1. PURPOSE

This SOP describes the global process of BRIM binder creation, and management of BeiGene submission binders that represent dossiers intended for submission to Regulatory Health Authorities (HA).

2. SCOPE

This SOP applies to all BeiGene GxP employees, consultants and contractors who create, manage, and support global regulatory submission dossier binders to Health Authorities. This includes all submission dossier type for BeiGene products, products in-licensed, or jointly developed with an external company, including cloned or re-use dossiers.

Situations which are out of scope:

2.1 Application/Submissions wholly owned by CRO (i.e., CTA and CTA maintenance)

2.2 CTN and CTN maintenance (for Australia only)

3. ABBREVIATIONS AND DEFINITIONS

3.1 **BRIM:** BeiGene Regulatory Information Management, the Veeva Vault RIM system that includes Veeva Vault Submissions, Vault Submissions Archive and Vault Registrations.

3.2 **CMC:** Chemistry, Manufacturing, and Controls

3.3 **CRO:** Contract Research Organization

3.4 **CTA:** Clinical Trial Application

3.5 **CTN:** Clinical Trial Notification

3.6 **HA:** Health Authority

3.7 **Lifecycle Amendment/Minor Variation:** A change to a marketing authorization that has a minimal or no impact on the quality, safety, or efficacy of a medicinal product.

3.8 **Major Supplement/Major Variation:** A change to a marketing authorization that may have a significant impact on the quality, safety, or efficacy of a medicinal product.

3.9 **RAL:** Regulatory Affairs Lead (i.e., RA Lead, RA Strategist, RA CMC)

3.10 **RO:** Regulatory Operations

3.11 **SOM:** Submission Operations Management

3.12 **SOM Lead:** Submission Operation Management assigned lead (Submission Dossier Manager and/or Publisher). This lead is assigned based on the submission dossier type.

3.13 **SOM SDM:** Submission Dossier Manager, a role within SOM which serves as the main contact and coordinator of submission filings.

3.14 **SOM Publishing:** A role within SOM who performs compilation of regulatory documents into a submission dossier to make it ready for HA submission.

3.15 **Submission Binder:** A logical organizational structure in BRIM used to prepare and compile the content of a regulatory submission within Veeva Vault Submissions.

3.16 **SCP**: Submission Content Plan

3.17 **SME:** Subject Matter Expert

3.18 **SOP:** Standard Operating Procedures

3.19 **WI:** Work Instruction

4. RESPONSIBILITIES

4.1 Submission Operations Management (SOM)

4.1.1 Creation of submission binder from SCP. Refer to Appendix 2: Submission Binder Management Roles and Responsibilities – Global.

4.1.2 Creates submission binder once the BRIM SCP document and/or section is approved and locked. Refer to WI (VV-QDOC-47124 Global Submission Content Plan Creation and Maintenance).

4.1.2.1 Performs ongoing maintenance and management of the submission binder

4.1.3 Updates to submission binder from SCP

4.1.3.1 Updates submission binder if edits are required based on updated SCP.

4.1.4 Coordinates approval of submission binders as required for finalization in BRIM

4.2 Regulatory Affairs Lead (RAL)

4.2.1 Ensures BRIM submission binder or final dossier package is complete.

4.2.2 Coordinates approval of submission binders as required for finalization in BRIM. Refer to SOP (VV-QDOC-12175 Approval Requirements for Regulatory Submissions).

5. PROCEDURE

5.1.1 Submission Binder

5.1.1.1 The SOM Lead will create submission binder from the SCP. Refer to Appendix 1: Submission Binder Management Plan Process Map.

5.1.1.2 SOM Lead coordinates final publishing activities for major applications, major supplement/major variation, and lifecycle/minor variation amendments.

5.1.1.3 SOM Lead or delegate coordinates the final dossier package submission quality review. Refer to WI (VV-QDOC-25072 Global Submission Dossier Technical Review).

5.1.1.4 RAL coordinates the final dossier package endorsement and submission binder approval. Refer to SOP (VV-QDOC-12175 Approval Requirements for Regulatory Submissions).

5.1.2 Updates to Submission Binder after approval

5.1.2.1 SME will update SCP.

5.1.2.2 SOM will update the submission binder and BRIM will automatically create a new draft version.

5.1.2.3 Continue from step 5.1.1.2 to step 5.1.1.4.

6. REFERENCES

6.1 Controlled Documents

6.1.1 SOP (VV-QDOC-12175 Approval Requirements for Regulatory Submissions)

6.1.2 WI (VV-QDOC-25072 Global Submission Dossier Technical Review)

6.1.3 WI (VV-QDOC-47124 Global Submission Content Plan Creation and Maintenance)

6.2 Regulatory References

6.2.1 N/A

6.3 Other References

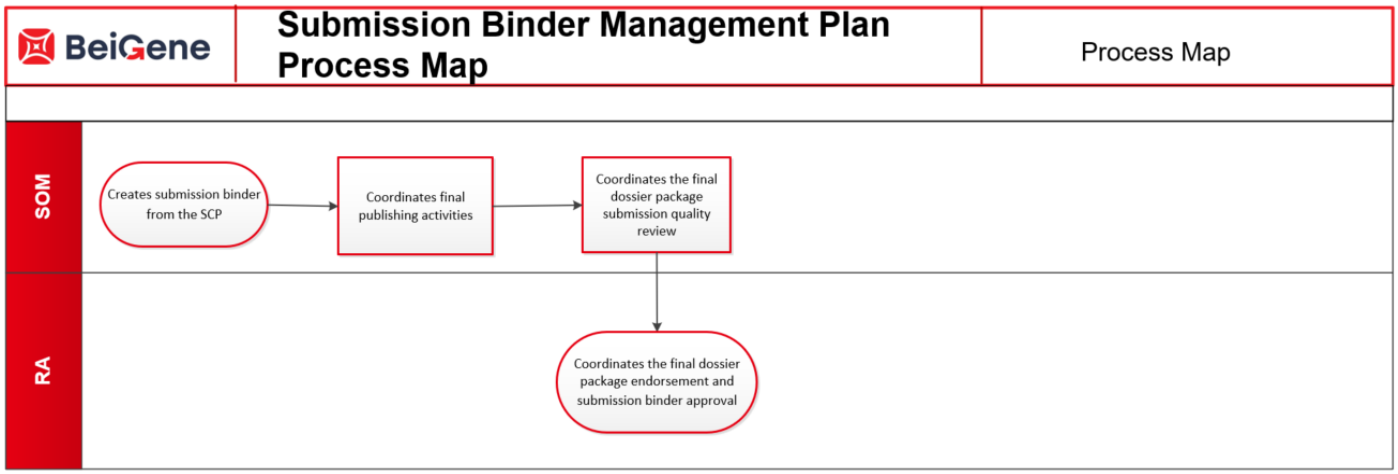
6.3.1 N/A

7. APPENDICES

7.1 Appendix 1: Submission Binder Management Plan Process Map

7.2 Appendix 2: Submission Binder Management Roles and Responsibilities – Global

Appendix 1: Submission Binder Management Plan Process Map



Appendix 2: Submission Binder Management Roles and Responsibilities – Global

Function Area	Create Submission Dossier Binder	Maintains Binders in Veeva Vault	Coordinated final publishing/ Quality Check	Coordinates final dossier endorsement and submission binder approval
Regulatory Affairs Lead				X
SOM	X	X	X	

8. DOCUMENT HISTORY PAGE

Version	Effective Date	Brief Description of Change
1.0	14 Jan 2022	Original SOP.
2.0	12 Dec 2022	Revisions: removal of steps and roles/responsibilities related to request of binder and creation of binder.

Document Approvals

Approved Date: 28 Nov 2022

Task: SME Approval Verdict: Approve changes & release	LaTonjia Wallace, (latonjia.wallace@beigene.com) Functional Area Representative 23-Nov-2022 20:50:33 GMT+0000

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Task: QA Approval Verdict: Approve changes & release	Kalpesh Patel, (Kalpesh.Patel@beigene.com) QA Approval 28-Nov-2022 15:11:44 GMT+0000