1. PURPOSE

This Work Instruction (WI) describes the process for the preparation, review, endorsement, and disclosure of study topline readout results as well as study-specific post press release communication where required.

2. SCOPE

This WI applies to all pivotal clinical studies sponsored by BeiGene and applies to both pre-specified interim (if applicable) and final analysis. The WI does not apply to the Investigator Sponsored Trials (ISTs) or Investigator Sponsored Research (ISRs) and does not apply to the trials where BeiGene does not have sponsor oversight over the trial database(es).

3. ABBREVIATIONS AND DEFINITIONS

3.1 **Flash Memo:** A document in PowerPoint format presenting study topline results.

3.2 **Topline Core Team:** The group of core members of the study team, consisting of but not limited to the Study Statistician, Study Medical Monitor, Development Core Team Lead (DCTL), Compound Statistical Lead, and Product Safety Lead.

3.3 **Topline Readout:** The procedure of controlling the communication of restricted topline results involving BeiGene pivotal clinical studies for obtaining alignment of the topline results interpretation and establishing next-step activities. The reviewers include Topline Core Team, Head of Global Statistics and Data Science (GSDS), Head of Statistics, Head of Safety Science and Chief Medical Officer (CMO) or delegate. Other functions may be included as required.

3.4 **Topline Results:** The most important results of the pivotal clinical study with the scope defined by the Topline Core Team including but not limited to the results for primary efficacy endpoint, key secondary endpoint and most important safety results.

4. RESPONSIBILITIES

4.1 Statistical Programming (SP)

4.1.1 Receives all required data and conducts the data acceptability check together with Statistician.

4.1.2 Generates the Study Data Tabulation Model (SDTM), Analysis Data Model (ADaM) datasets, and the Tables Figures Listings (TFLs) for topline result output.

4.2 Statistician

4.2.1 Leads the GSDS activities after all required data received to perform required analysis supporting topline readout.

4.2.2 Reviews all topline outputs and validates selected topline outputs from Scientific Programming team.

4.2.3 Provides statistical interpretation, prepares the Flash Memo.

4.2.4 Collaborates with PPM to provide Legal with a list of the names and email addresses of employees who have access to the timing of the database lock and/or readout as well as the aggregate topline result data and the date they first have access before the information is shared.

4.3 Portfolio and Program Management (PPM)

4.3.1 Drives and coordinates the topline result communications and related project management activities with the cross-functional team.

4.3.2 Prepares, reviews, and updates the study specific Topline Result Communication Plan in collaboration with Statistician.

4.3.3 Attends topline result communication key activities to ensure the communications follow the plan (e.g., topline results review meeting, Clinical Interpretation Meeting (CIM) meeting and press release review etc.).

4.3.4 Provides Legal with a list of the names and email addresses of employees who have access to the timing of the database lock and/or readout as well as the aggregate topline result data and the date they first have access before the information is shared, with Statistician's support. PPM leads with close collaboration with Statistician.

4.4 Medical Monitor (MM)

4.4.1 Performs topline readout activities that require medical or clinical expertise.

4.4.2 Provides medical interpretation and collaborates with members in Topline Core Team to formulate the interpretation of data as required and prepare the Flash Memo.

4.5 Product Safety Lead

4.5.1 Participates in topline readout activities that require safety expertise.

4.5.2 Provides safety interpretation and collaborates with members in Topline Core Team to prepare the Flash Memo.

4.6 Legal

4.6.1 Provides legal consultation regarding confidentiality obligation, insider trading compliance and public disclosure compliance throughout the topline result communication before the results are released to public by BeiGene.

4.6.2 Reviews and approves the Topline Result Communication Plan.

4.7 Data Disclosure & Transparency (DDT)

4.7.1 Provides consultation regarding trial transparency reporting compliance, as needed. DDT is not required to review the communication plan, but consults as needed.

4.8 Regulatory Affairs

4.8.1 Participates in topline readout related activities, as applicable, to provide expertise in regulations and input if necessary.

4.9 Chief Medical Officer (CMO) or Delegate

4.9.1 Reviews and approves the Topline Result Communication Plan.

Note: A delegate must be a qualified and authorized representative as per CMO's discretion (e.g., DCTL or clinical lead).

4.10 Corporate Affairs

4.10.1 Collaborates with cross-functional stakeholders including Legal, Medical, Regulatory, and Investor Relations, to develop recommended communications approach and gains organizational endorsement of approach. Develops materials to support communications approach (e.g., press release, reactive statement, Q&A, scenario plans).

4.10.2 Reviews and approves the Topline Result Communication Plan.

5. INSTRUCTION

5.1 Flash Memo Shell Development

5.1.1 Statistician follows WI (VV-QDOC-13240 Tables, Figures, and Listings Development and Maintenance) to select topline Clinical Summary Report (CSR) TFL shells 4 weeks before Database Lock (DBL).

5.1.2 Statistician drafts topline readout Flash Memo shell based on the selected topline CSR TFL shells before the finalization of Topline Result Communication Plan.

5.1.3 Statistician coordinates the review and approval of Flash Memo shell before DBL.

5.2 Prepare and finalize Topline Result Communication Plan before DBL.

5.2.1 Portfolio and Program Management drafts study specific Topline Result Communication Plan using Template (VV-QDOC-12116 Topline Result Communication Plan – Interim Analysis) or Template (VV-QDOC-61497 Topline Result Communication Plan – Final Analysis) and circulates to cross-functional team for review.

There are some key elements to consider in Topline Result Communication Plan:
- Steps and corresponding timeline before topline readout.
- Steps of communication flow and corresponding timeline after topline readout.

5.2.2 Portfolio and Program Management shares the Topline Result Communication Plan with Legal to decide the insider trading compliance process and procedure.

5.2.2.1 Portfolio and Program Management shares Topline Result Communication Plan with Legal and keeps Legal posted on any subsequent changes.

5.2.2.2 To the extent that Legal determines that the information about the trial, including the timing of the database lock and readout as well as the aggregate topline results, constitutes material nonpublic information, Legal will institute a special blackout for the Covered Employees according to the Company's Insider Trading Policy as necessary. PPM shall promptly notify Legal of any changes to the list with statistician's support until the end of the special blackout. With statistician's support, PPM shall provide Legal with a list of the names and email addresses of all employees who have access to the topline result data and the date they first have access before the information is shared (collectively "Covered Employees").

5.2.3 Portfolio and Program Management shares the Topline Result Communication Plan with Corporate Affairs team and Legal team for their consideration and decision on Press Release (PR) plan, which may include a standalone press release. Corporate Affairs team will assess and advise on the Topline Result Communication Plan related to this WI and timeline.

5.2.4 Portfolio and Program Management is responsible for the review of Topline Result Communication Plan within senior leadership and obtain approval by CMO or delegate, Functional Executive of Corporate Affairs and General Counsel or delegate before DBL.

Note: A delegate must be a qualified and authorized representative as per General Counsel's discretion.

5.3 All required raw data are available for Topline Readout on Day 0. When Interim Analysis is applicable, please refer to Template (VV-QDOC-00148 Data Monitoring Committee Charter). When study unblinding for planned Interim and Final Analysis is applicable, please refer to WI (VV-QDOC-01114 Scheduled Unblinding for Planned Interim and Final Analyses of a Randomized Clinical Study).

5.4 Conduct Topline Readout

5.4.1 Generally, GSDS generates and validates the topline outputs after receiving final data.

5.4.1.1 Statistical Programming maps SDTM datasets and generates ADaM datasets.

5.4.1.2 Statistical Programming generates and validates topline outputs per WI (VV-QDOC-00698 Verification of Statistical Programming Deliverables).

5.4.1.3 Statistician performs the internal review and validates the selected outputs.

5.4.2 Statistician updates Flash Memo with topline outputs. The Topline Core Team then authors the Flash Memo with interpretation:

- Statistician provides interpretation from statistical perspective for all topline outputs especially for efficacy analysis results.
- Clinical team (DCTL/Medical Monitor) provides interpretation from clinical perspective.
- Product Safety Lead provides interpretation from safety perspective.

5.4.3 According to Topline Result Communication Plan, Topline Core Team presents Flash Memo in topline readout meeting if topline readout meeting is required; if topline readout meeting is not required, Statistician shares Flash Memo per Topline Result Communication list.

5.5 Activities after Topline Readout

5.5.1 Medical Monitor leads the Clinical Interpretation Meeting (CIM) which is mandatory for all Phase III clinical studies and optional for phase II studies to review and discuss the key study results and the interpretation. Regulatory Project Manager (RPM) or designee to coordinate CIM.

5.5.2 CMO or delegate presents Flash Memo to Sr. Management via meeting or email depending on study specific requirements.

Note: For Sr. Management members, please refer to the distribution list approved by CMO or delegate.

5.5.3 Medical Monitor leads the Conference Abstracts and Publications referenced in SOP (VV-QDOC-01213 BeiGene Global Publications) and consults with Data Disclosure & Transparency to ensure trial transparency reporting compliance, collaborates with Corporate Affairs for press release inputs, as needed.

5.5.4 Per Topline Result Communication Plan, corresponding functions execute the activities post topline readout.

5.6 Post Press Release Data Access

5.6.1 For any requests to access the patient level study data, the request will be filled in the Form (VV-QDOC-11952 Clinical Data Access and Analysis Request Form) and approved by requestor's functional head, GSDS head and CMO or delegate.

5.6.2 For any requests to access the study summary results before the detailed results are released to the public, the request will be approved by the requestor's function head and DCTL/CMO delegate via email.

5.6.3 Study Statistician will be informed on all access requests for access maintenance and tracking.

6. REFERENCES

6.1 Controlled Documents

6.1.1 Form (VV-QDOC-11952 Clinical Data Access and Analysis Request Form)

6.1.2 SOP (VV-QDOC-01213 BeiGene Global Publications)

6.1.3 Template (VV-QDOC-00148 Data Monitoring Committee Charter)

6.1.4 Template (VV-QDOC-12116 Topline Result Communication Plan – Interim Analysis)

6.1.5 Template (VV-QDOC-61497 Topline Result Communication Plan – Final Analysis)

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

6.1.7 WI (VV-QDOC-01114 Scheduled Unblinding for Planned Interim and Final Analyses of a Randomized Clinical Study)

6.1.8 WI (VV-QDOC-13240 Tables, Figures, and Listings Development and Maintenance)

6.2 Regulatory References

6.2.1 N/A

6.3 Other References

6.3.1 N/A

7. APPENDICES

7.1 N/A

8. DOCUMENT HISTORY PAGE

Version	Effective Date	Brief Description of Change
1.0	18 Dec 2020	Original Work Instruction.
2.0	20 Jan 2023	Abbreviations & Definitions updated to remove Executive Committee from list. Responsibilities updated and added roles CMO and Functional Executive of Corporate Affairs. Instructions updated to align with the revised Topline Result Communication Plan templates.

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Approved Date: 13 Dec 2022

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