clinical Data Management Practices, Published July 2008, Society For Clinical Data Management (SCDM))

- ☐ The data coding and the use of dictionaries are addressed in a procedure...
- ☐ The data coding and the use of dictionaries are not addressed in a procedure.
- ☐ The procedure covers the following topics:
 - Dictionaries selection and versions management
 - Dictionaries installation and maintenance
 - Dictionaries list
 - Data coding process (autoencoding / manual coding / hybrid approach, coding validation methodology)
- ☐ The dictionaries used for data coding are:
 - ☐ MedDRA (version 11.1)
 - ☐ WHODRUG (version 2008)
 - ☐ WHO-ART (version 081)
 - ☐ COSTART (version 5.0)
 - ☐ ICD9
- ☐ The licenses for all the dictionaries used are available.
- ☐ The licenses for the coding dictionaries used are not all available.
- ☐ The coding is checked/approved (review of line listings) by... (Comparison raw data versus coded data) and documented.
- ☐ The coding is not checked / approved.
- ☐ The medical coding is performed / approved by a person with medical expertise.
- ☐ The persons in charge of coding are trained on the dictionary utilization.

7.21 Data Query Management

- ☐ The edit checks are run ... (frequency, period of time)
- ☐ Handling of data queries is addressed in a procedure...
- ☐ Handling of data queries is not addressed in a procedure...
- ☐ The procedure covers the following topics:
 - ☒ check of issued data queries accuracy prior the Investigators' review
 - ☐ data queries tracking
 - ☐ data queries workflow
 - ☐ entry of resolved queries in the database
 - ☐ Self-Evidence Corrections (SEC) management
 - list of SEC for each clinical trial (approval process, transmission to the Investigators, etc.)
 - entry of SEC in the database
- ☐ The procedure does not cover the following topics:
 -

7.22 Audit Trail

"An audit trail should reflect all deletions, updates, or additions to data after initial entry. The audit trail should reflect the date and time of the change and the user making the change. There should be clear documentation of the change as well as the reason for the change." (Chapter "Data entry and Data processing" - Good Clinical Data Management Practices, Published July 2009, Society For Clinical Data Management (SCDM))

Cf. (Code of Federal Regulations, Title 21, Part 11, Electronic Records; Electronic Signatures. Washington, DC: US Government Printing Office; 1997.

"6. DATABASE

... 4. For every database, there should be a **detailed data trail** allowing an external auditor to follow the progress of each data point from the original case report form, and any other original sources used, to the final electronic database. Items that should be considered in this process are:

"...

- techniques and documentation for editing errors on the database

- processing and documentation of data errors after delivery of the database to the statistician

- processing and documentation of data not included in the initial database design." (Guideline for Standard Operating Procedures for Good Statistical Practice in Clinical Research, versions 1-6, June 1999 – July 2001, Statisticians in the Pharmaceutical Industry (PSI))

- ☐ The management of the audit trail is addressed in a procedure.
- ☐ The management of the audit trail is not addressed in a procedure.
- ☐ The procedure addresses the following topics:
 - Documentation of access rights attribution / modifications
 - Audit trail modalities (start at the first entry, stop at the database freeze / same or different trail for data entry system & data management system, etc.)
 - Audit trail archiving (tamper-proof format)

- ☐ The audit trail reflects:
 - all deletions, updates or additions to data after initial entry,
 - initial and modified data
 - data and time of the change
 - user making the change
 - reason of the change

- ☐ The procedure does not address the following topics:
 -

In case of EDC:

- ☐ The audit trail is regularly checked by:
 - the Sponsor / monitor
 - the users
- ☐ The audit trail check is documented through...
- ☐ The audit trail check is not documented.

7.23 Electronic data from third party

- ☐ The collection of electronic data from third party is addressed in a procedure...
- ☐ The collection of electronic data from third party quality is not addressed in a procedure...
- ☐ The procedure covers the following topics:
 - Loading specifications (mandatory fields, critical variables, data format, etc.)
 - Collection and transfer tests and related documentation
 - Process to safeguard the blind when primary efficacy data are collected externally
 - Quality control at each stage of data handling
 - Management of data discrepancies / data updates
 - Validation of the programs and systems used for processing the data
 - Documentation of the process
- ☐ The procedure does not cover the following topics:
 -

7.24 Database on-line Quality Controls

- ☐ The on-line quality controls on the database are described in the procedure...
- ☐ The on-line quality controls on the database are not described in a procedure.
- ☐ The procedure covers the following topics:
 - ☐ scope of the quality controls: only some specific data (primary efficacy criteria, SAE, AE...) or the whole database
 - ☐ roles and responsibilities
 - ☐ quality controls documentation
 - ☐ Error rates calculation
 - ☐ Database acceptance criteria
- ☐ The procedure does not cover the following topics:
 -

7.25 Reconciliation with SAE database

- ☐ The reconciliation between the clinical database and the SAE database is addressed in a procedure...
- ☐ The reconciliation between the clinical database and the SAE database is not addressed in a procedure...
- ☐ The procedure covers the following topics:
 - ☐ roles and responsibilities
 - ☐ frequency and method (listings manually reconciled through direct comparison or databases programmatically compared with listing of differences reviewed manually)
 - ☐ validation of reconciliation programs if any
 - ☐ management of discrepancies
 - ☐ databases update
 - ☐ reconciliation documentation
- ☐ The procedure does not cover the following topics:
 -

7.26 Blind Review

- ☐ The blind review is addressed in a procedure...
- ☐ The blind review is not addressed in a procedure...
- ☐ The blind review is documented (minutes, report, etc.) with an actions plan
- ☐ The listings required for the blind review are prepared by...

7.27 Database closure / lock

"6. DATABASE

12. There must be a clear database closure process, including specification and proof of minimum data standards and of removal of write access and when the randomisation blind was broken.

The process for re-opening and re-closure of the database must also be clear."
 (Guideline for Standard Operating Procedures for Good Statistical Practice in Clinical Research, versions 1-6, June 1999 – July 2001, Statisticians in the Pharmaceutical Industry (PSI))

- ☐ The database closure is addressed in a procedure...
- ☐ The database lock is not addressed in a procedure.
- ☐ The procedure covers the following topics:
 - ☐ Requirements to close the database (e.g. SAE reconciliation performed, all data received and processed, all queries resolved)
 - ☐ approval process (roles and responsibilities, documentation)
 - ☐ Removal of database access
 - ☐ management of errors found after the database closure
 - ☐ re-opening conditions and procedure
- ☐ The closure is performed before the unblinding.
- ☐ The closure is performed after the unblinding.

7.28 Database unblinding

- ☐ The database unblinding is performed by (Statistician / Data Manager)

- ☐ The randomization list loading is controlled and this control is documented.
- ☐ The randomization list loading is not controlled.
- ☐ The authorization to unblind is documented.
- ☐ The authorization to unblind is not documented.
- ☐ The process of unblinding is described in a procedure.
- ☐ The process of unblinding is not described in a procedure.
- ☐ The interim analyses are carried out by a Statistician not otherwise involved in the trial to minimize access to unblinded information and treatment codes.

7.29 Data Export

"6. DATABASE

...9... the stored database may be passed over to another database for analysis, e.g. from ORACLE to SAS. In this case there must be full documentation and QC of the transfer process." (Guideline for Standard Operating Procedures for Good Statistical Practice in Clinical Research, versions 1-6, June 1999 – July 2001, Statisticians in the Pharmaceutical Industry (PSI))

- ☐ The data transfer process for analysis is addressed in a procedure...
- ☐ The data transfer process for analysis is not addressed in a procedure...
- ☐ The data transfer is controlled and the quality control is documented.
- ☐ There is no quality control on the data transfer.

7.30 Data Management Report

"6. DATABASE

10. The data manager should ensure that a data management report is provided with the final electronic database. The report should describe the procedures and conventions that were followed in the preparation of the database, and include similar topics to those in the data management plan. The report should also include:

- a full field listing and description of the file structure of the electronic database
- reference ranges and units for laboratory data
- a list and brief description of all programs run on the data
- level of errors found at each stage of checking the data
- general comments on data quality and significant problems encountered with the data
- a detailed list of any unresolved data queries
- a statement of any queries/errors which have not been corrected on the database
- a statement of the storage location of the electronic database." (Guideline for Standard Operating Procedures for Good Statistical Practice in Clinical Research, versions 1-6, June 1999 – July 2001, Statisticians in the Pharmaceutical Industry (PSI))

- ☐ The handling of the data management report is described in a procedure.

- ☐ The handling of the data management report is not described in a procedure.
- ☐ The data management report includes:
 - ☐ procedures and conventions that were followed in the preparation of the database
 - ☐ similar topics to those in the data management plan
 - ☐ a full field listing and description of the file structure of the electronic database
 - ☐ reference ranges and units for laboratory data
 - ☐ a list and brief description of all programs run on the data
 - ☐ level of errors found at each stage of checking the data
 - ☐ general comments on data quality and significant problems encountered with the data
 - ☐ a detailed list of any unresolved data queries
 - ☐ a statement of any queries/errors which have not been corrected on the database
 - ☐ a statement of the storage location of the electronic database
- ☐ The data management report does not include:
 -

7.31 Specific Aspects of "Remote Data Entry" Systems (e-CRF, IWRS)

"Chapter Data Entry and Data Processing

... Data Entry

... For heads-down data entry, the skill emphasis is on the number of keystrokes made and specific training on the database to be utilized. With EDC systems that utilize single entry, the skill emphasis is on the understanding of the trial. Site personnel entering data in an EDC system have received training on the specific system being used in the study as well as on study-specific issues..." (Good Clinical Data Management Practices, Published July 2008, Society For Clinical Data Management (SCDM))

Particular attention may be given the following topics:

- ☐ User management is described in the procedure ""
- ☐ User management is not described in a procedure.
- ☐ User management covers the following topics:
 - ☐ the users training to the system,
 - ☐ the documentation of training users to the system
- ☐ the provision of an user manual describing the manner of use the eCRF [*methods for correcting input errors such as*],
 - ☐ the documentation for users accessing to the system,
 - ☐ the management of the system access with a unique identifier for each user.
- ☐ The user management does not cover the following topics:
 -
- ☐ The completeness of data collection is guaranteed by:
 - ☐ the use of dropdown menus,
 - ☐ the use of check boxes,
 - ☐ setting input fields [*formats such as dates*],
 - ☐ the original data collection to calculate derived data.
- ☐ The code used to identify patients allows and unambiguous identification of each patient.

☐ The code used to identify patients does not allowed and unambiguous identification of each patient.

☐ The authorization for eCRF production is described in the document "".

☐ The authorization for eCRF production is not documented.

☐ The means by which the investigator has control of the data it generated [*if the data are stored on a central server*] is described in the document "".

☐ This method is demonstrably.

☐ This method is not demonstrably.

☐ The means by which the investigator is notified of data changes and approves the changes is described in the document "".

☐ Les modifications concernées incluent :

- ☐ changes in response to requests for correction,
- ☐ the 'Self Evident Corrections' managed by the data manager.

☐ The investigator has continuous access to data.

☐ The investigator investigator has no permanent access to data. [specify the conditions of maintenance management].

☐ The identification of data source and copies is described in the document "".

☐ This document specifies :

- ☐ the data source nature [*the source must be unique and unchanged during the trial*],
- ☐ data source location,
- ☐ copies location,
- ☐ the identification of the reference copy, when there are multiple copies,
- ☐ if necessary, the copies certification process [*to ensure that the copies are complete and accurate*], and the identification and accreditation of the certifier,
- ☐ the information procedures of the stakeholders when the data source location is changed during the trial.

☐ The method of copying data source (and méta-data) is described in the document "".

☐ The source data are printable.

☐ The source data are not printable.

☐ The availability of data for archiving on site is described in the procedure "".

☐ The availability of data for archiving on site is not described in the procedure "".

☐ On site, the data are archived:

- ☐ on paper (printing of electronic data)
- ☐ on an electronic support (such as CD-Rom)

☐ The archiving includes the data and the metadata of eCRF [*included trail audit*].

☐ The archiving does not include the metadata of eCRF.

☐ If the data sources are archived in a specialized service provider, the roles and the responsibilities of each part (sponsor, investigator and provider) are specified in a service contract...

□ The contract is written so as to preserve the roles and the responsibilities, under the GCP:

- □ of investigator, namely the generation of source data,
- □ of sponsor, namely the quality control, source data analysis and the resulting report.

7.32 Data management Computerized System Validation

7.32.1 Inventory of the Data management Computerized System

Main software of data management:

- ClinTrial (PhaseForward)
- Oracle Clinical (Oracle)
- SAS Capture (SAS)
- Capture System (Clinsight)
- ClinInfo (ClinInfo)

(SR Data Management – definition and software)

"6.1.5 Maintaining the System Inventory

Regulated companies **should maintain an inventory of computerized systems**, showing **which are GxP regulated**... The Inventory should provide summary information **such as the validation status**, the ownership, impact, current system version, and supplier..." (GAMP (Good Automated Practices), a risk-based approach to compliant GxP computerized systems, version 5, April 2008, ISPE)

"7.1.1 Inventaire des biens

... Il convient de clairement identifier tous les biens, de réaliser et de gérer un inventaire de tous les biens importants...

Il existe plusieurs types de biens, qui comprennent les éléments suivants:

...b) les **biens logiciels**: les applications logicielles les logiciels système, les outils de développement et les utilitaires;

c) les **biens physiques**: le matériel informatique, les moyens de communication, les supports amovibles et autre matériel;

d) les **services**: les services informatiques et de télécommunication, ...

e) les **personnes** et leurs qualifications, leur savoir-faire et leur expérience..."

(Norme ISO 27002:2005 (anciennement numéroté 17799:2005) : Technologies de l'information - Techniques de sécurité - Code de bonne pratique pour la gestion de la sécurité de l'information)

"3. Dependability System Documentation

For each study, **documentation should identify what software and hardware will be used to create, modify, maintain, archive, retrieve, or transmit clinical data**. Although it need not be submitted to FDA, this documentation should be retained as part of the study records and be available for inspection by FDA (either on-site or remotely accessible)." (FDA Guidance for Industry - Computerized Systems used in Clinical Investigations, May 2007)

Computerized Systems Inventory

- ☐ There is a Computerized Systems Inventory of Data Management.
- ☐ There is no Computerized Systems Inventory of Data Management.
- ☐ The Computerized Systems Inventory of Data Management includes:
 - ☐ network and connexions Plan,
 - ☐ the communications (internet, other systems...),
 - ☐ physical inventory items,
 - ☐ the relevant staff.
- ☐ The Computerized Systems Inventory is complete, maintained up-to-date and specifies all the systems in place at YYYY:
 - ☐ e-CRF,
 - ☐ data entry,
 - ☐ clinical databases manager,
 - ☐ other :

The listed systems are:

-

- ☐ The Computerized Systems Inventory is not maintained up-to-date.
- ☐ The Computerized Systems Inventory is not complete.
- ☐ The Computerized Systems Inventory is approved by
- ☐ The Computerized Systems Inventory is not approved.
- ☐ For each computerized System, a validation decision is available.
- ☐ The validation decision of each computerized System is described on the document... (Computerized Systems Inventory)
- ☐ The decision of computerized System validation is not documented.
- ☐ The functional description of each computerized system of Data Management covers:
 - ☐ les éléments constitutifs,
 - ☐ the supplier name
 - ☐ the version number
 - ☐ the processed data (regulatory / non-regulatory),
 - ☐ the status of computer system validation (*valid / invalide*),
 - ☐ the decision of computer system validation (*validate/ not be validated*),
 - ☐ the types of computer processing (*data entry, analysis, coding ...*).

7.32.2 Validation Policy

"Each regulated company should have a **defined policy** for ensuring that computerized systems are compliant and fit for intended use. The policy should typically include a commitment to:

- ... **follow a validation framework**, including the use of validation plans and validation reports as necessary ..." (GAMP (Good Automated Practices), a risk-based approach to compliant GxP computerized systems, version 5, April 2008, ISPE)

- ☐ YYY has defined a "Validation Policy" (reference), version#XX.
- ☐ The Validation Policy covers the following points:
 - ☐ responsibilities of the Managing director and staff,
 - ☐ staff Management,
 - ☐ documentation Management,
 - ☐ Computerized Systems Management (internally developed or not),
 - ☐ Systems retirement,
 - ☐ Quality Management,
 - ☐ Risks Management.
- ☐ The Validation Policy does not cover the following points:
 -
- ☐ There is no Computerized Systems Validation Policy.
- ☐ The Computerized Systems Validation Policy is approved by the Manager.
- ☐ The Computerized Systems Validation Policy is not approved by the Manager.

7.32.3 Associated Procedures

"6. DATABASE

... 5 **Procedures** should be defined to ensure that errors are not introduced into the database as a result of errors in computer programs. This includes the need to define programming standards. The following items should be considered:

(i) **general system validation:**

- software to be used for data entry
- structure and format of electronic data files
- documentation of methods of software checking and action to be taken when errors are found.

(ii) **study-specific checks:**

- checking of programs written for data entry (e.g. screen design)
- checking of programs written to conduct data derivations and data validation/plausibility checks
- checking of data manipulation programs written to transfer data from the entry format to the analysis format." (Guideline for Standard Operating Procedures for Good Statistical Practice in Clinical Research, versions 1-6, June 1999 – July 2001, Statisticians in the Pharmaceutical Industry (PSI))

"Chapter Database validation, programming and standards - Recommended Standard Operating Procedures:

- System Installation
- System Validation
- Change Control: outlines the validation procedure when a major system component is upgraded or changed

- Data Backup/Recovery: outlines the frequency of and archival strategy for database backups and the specific plan for recovery in the event of a system crash or other disaster that results in the loss of data

- Trial-specific Database Design

- Validation of Trial-specific Database Design

- Trial-specific Database Programming

- Validation of Trial-specific Database Programming

- Data Collection and Handling

- Receipt of Electronic Data

- Database and Systems Security " (Good Clinical Data Management Practices, Published July 2008, Society For Clinical Data Management (SCDM))

+ page 52 (Computerised systems validation in Clinical Research, a practical guide, 2nd edition, February 2004, CR-CSV Working Party)

GxP:

 " 6.1.1. Computerized systems policies and procedures

... These documents [more Detailed policies or SOPs] will typically address:

- maintaining the system inventory

- determining the impact of systems on patient safety, product quality, and data integrity

- defined roles and responsibilities

- the computerized system life cycle approach

- planning, supplier assessment, risk management, specification, verification, and reporting activities and documents system operation and management, including up to date operating procedures for end users and administrators, and all operational processes described in section 4.3 of this guide

- record and data management

- security management" (GAMP (Good Automated Practices), a risk-based approach to compliant GxP computerized systems, version 5, April 2008, ISPE - §6.1.1)

CLINIQUE:

 " 5.5.3. Si les données de la recherche biomédicale font l'objet d'un traitement ou sont gérées par des computerized systems, le proCore System:

... b) Mettre en place et assurer le suivi des procédures opératoires standardisées relatives à l'utilisation de ces systèmes ;..." (Décision du 24 novembre 2006 fixant les règles de bonnes pratiques cliniques pour les recherches biomédicales portant sur des médicaments à usage humain - § 5.5.3)

	"5.5.3 When using electronic trial data handling and/or remote electronic trial data systems, the Sponsor should:
	...maintains SOPs for using these systems,..." (Note for Guidance on Good Clinical Practice CPMP/ICH/135/95)
	"B. Standard Operating procedures
	There should be specific procedures and controls in place when using computerized systems to create, modify, maintain, or transmit electronic records, including when collecting source data at clinical trial sites. A list of recommended standard operating procedures (SOPs) is provided in Appendix A. Such SOPs should be maintained either on-site or be remotely accessible through electronic files as part of the specific study records, and the SOPs should be made available for use by personnel and for inspection by FDA.
	APPENDIX A -STANDARD OPERATING PROCEDURES
	Standard operating procedures (SOPs) and documentation pertinent to the use of a computerized system should be made available for use by appropriate study personnel at the clinical site or remotely and for inspection by FDA. The SOPs should include, but are not limited to, the following processes.
	- System sandup/installation (including the description and specific use of software, hardware, and physical environment and the relationship)
	- System operating manual
	- Validation and functionality Testing
	- Data collection and handling (including data archiving, audit trails, and risk assessment)
	- System maintenance (including system decommissioning)
	- System security measures
	- Change control
	- Data backup, recovery, and contingency plans
	- Alternative recording mandhods (in the case of system unavailability)
	- Computer user training
	- Roles and responsibilities of sponsors, clinical sites and other parties with respect to the use of computerized systems in the clinical trials"
	(FDA Guidance for Industry: Computerized Systems Used in Clinical Invisigations, May 2007)
	page 52 (Computerised systems validation in Clinical Research, a practical guide, 2nd edition, February 2004, CR-CSV Working Party)
	DATA MANAGEMENT:
	""Chapter EDC Principles - Recommended Standard Operating procedures:
	- System Sandup/Installation/Training
	- Data Collection and Handling

- System Maintenance	
- Data Backup, Recovery, and Contingency Plans	
- Security of the Server	
- Security of the EDC software	
- Change Control	
- Maintenance of Coding Dictionaries	
- Vendor Audits	
Chapter Database validation, programming and standards - Recommended Standard Operating procedures:	
- System Installation	
- System Validation	
- Change Control: outlines the validation procedure when a major system component is upgraded or changed	
- Data Backup/Recovery: outlines the frequency of and archival strategy for database backups and the specific plan for recovery in the event of a system crash or other disaster that results in the loss of data	
- Trial-specific Database Design	
- Validation of Trial-specific Database Design	
- Trial-specific Database Programming	
- Validation of Trial-specific Database Programming	
- Data Collection and Handling	
- Receipt of Electronic Data	
- Database and Systems Security	
- Site Qualification" (Good Clinical Data Management Practices, version 5.0, July 2008, Sociandy for Clinical Data Management)	
DATA MANAGEMENT AND STATISTIQUES :	
 "5.8 Integrity of data and computer software validity	
... The computer software used for data management and Statistical analysis should be reliable, and documentation of appropriate software Testing procedures should be available..." (Note for Guidance on Statistical Principles for Clinical Trials, CPMP/ICH/363/96, 5 February 1998)	
 "6. DATABASE	
... 5 procedures should be defined to ensure that errors are not introduced into the database as a result of errors in computer programs. This includes the need to define programming standards. The following items should be considered:	
(i) general system validation:	

- software to be used for data entry

- structure and format of electronic data files

- documentation of methods of software checking and action to be taken when errors are found.

(ii) study-specific checks:

- checking of programs written for data entry (e.g. screen design)

- checking of programs written to conduct data derivations and data validation/plausibility checks

- checking of data manipulation programs written to transfer data from the entry format to the analysis format." (Guideline for Standard Operating procedures for Good Statistical Practice in Clinical Research, versions 1-6, JA 1999 – July 2001, PSI)

PHARMACOVIGILANCE:

 "Chapitre 6 - Rôle du responsable de la mise sur le marché d'un médicament

10. procédures mises en place par le responsable de la mise sur le marché

Disposer de procédures and de techniques de contrôle de qualité, ainsi que de procédures opératoires standardisées relatives à la pharmacovigilance constituant les référentiels d'audits réguliers. Ces procédures doivent décrire de manière précise la structure et l'organisation du service de pharmacovigilance mis en place au sein de l'entreprise, la management des informations de pharmacovigilance ainsi que les fonctions and responsabilités de toute personne concernée par les opérations de pharmacovigilance." (Arrêté du 28 avril 2005 relatif aux bonnes pratiques de pharmacovigilance)

 "1.3.10 Confidentiality and Security

...In addition, procedures should be implemented to ensure security and non-corruption of data during data transfer. (VOLUME 9A of The Rules Governing Medicinal Products in the European Union - Guidelines on Pharmacovigilance for Medicinal Products for Human Use, September 2008)

☐ YYY has an applicable procedures list, up-to-date (version#X.X, date), on the computerized systems management.

☐ The procedures life cycle is adequate: writing, identification, approval and diffusion, as described in the procedure...

☐ The available operational procedures cover the different stages of computerized systems management.

☐ LABO PHARMA has written procedures for computerized systems management.

☐ The required following procedures are present and updated.

☐ The procedures cover the following points:

- ☐ systems identification and characterization,
- ☐ systems installation,
- ☐ systems validation (standards programs),
- ☐ the validation of programs developed specifically for a study,
- ☐ risks management,
- ☐ validation steps (tests),
- ☐ user documentation and user support (operational procedures),

- ☐ changes management,
- ☐ configuration management,
- ☐ periodical reviews,
- ☐ systems retirement,
- ☐ training,
- ☐ security,
- ☐ system maintenance,
- ☐ service contracts (SLA: Service Level Agreements) / of maintenance),
- ☐ backup and restore,
- ☐ activity continuity,
- ☐ archiving and data recovery,
- ☐ audit and review.
- ☐ "one-off programs" validation procedure of (e.g., specific macros to a data sand, for a specific study),
- ☐ Software Development procedure, if applicable,
- ☐ systems configuration and installation procedure (including inventories and systems description [hardware, software, environment, interfaces])
- ☐ use and system maintenance procedure
- ☐ services contracts management procedure/ suppliers management (including computerized systems purchase)
- ☐ Back-up and Recovery procedure
- ☐ Archiving procedure
- ☐ Security procedure:
 - ☐ logical, includes the user account and password management, security tools, system audit trail, antivirus, firewalls, logging connections, application firewall
 - ☐ physical / facilities
 - ☐ security incidents management
- ☐ continuity activity procedure, Continuity Plan, Recovery Plan, Contingency Plans associated.
- ☐ The procedures do not cover the following points:

7.32.4 Data Management Staff

The identification, the qualification and the training of data management staff are described on § "Qualification and staff training".

"Chapter Training - Computer Software and Technical Skills

*For data entry, cleaning, and analysis, data managers use various software applications, including clinical database management systems, case report form (CRF) imaging software, edit-specification development software, discrepancy management software, and others. **To use these software packages, employees require training.** Depending on time and budgetary restrictions, this training may be performed by the software vendor, a third party training vendor, or an in-house trainer." (Good Clinical Data Management Practices, Published July 2008, Society For Clinical Data Management (SCDM))*

- ☐ The staff is trained in the use of computerized systems of Data Management.
- ☐ The staff is not trained in the use of computerized systems of Data Management.
- ☐ The trainings are documented.
- ☐ The trainings are not documented.
- ☐ The trainings are updated and the staff is trained accordingly.

- ☐ The trainings are updated but the staff is not trained accordingly.
- ☐ The users have Manuals Systems.
- ☐ The users have not Manuals Systems.

7.33 Validation of the computerized system "SSS"

7.33.1 User Requirements Specifications

"Appendix D1 – 3.1 General Guidance

... The URS [User Requirements Specifications] defines, clearly and precisely, what the regulated company requires the system to do...

The content of a URS typically includes, but is not limited to:

- operational requirements
- functional requirements
- data requirements
- technical requirements
- interface requirements
- environment requirements
- performance requirements
- availability requirements
- security requirements
- maintenance requirements
- regulatory requirements
- migration of any electronic data
- constraints to be observed
- life cycle requirements " (GAMP (Good Automated Practices), a risk-based approach to compliant GxP computerized systems, version 5, April 2008, ISPE)

pages 35-36 (Computerised systems validation in Clinical Research, a practical guide, 2nd edition, February 2004, CR-CSV Working Party)

- ☐ User Requirements Specifications of the computerized system "SSS" of Data Management are described on the document ...
- ☐ User Requirements Specifications of the computerized system "SSS" of Data Management are not available.
- ☐ User Requirements Specifications of the computerized system "SSS" of Data Management specify the following topics:
 - ☐ User requirements :
 - operational,

- functional,
- data,
- technical,
- interfaces,
- environmental,
- performance,
- availability,
- security,
- maintenance,
- regulations.

- ☐ constraints,
- ☐ any other point considered significant for the users ...

☐ User Requirements Specifications of the computerized system "SSS" of Data Management do not specify the following topics:

-
-

☐ User Requirements Specifications of the computerized system "SSS" of Data Management is validated. This validation is documented.

☐ User Requirements Specifications of the computerized system "SSS" of Data Management is not validated.

7.33.2 Functional Description of the "SSS" Computerized System

For the systems developed in-house.

"Appendix D6 – system descriptions .. The need for a system description may be covered by one or more existing specifications or other documents, or a separate document may be produced... 3.1. General guidelines The system description should be maintained up to date... 3.2. Contents of the documents ... - main system functionality... key functions of the system, both GxP and non GxP... - regulatory impact... description of the key GxP functions of the system... - computing environment... infrastructure... interfaces... flow of data, ... security features... - system components...indication of the main hardware and software... - system interfaces... - access control... - security controls... - electronic records and signatures..." (GAMP (Good Automated Practices), a risk-based approach to compliant GxP computerized systems, version 5, April 2008,	
--	--

[SPE]

"Glossary"

Design specification: a specification that documents how a system is to be built. It typically includes system or component structures, algorithms, control logic, data structures, data set (file) use information, input/output formats, interface description...

Functional specifications: detailed specifications of the nature and structure of the system under evaluation, including the operating system" (Computerised systems validation in Clinical Research, a practical guide, 2nd edition, February 2004, CR-CSV Working Party)

☐ The Data Management Computerized System "SSS" is described:

- ☐ in the document...
- ☐ and/or in the technical specifications,
- ☐ and/or in the functional specifications...

☐ The Data Management Computerized System "SSS" is not described.

☐ This documentation covers the following topics:

- ☐ the description of the essential functions of the system (GxP et non GxP),
- ☐ the regulatory impact of the system,
- ☐ the system environment (infrastructures, users interfaces utilisateurs, interfaces with other systèmes, data flow...),
- ☐ system components and system softwares,
- ☐ keys interfaces with other systems and the flows between the systems,
- ☐ the control of the physical and logical access to the system ,
- ☐ the control of physical and logical security,
- ☐ an indication of the electronic data managed by the system, and electronic signatures used.

☐ This documentation does not cover the following topics:

-

☐ This documentation is updated.

☐ This documentation is outdated.

7.33.3 Risk Analysis

Pages 32-34 (Computerised systems validation in Clinical Research, a practical guide, 2nd edition, February 2004, CR-CSV Working Party)

☐ A Risk Analysis is available for the "XX" Core System:

- Date and version:
- Approved by:

☐ There is no Risk Analysis concerning the "XX" Core System.

☐ This Risk Analysis covers the following:

- ☐ potentials risks identification for the system functioning;
- ☐ materials (e.g.: breakdown, unavailability, replacement necessity...),
- ☐ Software (e.g.: crash, version changes, computer access rights, alteration or loss of files, design error, bug...),
- ☐ data (e.g.: data entry error, data loss, file loss or file corruption, back-up failure...),
- ☐ communication (e.g.: lack of communication, alteration during communication...),

- ☐ human factor (e.g.: malicious acts, fraud, theft, training lack, error, absence, espionage...),
- ☐ environment (e.g. : virus attack, electrical failure, power failure, fire / heat, frost, water damage, theft...),
- ☐ evaluation and identified risks analysis:
- ☐ possible causes / scenarios,
- ☐ consequences in terms of functionalities and responsibility exercise,
- ☐ criticality,
- ☐ likelihood of (occurrence frequency estimate),
- ☐ prevention possible measures (Prevention Plan),
- ☐ validation measures,
- ☐ Contingency Plan to apply in case of risk occurrence.

- ☐ The Risk Analysis is regularly reviewed and maintained up-to-date.
- ☐ The Risk Analysis is not regularly reviewed and maintained up-to-date.

7.33.4 Development of the Computerized System "SSS"

For the systems developed in-house:

Appendix D4 Management, development, and review of software

GAMP (Good Automated Practices), a risk-based approach to compliant GxP computerized systems, version 5, April 2008, ISPE

- ☐ The development of the data management computerized system "SSS" is described in the document XXX.
- ☐ This documentation covers the following topics:
 - ☐ the code source review and documentation
 - ☐ the design review (i.e. check adequacy with the requirements),
 - ☐ the documentation of the units tests,
 - ☐ the conservation of different source code versions.
- ☐ This documentation does not cover the following topics:
 - ☐ the code source review and documentation
 - ☐ the design review (i.e. check adequacy with the requirements),
 - ☐ the documentation of the units tests,
 - ☐ the conservation of different source code versions.
- ☐ The development of the data management computerized system "SSS" is not described in a document.

For the systems not developed in-house, the documentation of the "SSS" computerized system development can be evaluated during a supplier audit.

GxP:

"Appendix D4 Management, development, and review of software

... 3.3.1 Purchased Software

In most cases evidence of software control can be obtained through standard mechanisms for supplier assessment, such as supplier audit..." GAMP (Good Automated Practices), a risk-based approach to compliant GxP computerized systems, version 5, April 2008, ISPE

☐ The documentation of "SSS" computerized system development by the supplier was evaluated during a supplier audit.

☐ The documentation of "SSS" computerized system development by the supplier has not been evaluated.

7.33.5 Validation Plan

Appendix M1 Validation Planning - §5 Computerized system validation plans

GAMP (Good Automated Practices), a risk-based approach to compliant GxP computerized systems, version 5, April 2008, ISPE

☐ The management of the Data Management Computerized System "SSS" Validation Plan is described in the document XXX.

☐ The management of the Data Management Computerized System "SSS" Validation Plan is not described in a document.

☐ The Validation Plan covers the following topics:

- ☐ a general description of the system,
- ☐ the roles and responsibilities,
- ☐ the risks associated with the system,
- ☐ the validation strategy,
- ☐ the delivery,
- ☐ les critères d'acceptation du système,
- ☐ the change management,
- ☐ the associate procedures,
- ☐ the support processes (training, documentation management, configuration management...).

☐ The Validation Plan does not cover the following topics:

-

7.33.6 System Installation

Qualification d'installation (QI)

☐ The installation of the data management computerized system "SSS" is described in the document XXX.

☐ The installation of the data management computerized system "SSS" is not described.

☐ This documentation covers the following topics:

- ☐ the documentation of the system configuration,
- ☐ the execution of the configuration tests and the associated documentation,
- ☐ the execution of the functional tests and the associated documentation,
- ☐ the execution of the performance tests and the associated documentation.

☐ This documentation does not cover the following topics:

-

☐ The installation of the data management computerized system "SSS" is validated. This validation is documented.

☐ The installation of the data management computerized system "SSS" is not validated.

7.33.7 Functional Validation

Pour les systèmes développés en interne uniquement.

Qualification opérationnelle (QO) / de performance (QP) en environnement de développement

Appendix D5 Testing of Computerized systems

GAMP (Good Automated Practices), a risk-based approach to compliant GxP computerized systems, version 5, April 2008, ISPE

☐ The strategy of development tests applied to Data Management computerized systems "SSS" is described in the document XXX.

☐ The strategy of development tests applied to Data Management computerized systems "SSS" is not described.

☐ This documentation covers the following topics:

- ☐ the Tests Plans,
- ☐ the standard sheets for the tests execution,
- ☐ the tests execution and associated documentation,
- ☐ the fault management encountering during tests,
- ☐ the review and the approval of tests results tests (against acceptance criteria),
- ☐ tests reports.

☐ This documentation does not cover the following topics:

-

7.33.8 Operational Validation

Operational Qualification (OQ) / of Performance (PQ) in operational environment.

User acceptance testing

pages 39-40 (Computerised systems validation in Clinical Research, a practical guide, 2nd edition, February 2004, CR-CSV Working Party)

☐ The strategy of the User Tests applied to data management computerized "SSS" is described in the document XXX.

☐ The strategy of the User Tests applied to data management computerized "SSS" is not described in a document.

☐ This documentation covers the following topics:

- ☐ roles and responsibilities,
- ☐ tests references (user requirements, fonctionnal specifications, technical specifications),
- ☐ the identification of the tested functions,
- ☐ the identification of non-tested functions (and justification),
- ☐ the test terms for selected functions,
- ☐ the types of used tests,
- ☐ the acceptance criteria of tests results,
- ☐ the standard sheets for tests execution,
- ☐ tests execution and associated documentation,
- ☐ the fault management encountering during tests,
- ☐ the review and approval of tests (against the acceptance criteria),
- ☐ a review and a re-run of tests as soon as the operating environment is changed.

☐ This documentation does not cover the following topics:

-

7.33.9 Validation Report

Appendix M7 Validation Reporting

GAMP (Good Automated Practices), a risk-based approach to compliant GxP

☐ A Validation Report is available for the XX Study System:

- Date and version:
- Approved by:
- Core System Version:
- Application Version :

☐ There is no Validation Report for the XX Study System.

☐ A Summary Validation Report is available.

☐ There is no Validation Report Summary.

☐ The Validation Report covers the following:

- ☐ potential changes brought to the validation approach initially described in the Validation Protocol, and documentary evidences,
- ☐ for each validation step: performed activities, deviations, setting-up actions, and the conclusion of the step acceptance criteria,
- ☐ deliverables,
- ☐ the planned arrangements to maintain the system validated state,
- ☐ the validation system conclusion.

☐ The management of the validation report of data management computerized system "SSS" is described in the document ...

☐ The management of the validation report of data management computerized system "SSS" is not described in a document.

7.33.10 Validation Certificate

☐ A Validation Certificate is available for the XX study system:

- Date and version:
- Approved by:
- Core System Version:
- Application Version:

☐ There is no Validation Certificate for the XX study system.

7.33.11 Change Control

pages 48-49 (Computerised systems validation in Clinical Research, a practical guide, 2nd edition, February 2004, CR-CSV Working Party)

☐ The changes control of the data management computerized system "SSS" is described in the document ...

☐ The changes control of the data management computerized system "SSS" is not described in a document ...

☐ This documentation covers the following topics:

- ☐ the changes performed:
 - ☐ to hardware,
 - ☐ to software,
 - ☐ to operating environment,
 - ☐ to associated procedures,
 - ☐ to roles and responsibilities,
 - ☐ to access management,

- ☐ to needs for training,
 - ☐ to regulatory environment,
 - ☐ to data.
 - ☐ the changes documentation:
 - ☐ the change reason,
 - ☐ a registry of change requests,
 - ☐ a risk analysis and the impact of each change,
 - ☐ the approval/ the refusal of any change,
 - ☐ developments brought about by a change,
 - ☐ testing of each approved change prior to production.
 - ☐ to provide training
 - ☐ the updates documentation to provide
 - ☐ This documentation does not cover the following topics:
 - ☐
- <For an eCRF :
- ☐ The data changes management, if there is an amendment, is described in the procedure ...
- [For example, how to remove a review for patients already included and for which data have been collected]
- ☐ These changes are documented and validated.
 - ☐ These changes are not documented and not validated.

7.34 Additional Documentation for systems non-developed in-house

page 42-46 (Computerised systems validation in Clinical Research, a practical guide, 2nd edition, February 2004, CR-CSV Working Party)

- ☐ The Company XXX has conducted an audit of the supplier validation documentation for the data management computerized system "SSS".
- ☐ The Company XXX has not conducted an audit of the supplier validation documentation for the data management computerized system "SSS".
- ☐ The Company XXX has a summary of the supplier validation report for the data management computerized system "SSS".
- ☐ The Company XXX does not have a summary of the supplier validation report for the data management computerized system "SSS".
- ☐ The Company XXX has a supplier validation certificate for the data management computerized system "SSS".
- ☐ The Company XXX does not have a supplier validation certificate for the data management computerized system "SSS".

7.35 Specific Documentation for the validation of the clinical databases management system

""Chapter Database Validation, Programming, and Standards

Clinical Database Validation

... Data management software purchased off the shelf should have been heavily tested by the vendor who originally developed the software. These development-validation measures are typically referred to as "design-level validation" and do not need to be repeated by the end-user. However, documentation of the design-

level validation specifications and testing should, ideally, be available to the sponsor, at least for **audit** purposes and contractually through escrow.

Sponsors should ensure the completion and documentation of functional level testing, which includes documenting the effect of any known limitations, problems, and defects on functions used for the sponsor's study. Some examples of additional validation that might be performed and validated by sponsors using test data include the following:

- Testing of data entry screens to ensure that data are mapped to intended database structures
- Validation of any generic integrity constraints or data-checking routines that execute during data entry (e.g., range, date, format, coding, field discrepancies)
- Testing of data verification functions such as second-entry verification, file comparison, and batch verification
- Batch data transfer to the clinical trial database from separate data entry systems (e.g., electronically transferred data or remote data entry systems)

Some important documentation to be considered and addressed during database validation includes the following (see also this chapter's Recommended SOPs section):

- Prospectively written design specifications that describe what the software is intended to do and how it is intended to do it. A version controlled system manual can serve as design specifications.
- A test plan based on the design specification and the intended use of the database management system that outlines both how the testing will be conducted and the criteria for acceptance or rejection of the software based on testing outcomes.
- Results documentation that describes why the software will be accepted or rejected based on specific test results.
- Appropriate review and approval documents...

Trial-Specific Programming and Validation

After a clinical data management system has been validated and approved for use within a sponsor organization, validation must focus instead on specific study or protocol database design and implementation. Validation at this phase can be addressed in three major categories: database design, data entry, or capture and other study-specific programming.

...If use of standards is not possible, as in the case of a contract organization designing a database according to sponsor specifications, the specifications are sufficient.

At a minimum, database specifications should, provide the following information for each variable:

- ☐ Name and label
- ☐ Dataset label, panel, or other logical group to which the data belongs
- ☐ Type (e.g., numeric, character, integer, decimal, date)
- ☐ Length (including number of characters before and after the decimal point, where applicable)
- ☐ Definitions for all coded values

☒ Indication of the origin of the data

☒ Algorithms for derived or calculated variables

... The most important consideration is the need to ensure that data being entered through a data entry screen or captured via some other transfer process (e.g., electronic lab data transfers) map to the correct variables in the clinical trial database. Useful validation measures to consider when testing this functionality may include entering test or "dummy" data into the screens or loading test data transfer files so that output data listings from the database can be reviewed to ensure that the variables were correctly added and saved within the database structure. It is also critical to validate the data field definitions in terms of length and type...

Database entry or capture validation should also verify that key records management issues are addressed. The database should not accept entry of duplicate records, and primary key variables should be appropriately assigned and managed by the definition of the database's structure. When discrepancies between the first and second passes of data entry are resolved, validation should ensure that one record with the correct data is permanently and correctly inserted into the study database and can be extracted. Most importantly, the audit trail for the trial should be validated and protected so that all manipulation of the study database or external files is recorded by date, time, and user stamps in an audit trail that can be accessed as read-only for the life of the data.

Other examples of study-specific programming are data loading or transfer programming and programming done to validate the data (e.g., edit checks, query rules, procedures). This programming includes any code written to check the data and can occur at the time of entry or later as a batch job. This programming must be validated if action is taken regarding clinical data intended for submission as a result of the programming. Examples include programming that identifies data discrepancies such that queries are sent to clinical investigators or in-house data-editing conventions followed for items identified by the programming.

Best practices include identifying all intended uses of study-specific programming and testing each logic condition in the programming, based on a test plan. Algorithms for derived variables must be validated.

... The entire test plan can be a standard operating procedure that contains the testing methodology, scope, purpose, acceptance criterion, and approvals and that specifies the format for test data and problem reporting." (Good Clinical Data Management Practices, Published July 2008, Society For Clinical Data Management (SCDM))

pages 61-64 (Computerised systems validation in Clinical Research, a practical guide, 2nd edition, February 2004, CR-CSV Working Party)

General points

- ☐ The validation of the clinical databases management system is documented.
- ☐ This documentation covers the following topics:
 - ☐ the validation of the database implementation (standard tables),
 - ☐ if applicable, the validation of the data transfer of a data acquisition system to the clinical databases system,
 - ☐ the validation of algorithms to calculate derived data,
 - ☐ the validation of data control programs,
 - ☐ the validation of system trail audit,
 - ☐ the validation of data extraction,
 - ☐ the validation of database security access.
- ☐ The validation of the clinical databases management system is not documented.

Specific points:

a/ Database Set up

- ☐ The validation of tables changed specifically for a trial is documented.
- ☐ This documentation covers the following topics:
 - ☐ entry tests (fields, formats, self-coding, calculation of derived data, opportunity to confirm the missing data or non-standard...),
 - ☐ the conformity between the mask fields and the tables fields,
 - ☐ the conformity between the entered variables and transfered data into the base (i.e. variables in the good field of the good table).
- ☐ The validation of tables changed specifically for a trial is not documented.

b/ Data transfer

- ☐ The validation of data transfer of a data acquisition system to the management of clinical databases is documented.
- ☐ This procedure covers the following topics:
 - ☐ the transfer of data from double entry,
 - ☐ the other data transfer (i.e. electronic data of laboratory),
 - ☐ the transfer check (i.e. transferred data in the good field of the good table),
 - ☐ detection and management of duplicate data,
 - ☐ alerts if the data are not transferred.
 - ☐ the presence of transfer trail audit, validated, in the receiving system.
- ☐ This procedure does not cover the following topics:
 - ☐ the transfer of data from double entry,
 - ☐ the other data transfer (i.e. electronic data of laboratory),
 - ☐ the transfer check (i.e. transferred data in the good field of the good table),
 - ☐ detection and management of duplicate data,
 - ☐ alerts if the data are not transferred.
 - ☐ the presence of transfer trail audit, validated, in the receiving system.
- ☐ The validation of data transfer of a data acquisition system to the management of clinical databases is not documented.

c/ Derived data

- ☐ The algorithms validation of derived data calculating is documented.
- ☐ This documentation covers the following topics:
 - ☐ tests in limits (i.e. with extremes, limits and missing data),
 - ☐ algorithm standard tests (i.e. for all source data types),
 - ☐ the verification of the value of calculated derived variables,
 - ☐ the verification of the adequacy between the field name of source variables and the field name of derived variables in the database,
 - ☐ the control of dictionaries and tables versions.
- ☐ This documentation does not cover the following topics:
 - ☐ tests in limits (i.e. with extremes, limits and missing data),
 - ☐ algorithm standard tests (i.e. for all source data types),
 - ☐ the verification of the value of calculated derived variables,
 - ☐ the verification of the adequacy between the field name of source variables and the field name of derived variables in the database,
 - ☐ the control of dictionaries and tables versions.
- ☐ The algorithms validation of derived data calculating is not documented.

d/ Data Validation

- ☐ The validation of data control programs is documented.
- ☐ This documentation covers the following topics:
 - ☐ The validation of standard controls programs:
 - ☐ the verification that each control does apply to each involved,
 - ☐ the verification of the reproducibility programs (if a check does not reveal any abnormality, it should not do so until the relevant data are not changed),
 - ☐ the management of programming errors,
 - ☐ tests performed with data adapted to the detection of false positives and false negatives.
 - ☐ the validation of control programs specifically for a trial:
 - ☐ the verification that each control does apply to each involved,
 - ☐ the verification of the reproducibility programs (if a check does not reveal any abnormality, it should not do so until the relevant data are not changed),
 - ☐ the management of programming errors,
 - ☐ tests performed with data adapted to the detection of false positives and false negatives.
- ☐ This documentation does not cover the following topics:
 - ☐ The validation of standard controls programs:
 - ☐ the verification that each control does apply to each involved,
 - ☐ the verification of the reproducibility programs (if a check does not reveal any abnormality, it should not do so until the relevant data are not changed),
 - ☐ the management of programming errors,
 - ☐ tests performed with data adapted to the detection of false positives and false negatives.
 - ☐ the validation of control programs specifically for a trial:
 - ☐ the verification that each control does apply to each involved,
 - ☐ the verification of the reproducibility programs (if a check does not reveal any abnormality, it should not do so until the relevant data are not changed),
 - ☐ the management of programming errors,
 - ☐ tests performed with data adapted to the detection of false positives and false negatives.
- ☐ The validation of data control programs is not documented.

e/ Audit Trail Validation

- ☐ The validation of the system trail audit is not documented.
- ☐ This documentation covers the following topics:
 - ☐ compliance tests of the trail audit :
 - ☐ registration for any initial data: date, time, user identification, data value,
 - ☐ registration for any changed data : date, time, user identification, new data value, heure, change reason.
 - ☐ tests of non-accessibility of the writing trail audit.
- ☐ This documentation does not cover the following topics:
 - ☐ compliance tests of the trail audit :
 - ☐ registration for any initial data: date, time, user identification, data value,
 - ☐ registration for any changed data : date, time, user identification, new data value, heure, change reason.
 - ☐ tests of non-accessibility of the writing trail audit.

☐ The validation of the system trail audit is not documented.

f/ Validation of data extraction

- ☐ The validation of system data extraction is documented.

☐ This documentation covers the following topics:

- ☐ the validation of the data extraction programs:
 - ☐ verification that the retrieved data are those of good study,
 - ☐ verification that the retrieved data are those of good tables,
 - ☐ verification that the retrieved data are those in a correct format.
- ☐ the programs developed in an separate environment from the use of validated programs,
- ☐ the documentation of extractions, including the source-program, the date and the generation time, the page number and the total number of pages.

☐ This documentation does not cover the following topics:

- ☐ the validation of the data extraction programs:
 - ☐ verification that the retrieved data are those of good study,
 - ☐ verification that the retrieved data are those of good tables,
 - ☐ verification that the retrieved data are those in a correct format.
- ☐ the programs developed in an separate environment from the use of validated programs,
- ☐ the documentation of extractions, including the source-program, the date and the generation time, the page number and the total number of pages.
- ☐ The validation of system data extraction is not documented.

g/ Access – Database lock

☐ The validation of the security of access to database and procedures for locking/unlocking is documented.

☐ This documentation covers the following topics:

- ☐ the limiting of the access rights,
- ☐ the management of rights access (in writing),
- ☐ the process of locking / unlocking.

☐ This documentation does not cover the following topics:

- ☐ the limiting of the access rights,
- ☐ the management of rights access (in writing),
- ☐ the process of locking / unlocking.

☐ The validation of the security of access to database and procedures for locking/unlocking is not documented.

7.36 Specific Documentation for the validation of a clinical data entry system

page 57 (Computerised systems validation in Clinical Research, a practical guide, 2nd edition, February 2004, CR-CSV Working Party)

☐ The validation of the data entry system is documented.

☐ This documentation covers the following topics:

- ☐ data input mask tests (type and size of fields)
- ☐ functional tests of entry controls (format, limits values, coding, interdependence of certain fields...),
- ☐ the tests of input features (comparing data in case of double entry, data verification if simple entry ...),

- ☐ transfer tests to a clinical databases management system.
 - ☐ tests of data extraction reports.
- ☐ This documentation does not cover the following topics:
- ☐ data input mask tests (type and size of fields)
 - ☐ functional tests of entry controls (format, limits values, coding, interdependence of certain fields...),
 - ☐ the tests of input features (comparing data in case of double entry, data verification if simple entry ...),
 - ☐ transfer tests to a clinical databases management system.
 - ☐ tests of data extraction reports.
- ☐ The validation of the data entry system is not documented.

7.37 Specific Documentation for validation of the electronic data collection system ('Remote Data Entry')

pages 57-58 (Computerised systems validation in Clinical Research, a practical guide, 2nd edition, February 2004, CR-CSV Working Party)

- ☐ The system of electronic data collection is:
- ☐ 'on line' (hosted on a website),
 - ☐ 'off line' (installed on a local computer, the data transfer from the local database to the central database, requiring the setting up of an internet type connexion),
 - ☐ a system developed in-house,
 - ☐ a system not developed in-house,
- ☐ The validation of electronic data collection system is documented.
- ☐ This documentation covers the following topics:
- ☐ The constraints on the use of materials on site (matériel des clients) for the installation of the data collection system:
 - ☐ the management of technical constraints,
 - ☐ the management of configuration constraints,
 - ☐ the system compliance with the User specifications,
 - ☐ the system compliance with the specifications for data extraction,
 - ☐ implementation of the electronic signature,
 - ☐ the verification of the logic control programs of the data, when entering,
 - ☐ the verification of correction requests processing, (send / receive / reply / forwarding),
 - ☐ the performances of the system trail audit,
 - ☐ the process of the clock synchronization system (time zone support),
 - ☐ the security of the data transfer (par exemple : dedicated telephone lines, secure internet https, VPN, ...),
 - ☐ for the "off line" systems, the verification and the security (encryption, passwords, anti-virus, firewall application, ...) of data transfer of the local database to central database,
 - ☐ the security of the central database,
 - ☐ the control of the developer's local source code and / or supplier (if the system is developed in-house or not),
 - ☐ tests with interfaces (exemple: en cas d'import de données de laboratoire centralisé),
 - ☐ the training of end users, on site,
 - ☐ a Help Desk,
 - ☐ The management of physical and logical access, on site :
 - ☐ the computers on site are dedicated to data collection system,

- ☐ the computers on site are not dedicated to data collection system but the system is physically and logically isolated from other software,
 - ☐ the computers on site are not dedicated to data collection system and the system is not physically and logically isolated from other software.
 - ☐ the physical security of equipments on site,
 - ☐ for the "off line" systems, the backup and the recovery of data on local computers,
- ☐ This documentation does not cover the following topics:
- ☐ The constraints on the use of materials on site (matériel des clients) for the installation of the data collection system:
 - ☐ the management of technical constraints,
 - ☐ the management of configuration constraints,
 - ☐ the system compliance with the User specifications,
 - ☐ the system compliance with the specifications for data extraction,
 - ☐ implementation of the electronic signature,
 - ☐ the verification of the logic control programs of the data, when entering,
 - ☐ the verification of correction requests processing, (send / receive / reply / forwarding),
 - ☐ the performances of the system trail audit,
 - ☐ the process of the clock synchronization system (time zone support),
 - ☐ the security of the data transfer (par exemple : dedicated telephone lines, secure internet https, VPN, ...),
 - ☐ for the "off line" systems, the verification and the security (encryption, passwords, anti-virus, firewall application, ...) of data transfer of the local database to central database,
 - ☐ the security of the central database,
 - ☐ the control of the developer's local source code and / or supplier (if the system is developed in-house or not),
 - ☐ tests with interfaces (exemple: en cas d'import de données de laboratoire centralisé),
 - ☐ the training of end users, on site,
 - ☐ a Help Desk,
 - ☐ The management of physical and logical access, on site :
 - ☐ the computers on site are dedicated to data collection system,
 - ☐ the computers on site are not dedicated to data collection system but the system is physically and logically isolated from other software,
 - ☐ the computers on site are not dedicated to data collection system and the system is not physically and logically isolated from other software.
 - ☐ the physical security of equipments on site,
 - ☐ for the "off line" systems, the backup and the recovery of data on local computers,
- Additional documentation for systems not developed in-house:
- ☐ complete documentation of tests, including "User Acceptance Testing",
 - ☐ functional and technical specifications of the system approved by the client,
 - ☐ documentation for system change management,
 - ☐ the procedures for the end users,
 - ☐ the procedures for system management.
- ☐ The validation of the electronic data collection system is not documented.

7.38 Change Management

pages 48-49 (Computerised systems validation in Clinical Research, a practical guide, 2nd edition, February 2004, CR-CSV Working Party)

□ The change management to data management computerized systems is described in the procedure "".

□ The change management to data management computerized systems is not described in a procedure.

□ This procedure covers the following topics:

- □ the change control,
- □ the system configuration management,
- □ the version control of the system,
- □ The change documentation consist of:
 - □ change history,
 - □ risk analysis,
 - □ impact analysis,
 - □ approval and authorization circuit.

□ This procedure does not cover the following topics:

-

7.39 Security

"6. DATABASE ... 7 The integrity and physical security of the database must be protected. Techniques should be in place to prevent the creation of multiple versions of the database. Security procedures should consist of the following items: - documentation of techniques for database 'locking' and security (including backups) - documentation and start time (e.g. before or after database locking) of an audit trail of - database edits - documentation of controls on access to the database - archiving of the database (see GSOP 9, Archiving and Documentation)." (Guideline for Standard Operating Procedures for Good Statistical Practice in Clinical Research, versions 1-6, June 1999 – July 2001, Statisticians in the Pharmaceutical Industry (PSI)) "Chapter Data Storage Minimum standards ... Document the procedures for granting access to database servers... The physical security of original data sources (e.g., case report forms, electronic data files, and other original data documents) should be maintained carefully. Original paper and electronic documents should be warehoused in secure rooms or file cabinets with controlled access. ... Database servers can be the primary warehouse of clinical data and should be physically secured, and appropriate standard operating procedures (SOPs) should exist to regulate access to them. Direct access to database servers should be restricted to individuals who are responsible for monitoring and backing up the system. ... If any data are stored locally at the study site before being sent to a central server (as is the case with a hybrid or "offline" system), the physical security of the system at the source of data entry is more critical. In either case, care must be taken to ensure the physical and logical security of computers that are used to store clinical data for any period of time.

...

Chapter Data Privacy - Best Practices

...Data should be stored in **protective environments** relevant to the type of media being stored..."(Good Clinical Data Management Practices, Published July 2008, Society For Clinical Data Management (SCDM))

+ pages 20-21 (Computerised systems validation in Clinical Research, a practical guide, 2nd edition, February 2004, CR-CSV Working Party)

- ☐ The security policy of data management computerized systems is described in the document ...
- ☐ The security policy of data management computerized systems is not described in a document.
- ☐ The security applied to data management computerized systems is described in the procedure ...
- ☐ The security applied to data management computerized systems is not described in a procedure.
- ☐ This procedure covers the following topics:
 - ☐ physical security,
 - ☐ logical security,
 - ☐ security incidents management,
 - ☐ backup and recovery,
 - ☐ archiving,
 - ☐ activity continuity.
- ☐ This procedure does not cover the following topics:
 -

Si il est nécessaire de détailler davantage les différents points de sécurité, se référer au chapitre "Sécurité" de la check-list d'audit de validation de systèmes informatisés.

8 Curriculum Vitae de l'Auditeur

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