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9.2. Laboratory Systems and Process Risk Assessment

1) Scenario:

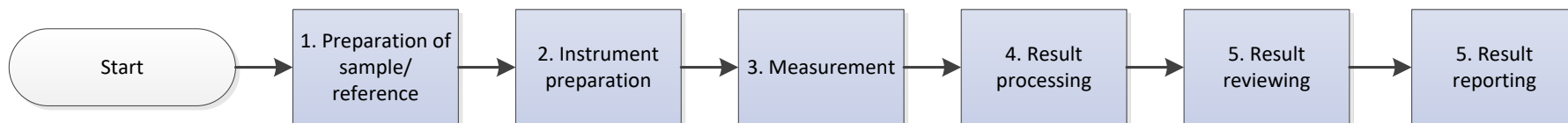
The UV device is a stand-alone instrument, not connected to a network. This device is delivered with a standard desktop computer with Windows 7 as the operating system. The weighing activities are completed using balances that are connected to a printer. These balances are calibrated, and calibration status is controlled and verified through procedure. The balance configuration is locked. The access to the balance is segregated from lab personal. Prepared analytical worksheets are available for the UV-assay test and these sheets are part of the documentation control process.

2) Business process mapping

For this example, the business process mapping is done through the 6 FDA systems and their subsystems.

➔ Laboratory control system -> Sample Analysis -> UV-Assay

The sub-process is as follows:



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3) Data (paper/electronic) and system identification

a. System identification (see section 3 step A)

| | 1 | 2 | 3 | 4 | 5 | 6 |
|----------|---------------------------------|----------------------|---------------|----------------|----------------------|------------------|
| Start | Preparation sample/Ref | Instrument Prep | Measurements | Result process | Result reviewing | Result reporting |
| GxP Data | Paper | paper/electronic | electronic | paper | paper/electronic | electronic |
| System | Raw data sheet (RDS) balance | RDS UV instrument | UV instrument | RDS | RDS UV instrument | LIMS |

b. Data Identification (see section 3 step B)

| Step | 1. Preparation sample/Ref | 2. Instrument Prep | 3. Measurements | 4. Result process | 5. Result reviewing | 6. Result reporting |
|--------------------------|---|--|-----------------|---|--|---------------------|
| System 1: RDS | | | | | | |
| GxP Data elements | Method ID Sample ID Ref-sample ID Analyst Date and time Balance ID Weights (ticket) Solvents/Reagents ID | Method ID Sample ID Ref-sample ID Analyst Date and time UV ID SST data | | Run ID UV absorbances (print or manual) Calculated assay(s) | Reviewer ID Date and time Comments Documentation Audit trail review | |
| System 2: Balance | | | | | | |
| GxP Data elements | Date/Time* Configuration | | | | | |
| System 3: UV | | | | | | |

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| | | | | | | |
|-----------------------|--|--|---|--|------------------------------|---|
| GxP Data elements | | Date/Time* Configuration* Analyst Method ID SST data | UV absorbances* Meta data* (run ID, analyst, time and date, sequence, sample ID, ..) | | Raw data Audit trail data | |
| System 4: LIMS | | | | | | |
| GxP Data elements | | | | | | Sample ID Analyst ID Date and time Sample result |

c. Highlight electronic GxP data that can be modified/deleted or re-processed after creation. (asterix in above table) (see section 3 step C)

4) Data and System categorisation

a. Data severity assessment: (see section 4.1)

For this exercise we only continue with the UV-instrument. The raw GxP data sheets (RDS), the balances and LIMS are out of the scope. These systems should be handled in a separate assessment.

The UV-instrument is used for RM, intermediates and APIs. According to the severity definitions, we will apply the API categorisation which will result in very high severity.

b. System profiling: (see section 4.2, decision tree figure 3)

System 1: RDS -> cat 1

System 2: Balance -> cat 3

System 3: UV-instrument -> cat 6

System 4: LIMS -> cat 6

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c. System assessment: (according to checklist 4.3 table 2)

Only the gaps are in below overview.

| Topic | Sub topic | Question | Acceptance criteria | Does the system meet the criteria? | Description of gaps |
|------------------------------|--------------------|--|--|------------------------------------|---|
| Data lifecycle management | Data capture/entry | Does the system enforces saving at the moment of GxP data entry? | The system should enforce saving immediately after critical data entry. Data entry prior to saving to permanent memory with audit trail (server, database) is considered to be temporary memory. The length of time that data is held in temporary memory should be minimized. | No | It is possible that data is not saved at the end of the measurement. The system is asking if data need to be saved or not. |
| Data lifecycle management | Backup/restore | Is a scheduling system maintained for manual data backups and are manual backup processes traceable throughout the process of performing the activity? | For manual Data Backup, a scheduling system shall be maintained. The scheduling system shall track and notify the appropriate personnel when backup is required. Manual backup processes shall be traceable throughout the process of performing the activity. | No | There is no system in place for back-up and storage of standalone systems. (not connected to a network) There is no fixed schedule. |
| Data lifecycle management | Backup/restore | Do changes to the Data Backups process follow a formal change control process? | Any changes to scheduled Data Backups shall follow the formal change management process. | No | See question 14 |
| Audit trail | Functionality | Is there an audit trail in place for user management and system settings? | Where computerized systems are used to capture, process, report or store raw data electronically, the data shall include user management- and system settings. The items included in audit trail should be those of relevance to permit reconstruction of the generation, modification and deletion of the user management- and system settings. | No | No user management audit trail available |
| Security/User Access Control | Authentication | Does the system require enforcing for password change at a defined interval? | The system must require enforcing for a passwords change at a defined interval. | No | The system doesn't require periodic password change. |
| Time Stamps | Access security | Can non-IT administrator roles change systems date and time settings (including time zone settings)? | Only system administrators shall have sufficient authority to change systems date and time settings. Non-administrator roles shall have read only access. | No | All users can change date and time. (including time zone) |

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5) Risk Assessment (FMEA to calculate the gaps and their current individual Risk Priority Numbers (RPN)) (see section 5)

| Checklist ID | Step | Function/Requirement or Data flow Step | Potential Failure Mode | Effect | Severity | Occurrence | Detectability | RPN |
|--------------|--------------------|--|---|--|----------|------------|---------------|-----|
| 8 | Data capture/entry | Does the system enforces saving at the moment of GxP data entry? | It is possible that data is not saved at the end of the measurement. The system is asking if data need to be saved or not. | Data can be lost. | 5 | 3 | 4 | 60 |
| 14 | Backup/restore | Is a scheduling system maintained for manual data backups and are manual backup processes traceable throughout the process of performing the activity? | There is no system in place for back-up and storage of stand alone systems. (not connected to a network) There is no fixed schedule. | Data can be lost. | 5 | 4 | 2 | 40 |
| 17 | Backup/restore | Do changes to the Data Backups process follow a formal change control process? | see question 14 | see question 14 | 5 | 4 | 2 | 40 |
| 23 | Functionality | Is there an audit trail in place for user management and system settings? | No user management audit trail available | User levels can be changed. (e.g. an analyst can receive admin rights) | 5 | 3 | 4 | 60 |
| 34 | Authentication | Does the system require enforcing for password change at a defined interval? | The UV systems doesn't require periodic pasword change. | Possible misabuse of someones password | 5 | 1 | 4 | 20 |
| 44 | Access security | Can non-IT administrator roles change systems date and time settings (including time zone settings)? | Date and time settings (including time zones) are accessible by all users. | Time of creating data can be adulterated. | 5 | 2 | 4 | 40 |

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6) Risk management (see section 6)

The above table shows that 5 of the 6 gaps have a high RPN (Red). Actions have been defined to address these issues immediately. Additional actions have also been defined to mitigate the other gaps

In the next table the RPNs are recalculated after implementation of the defined actions.

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| Checklist ID | Step | Potential Failure Mode | Effect | RPN | Intermediate Action | Severity | Occurrence | Detectability | RPN | Long term Recommended Action | Severity | Occurrence | Detectability | RPN |
|--------------|--------------------|--|--|-----|---|----------|------------|---------------|-----|--|----------|------------|---------------|-----|
| 8 | Data capture/entry | It is possible that data is not saved at the end of the measurement. The system is asking if data need to be saved or not. | Data can be lost. | 60 | Introduce a procedure to describe the different steps for the user during UV analysis, including a review process at the end. | 5 | 2 | 2 | 20 | Update the software to go to the version which is storing automatically all of the runs. | 5 | 1 | 1 | 5 |
| 14 | Backup/restore | There is no system in place for back-up and storage of stand alone systems. (not connected to a network) There is no fixed schedule. | Data can be lost. | 40 | Introduce a manual back-up process | 5 | 2 | 2 | 20 | Install a full automated back-up system with a defined customized interval | 5 | 1 | 1 | 5 |
| 17 | Backup/restore | see question 14 | see question 14 | 40 | See question 14 | 5 | 1 | 1 | 5 | NA since short term implementation is sufficient | | | | 0 |
| 23 | Functionality | No user management audit trail available | User levels can be changed. (e.g. an analyst can receive admin rights) | 60 | Install a logbook and periodic user/access review | 5 | 2 | 2 | 20 | Even the new software doesn't have the audit trail function for user management | 5 | 2 | 2 | 20 |
| 34 | Authentication | The UV systems doesn't require periodic password change. | Possible misuse of someones password | 20 | Implement a procedure to regularly change of passwords | 5 | 1 | 2 | 10 | Implement automatic password rules in system. (or update software) | 5 | 0 | 1 | 0 |
| 44 | Access security | Date and time settings (including time zones) are accessible by all users. | Time of creating data can be adulterated. | 40 | Include a procedure to define R&R towards time and date settings and include check in the periodic review. | 5 | 1 | 4 | 20 | Update the software to include user level access on date and time settings (including time zone) | 5 | 0 | 1 | 0 |

To close out the risk in a documented and formal way, an additional column can include a reference to the objective evidence that has been implemented to remediate the gaps.

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| Checklist ID | Step | Potential Failure Mode | Effect | Long term Recommended Action | Severity | Occurrence | Detectability | RPN | References |
|--------------|--------------------|---|--|--|----------|------------|---------------|-----|--|
| 8 | Data capture/entry | It is possible that data is not saved at the end of the measurement. The system is asking if data need to be saved or not. | Data can be lost. | Update the software to go to the version which is storing automatically all of the runs. | 5 | 1 | 1 | 5 | 1) Change control document upgrade UV software 2) Qualification report of UV software NameX, version xx 3) Training records analysts 1, 2, x |
| 14 | Backup/restore | There is no system in place for back-up and storage of stand alone systems. (not connected to a network) There is no fixed schedule. | Data can be lost. | Install a full automated back-up system with a defined customized interval | 5 | 1 | 1 | 5 | 1) Change control document connecting UV to network 2) Qualification report of back-up/restore software NameY, version xx |
| 17 | Backup/restore | see question 14 | see question 14 | NA since short term implementation is sufficient | | | | 0 | 1) Change control procedure version xx |
| 23 | Functionality | No user management audit trail available | User levels can be changed. (e.g. an analyst can receive admin rights) | Even the new software doesn't have the audit trail function for user management | 5 | 2 | 2 | 20 | 1) logbook reference xxx |
| 34 | Authentication | The UV systems doesn't require periodic password change. | Possible misuse of someones password | Implement automatic password rules in system. (or update software) | 5 | 0 | 1 | 0 | 1) Change control document upgrade UV software 2) Qualification report of UV software NameX, version xx |
| 44 | Access security | Date and time settings (including time zones) are accessible by all users. | Time of creating data can be adulterated. | Update the software to include user level access on date and time settings (including time zone) | 5 | 0 | 1 | 0 | 1) Change control document upgrade UV software 2) Qualification report of UV software NameX, version xx |