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| SOP No. |  |
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| Author: |  |
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| Document information | |
| Revision period |  |

1. **Purpose**

This Procedure is applied to the process of generating dynamic and reproducible reports using R Markdown for clinical trial data analysis and reporting.

This Procedure is mandatory for compliance by all statistical programmers and analysts involved in process of planning, creation, validation, and documentation of dynamic reports.

The requirements of this Procedure are mandatory for compliance by Biostatisticians, Quality Control Reviewers (QCR), and Project Managers responsible for ensuring accuracy, consistency, and adherence to regulatory requirements and sponsor guidelines.

## **2. Scope**

This SOP applies to all statistical programmers and analysts involved in generating dynamic reports for clinical study reports (CSRs), regulatory submissions, and other research deliverables using R Markdown.

## **3. Responsibilities**

* **Statistical Programmers (SP)**: Develop, validate, and document R Markdown reports.
* **Biostatisticians (BST)**: Provide statistical analysis plans (SAPs) and review reports.
* **Quality Control Reviewers QCR**: Perform independent validation and ensure compliance.
* **Project Managers**: Ensure timelines and deliverables align with study requirements.

## **4. Definitions**

* **R Markdown**: A framework for creating dynamic, reproducible reports combining R code, text, and visualizations.
* **TLFs**: Tables, Listings, and Figures summarizing clinical trial data.
* **SAP**: Statistical Analysis Plan, outlining methodology and specifications for reporting.
* **SAR**: Statistical Analysis Report.
* **CDISC**: Clinical Data Interchange Standards Consortium, defining standard data formats.
* **ADaM**: Analysis Data Model, providing datasets used for statistical analysis.

## **5. Procedure**

### **5.1 Preparation**

**5.1.1. Review of SAP and study protocol to determine reporting specifications**

* **SP** and **BST** identify key analysis objectives and endpoints and draw out the basic chapter structure of SAR.
* **SP** ensure consistency of the structure of the expected SAR with SAP, protocol requirements and corporate reporting templates.

#### **5.1.2. Obtaining necessary input datasets and metadata**

* **SP** access and validate the availability of pre-made datasets and TLFs.
* **SP** confirm dataset structures and variable mappings align with the specifications.
* **SP** check for data integrity issues such as missing values and outliers.

#### **5.1.3. Defining the output structure**

* **SP** specify TLFs and textual summaries based on reporting requirements for each chapter.
* **SP** align titles, footnotes, and captions with study reporting guidelines.
* **SP** ensure consistency in statistical methods and presentation across outputs.

### **5.2 Programming**

#### **5.2.1.** Setting up the R Markdown environment

#### **SP** load required packages (e.g., rmarkdown, knitr, gt, flextable, ggplot2).

#### **SP** configure YAML settings for document format (PDF, Word, or HTML), initial design features, object numeration.

#### **SP create, configure and connect a template that defines such features as custom styles, font type, font size, page orientation, spacing.**

#### **SP d**efine parameters for dynamic content generation, specifying different all report rendering options necessary.

#### **SP assign titles to** report rendering options. The draft version of dynamically generated SAR is assigned manually in local environment of **SP.**

#### **5.2.2.** Developing R Markdown scripts for analysis and visualization**.**

#### **SP** fill chapters with pre-made TLFs, configure dynamic referencing, captions, placement on the page.

#### **SP c**reate necessary dynamic tables outside of the scope of TLFs using appropriate packages (e.g., gtsummary, gt, or flextable).

#### **SP g**enerate necessary figures tables outside of the scope of TLFs using ggplot2 or other visualization libraries.

#### **5.2.3.** Applying best practices for dynamic reporting

* **SP** create complex and layered dynamic descriptions using inline R code, custom functions, code chunk options.
* **SP i**mplement conditional logic for adaptive reporting.
* **SP a**utomate formatting for consistency applying pre-defined custom styles to text portions of the document.
* **SP regularly update dynamically rendered draft version of SAR manually specifying its version number.**

#### **5.2.4. Ensuring traceability by documenting data derivation and transformations**

* **SP m**aintain version-controlled scripts.
* **SP a**nnotate R Markdown scripts with clear documentation.
* **SP s**ave key intermediate datasets for validation and audit purposes.

### 5.3 Validation

**5. 3. 1. Performing independent review of generated reports**

* **SP and BST** compare outputs against expected results from the SAP. If quality check is passed, **SP and BST proceed to the next step. If** quality check is failed the code is updated with necessary changes.
* **SP v**erify consistency between TLFs and textual summaries. If quality check is passed, **SP proceed to the next step. If** quality check is failed the code is updated with necessary changes.

**5. 3. 2. Conducting QC checks for accuracy and completeness**

* **BST v**alidate all statistical calculations and visualizations.
* **BST e**nsure formatting consistency and regulatory compliance.
* **SP and BST p**erform cross-checks against source datasets.
* If quality check is passed, **the team proceeds to the next step. If** quality check is failed the code is updated with necessary changes by **SP.**

**5. 3. 3. Documenting validation findings and corrective actions.**

* **SP m**aintain QC logs and track issue resolutions.
* **SP a**rchive reviewed reports and validation reports.

### 5.4 Submission and Reporting

* **SP format reports per sponsor and regulatory guidelines (e.g., FDA, EMA).**
* **SP and BST integrate dynamic reports into clinical study reports and submissions.**
* **SP store final validated reports in the appropriate repository.**

### 6. Documentation and Compliance

* **SP m**aintain logs of R Markdown development and validation activities (QC logs).
* **SP e**nsure compliance with Good Clinical Practice (GCP) and company SOPs.
* **SP a**rchive final reports and scripts per regulatory retention policies.

## **7. References**

* Statistical Analysis Plan (SAP)
* Clinical Study Protocol
* CDISC, ADaM and SDTM Guidelines
* Regulatory Guidance Documents (e.g., FDA, EMA)

## **8. Supporting documents**

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| **No.** | **Name** | **SD No.** |
| 1. | QC Logs |  |
| 2. | SAP review reports |  |

## **10. Revision History**

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| **Version** | **Effective date** | **Reason for changes / description** |
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