## 1. PURPOSE

This Work Instruction (WI) describes the process for the development, review, and maintenance of Tables, Figures and Listings (TFLs) statistical output.

## 2. SCOPE

This WI applies to all clinical studies reports sponsored by BeiGene, including clinical pharmacology studies if deemed appropriate and corresponding integrated analysis. The WI does not apply to Investigator Sponsored Trials (ISTs).

## 3. ABBREVIATIONS AND DEFINITIONS

3.1 **AWS:** BeiGene's internally hosted Amazon Web Service environment

3.2 **BEEP:** BeiGene Employee Engagement Portal

3.3 **Clinical Study Team (CST):** A team of cross-functional representatives responsible for the coordination, planning and execution of clinical studies from protocol to study closeout.

3.4 **CMO:** Chief Medical Officer

3.5 **Database Lock (DBL):** A lock of data in the EDC system/external data preventing system users from updating and/or adding new data.

3.6 **Dry Run TFLs:** Draft run of programmed TFLs containing live or dummy data before a database snapshot or database lock including intext and appendix

3.7 **GSDS:** Global Statistics and Data Science

3.8 **Statistical Analysis Plan (SAP):** A document that contains a detailed elaboration of the principal features of the analysis described in a clinical protocol, and which includes procedures for statistical analysis of the primary and secondary endpoints and other data.

3.9 **TFLs:** Tables, Figures and Listings including intext and appendix

3.10 **TFL shells:** Shells of Tables, Figures, and Listings including intext and appendix

3.11 **TOC:** Table of Content including intext and appendix

## 4. RESPONSIBILITIES

### 4.1 Portfolio and Program Management (PPM)

4.1.1 Provides user access list for pivotal studies and corresponding integrated analysis.

### 4.2 Study Statistician

4.2.1 Develops, and maintains TFL shells.

4.2.2 Creates SharePoint folder.

4.2.3 Requests access to the TFLs.

4.2.4 Coordinates the review of TFLs.

4.2.5 Performs statistical validation of key results in TFLs.

### 4.3 Statistical Programmer

4.3.1 Reviews the TFL shells.

4.3.2 Develops, reviews, and maintains TFLs and verification of TFLs.

### 4.4 Clinical Study Team (CST)

4.4.1 Reviews the TFL TOC, TFL shells, and TFLs.

### 4.5 Product Lead of Global Statistics or Global Statistics delegate and Development Core Team Lead (DCTL)/(Global Product Team Lead) GPTL or DCTL/GPTL delegate

4.5.1 Approves of TFL shells.

## 5. INSTRUCTION

5.1 Development of Draft TFL Shells

5.1.1 Study Statistician, in collaboration with the Statistical Programmer, plans the timing of the TFL shells development following the study-specific delivery timeline.

5.1.2 Study Statistician prepares the TFL TOC, based on a draft version of the SAP and circulates to the Medical Monitor, Global Patient Safety, Medical Writer, and other applicable CST members for review and obtains agreement before the draft TFL shells is developed.

5.1.3 Study Statistician prepares the draft TFL shells and circulates them to the Statistical Programmer for review.

5.1.3.1 Study Statistician prepares the draft TFL shells using Template (VV-QDOC-13241 Tables, Figures, Listings (TFLs) Shells), a draft version of the SAP, and General Reporting Guidelines for Tables, Figures and Listings.

5.1.3.2 Study Statistician maintains track changes from the Template Shell including modifications from the Template Shell and additions of study/indication specific shells.

5.1.4 Statistical Programmer reviews the draft TFL shells and provides feedback to the Study Statistician.

5.1.5 Study Statistician revises the TFL shells to incorporate Statistical Programmer's feedback.

5.1.6 Study Statistician circulates the draft TFL shells for review to Functional Lead Statistician, Medical Monitor, Global Patient Safety, Medical Writer, and other CST members if applicable.

5.1.6.1 Study Statistician incorporates any required revisions into the draft TFL shells from CST review and declares stable TFLs shells.

5.1.7 Study Statistician manages version history manually in the draft TFL shell to track the changes, with unique names given for each shell to distinguish between a series of draft TFL shells.

5.1.8 In accordance with study specific deliverable timelines and prior to TFL development by Statistical Programmer, the Study Statistician prepares the TFL shells and circulates to the following functional representatives for review and approval:

- Development Core Team Lead Statistician
- Development Core Team Lead or Global Product Team Lead
- Lead Statistical Programmer
- Clinical Development Representative(s)
- Medical Writer
- Global Patient Safety
- Regulatory Affairs Representative
- Clinical Pharmacology
- Any other function as required

Approvals are obtained using Template (VV-QDOC-99239 Tables, Figures, and Listings (TFL) Shell Approval Form), the approved TFL Shells and Approval Form should be stored in AWS.

5.2 Development of Draft TFLs

5.2.1 As per study specific deliverable timelines, the Statistical Programmer and Study Statistician plan the timing of the TFL development after SAP and TFL shells are developed.

5.2.2 The Statistical Programmer and Study Statistician consult with the Medical Monitor, Medical Writer, Global Patient Safety, Clinical Operations Manager, and other applicable CST members to confirm TFL delivery timelines and review of draft TFLs (Dry Run).

5.2.3 Study Statistician collaborates with PPM or CST to obtain the user access list for the Dry Run TFLs.

5.2.3.1 For single arm pivotal studies and corresponding integrated analysis, Study Statistician collaborates with PPM to obtain a list of the names and email addresses of individuals who have access.

5.2.3.2 For non-pivotal studies or pivotal studies with blinded/masked TFLs and corresponding integrated analysis, Study Statistician collaborates with CST to initiate and generate the team list to access the Dry Run TFLs.

5.2.4 Study Statistician submits an access request using the Clinical Programs SharePoint Access Management Form in Service Desk System Portal and obtains its approval. Refer to SOP (VV-QDOC-12052 GSDS Data Access and Control) for further guidance on the process for requesting access.

5.2.5 Statistical Programmer prepares the draft TFLs following the stable TFL shells, WI (VV-QDOC-00169 Statistical Programming), and SOP (VV-QDOC-00697 Statistical Programming Development and Verification).

5.3 Review of Draft TFLs

5.3.1 Study Statistician reviews the draft TFLs and provides feedback to Statistical Programmer.

5.3.2 Statistical Programmer incorporates feedback from Study Statistician into the draft TFLs. If necessary, Study Statistician makes TFL shells updates prior to updating the draft TFLs.

5.3.3 Study Statistician circulates the draft TFLs for review to following functional representatives:

- Development Core Team Lead Statistics
- Development Core Team Lead or Global Product Team Lead
- Lead Statistical Programmer
- Clinical Development Representative(s)
- Medical Writer
- Global Patient Safety Representative
- Regulatory Affairs Representative
- Clinical Pharmacology Representative
- Any other function as required

5.3.4 If TFL shell revisions are needed, Study Statistician incorporates the required revisions into the TFL shells. The revised TFL shells must be approved by the functions listed in section 5.1.8 before TFL revisions. Statistical Programmer incorporates update(s) into draft TFL per the updated TFL shells. Study Statistician circulates the revised TFLs for review to functional representatives as per section 5.3.3 mentioned if needed.

**NOTE:** If revisions impact resources and study timelines, the revisions along with impact assessment must be endorsed by Head of GSDS and CMO or delegate. The revised TFL shells to be re-circulated for review by CST as per step 5.1. Study timelines to be updated accordingly.

5.4 Delivery, Revision and Maintenance of TFLs

5.4.1 In accordance with study specific deliverable timelines and prior to database lock (DBL)/database snapshot, Study Statistician may circulate the draft TFL to the following functional representatives for review:

- Functional Heads of GSDS
- Clinical Development
- Global Patient Safety
- Regulatory Affairs Representative
- Functional Head from Clinical Pharmacology, if required
- Biomarker & Translational Science, if required

- Any other function as required

5.4.2 Prior to DBL/database snapshot, if SAP amendment and/or addendum takes place and it is deemed that the TFLs need to be revised, then the updated TFL shells must be approved by the functions listed in section 5.1.8 before TFL revisions.

**NOTE**: If revisions impact resources and study timelines, the revisions along with impact assessment must be endorsed by Head of GSDS and CMO or delegate. The revised TFL shells to be re-circulated for review by CST as per step 5.1. Study timelines to be updated accordingly.

5.4.3 Prior to DBL/database snapshot, Study Statistician performs statistical validation of key results in TFLs following WI (VV-QDOC-00698 Verification of Statistical Programming Deliverables).

5.4.4 Study Statistician collaborates with PPM to provide a list of the names and email addresses of individuals who have access following WI (VV-QDOC-12115 Topline Result Communication) for pivotal studies and corresponding integrated analysis.

5.4.5 Study Statistician submits access request using the Clinical Programs SharePoint Access Management Form in Service Desk System Portal and obtains its approval. Refer to SOP (VV-QDOC-12052 GSDS Data Access and Control) for further guidance on the process for requesting access.

5.4.6 After DBL/database snapshot, Statistical Programmer generates the TFLs. Study Statistician reviews the TFLs and circulates to Medical Monitor, Medical Writer, Global Patient Safety, and other applicable CST members. The below points must be considered for blinded studies:

- For Final DBL and Interim database lock after which Study Statistician and Statistical Programmer are unblinded, Study Statistical Programmer generates the TFLs and Study Statistician reviews the TFLs and circulates to CST review.
- For database snapshot and DBLs of Interim Analysis after which Study Statistician and Statistical Programmer remain blinded, the TFLs will be generated by an independent team (independent statistical programmer and statistician) and delivered to the designated unblinded personnel/committee following WI (VV-QDOC-01327 Data Integrity Protection for Clinical Trials), WI (VV-QDOC-12115 Topline Result Communication) and study Data Integrity Protection Plan.

5.4.7 Study Statistician informs Medical Writer that the TFLs are ready such that writing of the Clinical Study Report and any other document may begin.

5.5 TFLs for Topline Readout

5.5.1 Study Statistician selects topline CSR TFL shells at least 4 weeks prior to DBL or date of database snapshot following WI (VV-QDOC-12115 Topline Result Communication). The TLFs to be considered for topline include but are not limited to:

- **Study Population**: patient disposition, demographics, and baseline characteristics
- **Efficacy**: primary efficacy analysis and key secondary efficacy analyses
- **Safety**: most important safety analysis

5.5.2 After DBL or date of database snapshot, Statistical Programmer generates topline TFLs following WI (VV-QDOC-00698 Verification of Statistical Programming Deliverables) and Study Statistician performs the topline readout per WI (VV-QDOC-12115 Topline Result Communication).

5.5.3 For blinded studies, after unblinding has occurred, any additional analysis requires TFLs shell addendum. The final TFLs shell addendum which contains all additional analysis in Clinical Study Report, or any other document should be approved before the Clinical Study Report or any other document signoff by below function representatives:

- Development Core Team Lead Statistics
- Development Core Team Lead or Global Product Team Lead
- Lead Statistical Programmer
- Clinical Development Representative(s)
- Any other function if required

## 6. REFERENCES

### 6.1 Controlled Documents

#### 6.1.1 SOP (VV-QDOC-00697 Statistical Programming Development and Verification)

#### 6.1.2 SOP (VV-QDOC-12052 GSDS Data Access and Control)

#### 6.1.3 Template (VV-QDOC-13241 Tables, Figures, Listings (TFLs) Shells)

#### 6.1.4 Template (VV-QDOC-99239 Tables, Figures, and Listings (TFL) Shell Approval Form)

#### 6.1.5 WI (VV-QDOC-00169 Statistical Programming)

#### 6.1.6 WI (VV-QDOC-00698 Verification of Statistical Programming Deliverables)

#### 6.1.7 WI (VV-QDOC-01327 Data Integrity Protection for Clinical Trials)

#### 6.1.8 WI (VV-QDOC-12115 Topline Result Communication)

### 6.2 Regulatory References

#### 6.2.1 N/A

### 6.3 Other References

#### 6.3.1 General Reporting Guidelines for Tables, Figures and Listings

## 7. APPENDICES

### 7.1 N/A

## 8. DOCUMENT HISTORY PAGE

| Version | Effective Date | Brief Description of Change |
|---|---|---|
| 1.0 | 08 Jan 2021 | Original Work Instruction. |
| 2.0 | 12 Sep 2023 | • Revised the Responsibilities section for clarity.<br>• Added Portfolio and Program Management (PPM) to Responsibilities section.<br>• Revised the Instruction section for process efficiency.<br>• Removed Template VV-QDOC-15017 Tables, Figures, and Listings Review Form from sections 5.1.6, 5.3, 5.3.4, and 6.0.<br>• Removed Template VV-QDOC-13242 from section 6.0.<br>• Added Template VV-QDOC-99239 Tables, Figures, and Listings (TFL) Shell Approval Form in sections 5.1.8 and 6.0 |

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