# Duke Medicine

Pediatric Blood and Marrow Transplant
Adult Blood and Marrow Transplant
Stem Cell Laboratory

<table>
<thead>
<tr>
<th>DOCUMENT NUMBER:</th>
<th>COMM-PAS-004</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOCUMENT TITLE:</td>
<td>Change Control</td>
</tr>
</tbody>
</table>

**DOCUMENT NOTES:**

**Document Information**

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- **Vault:** COMM-PAS-rel
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- **Document Type:** COMM-PAS

**Date Information**

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- **Expiration Date:**

**Control Information**

- **Author:** BS76
- **Owner:** RB232
- **Previous Number:** COMM-PAS-004 Rev 05
- **Change Number:** PAS-CCR-035

CONFIDENTIAL - Printed by: ACM93 on 20 May 2019 08:13:37 am
COMM-PAS-004 CHANGE CONTROL

1 PURPOSE
   1.1 To describe the process required to initiate and evaluate change control within MasterControl for the Adult Blood and Marrow Transplant (ABMT) Program, the Pediatric Blood and Marrow Transplant (PBMT) Program, and the Stem Cell Laboratory (STCL).
   1.2 To identify potential risk(s) and impact of proposed change(s).
   1.3 To describe when an effectiveness check is required and describe the steps for completing an effectiveness check.

2 INTRODUCTION
   2.1 Regulated environments require specific rules for processes including change control. The establishment of a change control system supports quality, consistency, and protects the integrity of controlled documents.

3 SCOPE AND RESPONSIBILITIES
   3.1 This procedure applies to the creation of or modification(s) to controlled documents.
   3.2 This procedure applies to archiving controlled documents.
   3.3 This procedure applies to changes involving a Program’s design, software, equipment, service provider, and/or other changes requiring review through the change control system.
   3.4 The process for handling emergency change control requests is addressed in Section 8.5.
   3.5 The Medical/Program Director, Quality Systems Unit (QSU), MasterControl System Administrator, and all personnel in programs involved with initiating, reviewing and approving changes via the change control process are responsible for ensuring the requirements of this procedure are met.
   3.6 The Training Coordinator, as applicable, is included in the notification step of the route when the Change Control Request (CCR) is approved, to allow for early identification of potential training needs.
   3.7 MasterControl Document Control Operations (DCO) is notified when a CCR is approved so that appropriate action can be taken in MasterControl.

4 DEFINITIONS/ACRONYMS
   4.1 AR – Annual Report
   4.2 ABMT – Adult Blood and Marrow Transplant
   4.3 BLA – Biologics License Applications
   4.4 CBE – Changes Being Effected
4.5 CCR – Change Control Request

4.6 Change Control – The process of approving and documenting changes to controlled documents, processes, equipment, operations, and design change(s) to ensure compliance with applicable regulatory requirements.

4.7 Controlled Documents – Documents which are subject to review, approval, and version control.

4.8 Detectability – The ability to detect a failure before it causes harm. The purpose of considering detection in any scenario is to ensure that potential or actual failures can be identified with enough time to take action before the user is adversely affected.

4.9 Design Change – The disciplined approach and investment during the design phase that predicts the success of a change or innovation. Includes but is not limited to Program construction or remodeling.

4.10 Document Control Operations (DCO) – Consists of the MasterControl System Administrator and document control specialist(s).

4.11 Effectiveness Check (EC) – Process of evaluating a change after implementation to confirm the change has met the desired outcome. Requirements for each effectiveness check are agreed to before the change is approved and implemented.

4.12 Emergency Request – Allowed when SQIPP is compromised.

4.13 EMMES – Dedicated, validated, web application, database, and online data entry system provided by EMMES Corporation also referred to as AdvantageEDC℠ database.

4.14 Impact – A risk, by its very nature, always has a negative impact. However, the size of the impact varies in terms of cost and impact on health, human life, or some other critical factor. Impact can range from trivial to extreme.

4.15 Initiator – The initiator is responsible for initiating and routing the Change Control Request (CCR) in MasterControl. A subject matter expert (SME), author, or designee trained in MasterControl.

4.16 JA – Job Aid


4.18 PAS – Pediatric, Adult, and Stem Cell Laboratory

4.19 PAS – Prior Approval Supplement

4.20 PBMT – Pediatric Blood and Marrow Transplant

4.21 Probability – A risk is an event that “may” occur as a result of the change. The probability of it occurring can range anywhere from rare to very likely.

4.22 Quality Systems Unit (QSU) – Responsible for ensuring quality system(s) are effectively established and maintained, and who reports on its performance to management with executive responsibility review. QSU has sign-off authority on new and changes to existing documents, processes, or products.

4.23 RA – Regulatory Affairs
4.24 **Risk** – The combination of the probability of occurrence of harm and the severity of that harm. The potential impact to product Safety, Quality, Identity, Purity and Potency (SQIPP).

4.25 **SCR** – System Change Request for EMMES

4.26 **SME** – Subject Matter Expert

4.27 **Software Change** – Includes, but is not limited to, upgrades or changes in computer software/systems.

4.28 **SOP** – Standard Operating Procedure

4.29 **SQIPP** – Safety, Quality, Identity, Purity and Potency

4.30 **STCL** – Stem Cell Laboratory

5 **MATERIALS**

5.1 N/A

6 **EQUIPMENT**

6.1 Computer access to MasterControl and EMMES

7 **SAFETY**

7.1 N/A

8 **PROCEDURE**

8.1 **Change Control Request Form**

8.1.1 The Change Control Request form should be initiated in MasterControl and approval should be completed before implementing a change.

8.1.1.1 Revisions to an SOP and associated form or job aid can be combined in the same CCR if the change description can be clearly documented together.

8.1.1.2 Changes to facilities or equipment (including repairs) should be documented on a CCR with applicable supporting documentation such as facility drawings. If multiple changes/repairs are required, they should be documented on separate CCR requests; however, if the change description can be clearly documented together, they may be submitted on one CCR.

8.1.1.3 All software changes should be documented in a CCR. If multiple changes are required, they should be documented on separate CCR requests; however, if the change description can be clearly documented together, they may be submitted on one CCR.

8.1.1.4 All service provider changes should be documented in a CCR. If multiple changes are required, they should be documented on separate CCR requests; however, if the
change description can be clearly documented together, they may be submitted on one CCR.

8.1.1.5 If one change affects multiples areas (for example, documents, equipment, and a service provider), one CCR is encouraged as long as the description of applicable changes is clear.

8.1.2 The initiator completes COMM-QA-019 FRM1 Change Control Request (Effectiveness Check) FRM1 or COMM-QA-019 FRM2 Change Control Request (No Effectiveness Check) FRM2 in MasterControl.

8.1.2.1 COMM-QA-019 FRM1 Change Control Request (Effectiveness Check) FRM1 can be routed if the initiator determines the change to be medium or high risk. Refer to Appendix I for specific routing structures for this form.

8.1.2.1.1 Examples of changes that require effectiveness checks include updates to critical equipment and changes to critical service providers.

8.1.2.2 COMM-QA-019 FRM2 Change Control Request (No Effectiveness Check) FRM2 can be routed if the initiator determines the change to be low risk or medium risk. This form contains the same information as COMM-QA-019 FRM1 Change Control Request (Effectiveness Check) FRM1 excluding sections V and VI and their associated routing steps in MasterControl. Refer to Appendix II for specific routing structures for this form.

8.1.2.2.1 Examples of changes that do not require effectiveness checks include document title changes and changes that do not affect SQIPP. Changes with an associated with COMM-QA-076 FRM1 CAPA Report should use this form since the effectiveness check of the associated change will be tracked as part of the CAPA.

8.1.2.2.2 QSU may determine during routing that an effectiveness check is required for the change. COMM-QA-019 FRM2 Change Control Request (No Effectiveness Check) FRM2 would be aborted and COMM-QA-019 FRM1 Change Control Request (Effectiveness Check) FRM1 would be initiated to include an effectiveness check.

8.1.3 The initiator of the CCR starts the appropriate form in MasterControl, selecting the associated program/department.

8.1.3.1 The CCR number auto-populates on the form.

8.1.4 Sections I and II are completed by the initiator by checking applicable items and providing explanation where requested. Any sections that do not apply to the requested change should be checked N/A. Section V is
completed by the initiator for COMM-QA-019 FRM1 Change Control Request (Effectiveness Check) FRM1.

8.1.5 Document Changes (Section I)

8.1.5.1 Check whether requesting a new document or a revision or archival of an existing document. List all applicable document titles, document numbers, and revision numbers.

8.1.5.2 Collaborators for new or revised documents should include Subject Matter Expert (SME) and/or personnel associated with the document who are trained in MasterControl as power users.

8.1.5.3 Under document training requirements, select if development of training tools is required (e.g., checklist, quiz, other).

8.1.5.3.1 The training coordinator will follow-up with the initiator in the document collaboration process to implement training tools.

8.1.5.4 The initiator of the CCR lists MasterControl job codes to ensure training assignments are appropriate and inclusive. Refer to COMM-QA-069 Job Codes – Roles and Users within Job Codes.

8.1.5.4.1 All new and revised SOPs, FRMs, and JAs require training in MasterControl.

8.1.5.4.2 For revised SOP/controlled documents, the initiator may select to utilize previously established training assignments if, after reviewing them, the initiator determines that there is no need to update the assignments.

8.1.5.4.3 Some documents in MasterControl, such as organizational charts for example, may not require training.

8.1.6 Equipment Changes (Section I)

8.1.6.1 List Equipment Type, Name, and Serial Number, and Criticality as applicable under the relevant selection.

8.1.6.2 If equipment parts are being replaced per a standard, SOP-driven process (like for preventative maintenance) and are “like for like”, submission of a Change Control is not required.

8.1.6.3 If the change is to existing equipment, document if the requested change affects the qualification status of the equipment.

8.1.6.4 Equipment qualification status should be assessed upon changes to SOPs associated with the use of the equipment.
8.1.6.4.1 Equipment should be requalified if any changes are made which significantly alter the validated state of the equipment.

8.1.6.4.2 Requalification may be warranted following any significant equipment repair, replacement of major components, relocation or observation of drifts in performance trends.

8.1.6.4.3 Repairs or changes that are due to equipment failure may have the potential to impact product quality and should be documented and investigated per COMM-QA-042 Deviations and Investigations. Repairs or changes documented under a deviation report are not required to be duplicated in a change control request.

8.1.7 Software Changes (Section I)
8.1.7.1 List Software Type, Name, and Version Number of the requested change.

8.1.7.2 An EMMES change will also need to be accompanied by STCL-FORM-034 Data Verification Form.

8.1.8 Service Provider Changes (Section I)
8.1.8.1 List Service Provider Name, Type of service provided, and Criticality of the requested change.

8.1.9 Explain any other requested changes that do not fall under the above categories.

8.1.10 The description and reason for the requested change(s) to a document, design, software, equipment, or other, should include as much detail as possible.

8.1.10.1 Include applicable CAPA Report number in the description of change(s) if this change is a result of a CAPA.

8.1.11 Determine if the requested change impacts compliance with any regulatory standards including FACT, CAP, etc.

8.1.12 Impact and Risk Assessment (Section II)
8.1.12.1 Documentation of impact and risk assessment is required for all changes.

8.1.12.2 Select all areas that could be affected by this change.

8.1.12.2.1 List specific projects, as applicable, to better categorize changes and determine reporting requirements.

8.1.12.3 Select any additional items that will need to be completed before the requested change can be implemented.

8.1.12.3.1 Validations/Qualifications may be required for any changes affecting the process, testing, or
equipment used in GMP processing. List requested validation numbers.

8.1.12.3.2 External reporting may be selected when the department acts as a contract service provider to an external company. The service contract or quality agreement, as applicable, should be reviewed to determine reporting requirements.

8.1.12.3.3 Any change to the EMMES software also requires documentation and verification per STCL-FORM-034 Data Verification Form.

8.1.12.3.4 Supplier/Service Provider Qualification is required for any change to service providers.

8.1.12.3.5 All required items must be appropriately complete before the change is implemented.

8.1.12.4 List all documents referencing the SOPs requested for change.

8.1.12.4.1 This can be completed by running a search in MasterControl or contacting Document Control.

8.1.12.4.2 Review all identified documents to determine whether additional changes are needed.

8.1.12.5 Risk Assessment is determined by evaluating the impact, probability, and detectability of identified risks. The change is then categorized as a low, medium, or high-risk assessment.

8.1.12.5.1 See Table I for CCR risk examples.

Note: This table acts as a guide only; Specific circumstances may result in a different risk grade than depicted in the table. The initiator should collaborate with QSU to evaluate risks for each proposed change.

CCR Risk Assessment (See Table 1 for examples)

- **Low**
  - Risks are low level and do not require additional intervention outside of completing any identified pre-implementation mitigation tasks. Effectiveness checks are not required.

- **Medium**
  - Risks of moderate importance. Mitigation strategy may include pre-implementation tasks such as validations, qualifications, SCRs, external reporting etc. QSU and initiator will collaborate to determine if effectiveness checks are required to identify new risk events after implementation.

- **High**
  - Risks are of critical importance and mitigation and contingency planning must be a top priority. Mitigation of risk prior to implementation may include tasks such as validations, qualifications, SCRs, etc. Effectiveness checks will be required for these changes to identify new risk events after implementation.
### Table 1: Risk level Examples

<table>
<thead>
<tr>
<th>CCR Risk Assessment</th>
<th>CCR Request</th>
<th>Risk</th>
<th>Mitigation before Implementation</th>
<th>Effectiveness Check</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Formatting or grammatical changes in SOP</td>
<td>Training not completed in MC before completing task</td>
<td>No additional requirements outside of normal document revision process</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SOP title changes</td>
<td>Documents referencing SOP will not be updated</td>
<td>Identify all document references to SOP title and assess if additional concurrent changes are needed.</td>
<td>Not required</td>
</tr>
<tr>
<td></td>
<td>Additional instructions for clarity, SOP change with no impact to SOIPP</td>
<td>Operator may not train on revision changes before completing task resulting in deviation</td>
<td>Determine if additional training practices are required.</td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td>New like-for-like processing equipment, moving in-use equipment</td>
<td>Equipment not qualified before use</td>
<td>Verify qualification completion</td>
<td>Review Troubleshooting logs for any issues with equipment</td>
</tr>
<tr>
<td></td>
<td>Updated QC or assay processes</td>
<td>QC process/assay not validated before implementation</td>
<td>Verify Validation completion</td>
<td>Review QC data for failed QC, review OOS and sample repeat data</td>
</tr>
<tr>
<td></td>
<td>EMMES updates</td>
<td>Errors in EMMES release</td>
<td>Verify SCR completed before implementation</td>
<td>Review events for inaccurate data reporting in EMMES</td>
</tr>
<tr>
<td>High</td>
<td>New infectious disease testing service provider</td>
<td>Infectious disease testing could be inaccurate</td>
<td>Verify service provider qualification before implementation</td>
<td>Review events for issues relating to infectious disease testing</td>
</tr>
<tr>
<td></td>
<td>New sterility testing method</td>
<td>Sterility testing could be inaccurate</td>
<td>Verify analytical validation completed before implementation</td>
<td>Review OOS events, sterility rate, proficiency testing results</td>
</tr>
<tr>
<td></td>
<td>New processing facility</td>
<td>facility may not meet GMP specifications</td>
<td>Verify site qualification completed before implementation</td>
<td>Review ongoing EM results, facility audits</td>
</tr>
</tbody>
</table>

8.1.13 The risk assessment is used to determine whether an effectiveness check (EC) is required.

8.1.13.1 High risk changes require an EC.

8.1.13.2 Medium risk changes may require an EC at discretion of initiator and QSU.

8.1.13.3 Low risk changes do not require an EC.

8.1.13.4 If the initiator determines an EC is required on COMM-QA-019 FRM2 Change Control Request (No Effectiveness Check) FRM2, the form should be aborted and COMM-QA-019 FRM1 Change Control Request (Effectiveness Check) FRM1 should be initiated to include an effectiveness check.

8.1.13.5 CCRs associated with a CAPA will record the EC solely in the CAPA Report.
8.1.14 Effectiveness Check Requirements (Section V)

8.1.14.1 This section is applicable to COMM-QA-019 FRMI Change Control Request (Effectiveness Check) FRMI only.

8.1.14.2 The method to assess effectiveness of the change is selected based off the type of change and impact. This can include inspection, review of documentation, data analysis, etc.

8.1.14.3 An estimated completion date for the EC should be listed taking into account the method of the check and the time required to properly assess the effectiveness of the change.

8.1.15 The initiator submits the CCR in MasterControl after completion of Steps I, II, and V (Section V applies to COMM-QA-019 FRMI Change Control Request (Effectiveness Check) FRMI only).

8.2 Change Control Plan Review and Approval

8.2.1 Change control routes are established within MasterControl based on the form and program/department. See Appendix I and II for detailed routing diagram. After the initiator submits the CCR in MasterControl, the review route consists of the following:

8.2.1.1 Program/Medical Director (COMM-QA-019 FRMI Change Control Request (Effectiveness Check) FRMI only) – Provides initial review of the CCR, approving or rejecting the request based on program need.

8.2.1.2 RA – Reviews STCL CCRs related to CCBB Biologics License Applications (BLA). If the initiator is routing a CCR for a program where no RA review is required, the initiator should check N/A at the top of Section III.

8.2.1.2.1 RA documents an assessment in Section III, as necessary, to facilitate communication with Quality and Training Coordinator to ensure appropriate timing for release of documents and change implementation.

8.2.1.2.2 RA designates the appropriate classification of the change based on FDA requirements and the potential for an adverse effect on the product (Table 2).
Table 2

<table>
<thead>
<tr>
<th>Classification</th>
<th>FDA Requirement(s)</th>
<th>Reporting Type</th>
<th>Guidelines for Release (Confirm with RA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major</td>
<td>Prior FDA approval required</td>
<td>PAS - Prior Approval Supplement</td>
<td>Wait for FDA feedback. Confirm release date with RA.</td>
</tr>
<tr>
<td>Moderate</td>
<td>Submit supplement</td>
<td>CBE -30 – Changes Being Effected in 30 days</td>
<td>30 Days after FDA Receipt of Supplement. Confirm release date with RA.</td>
</tr>
<tr>
<td>Moderate</td>
<td>Submit supplement</td>
<td>CBE 0 - Changes Being Effected immediately</td>
<td>Immediately after FDA Receipt. Confirm release date with RA.</td>
</tr>
<tr>
<td>Minor</td>
<td>Submit change in Annual Report (AR)</td>
<td>AR</td>
<td>Effective Immediately. No confirmation required from RA.</td>
</tr>
<tr>
<td>N/A</td>
<td>Not applicable</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

8.2.1.3 **Quality Review** – Completes final review on all initial CCR plans (during first routing) to ensure completeness and impact and risk assessment are documented. Final approval by Quality is required on all CCRs.

8.2.1.3.1 When a CCR is rejected, a comment is added by Quality to provide explanation to the initiator of the CCR.

8.2.1.3.2 Quality also ensures that an approved CCR is completed on all new and revised documents prior to issuing approval.

8.2.1.3.3 The Quality review evaluates the CCR in terms of required corrective action or system/process enhancement, technical design, risk and impact assessment, and proposed effectiveness checks.

8.2.1.3.4 If the CCR is incomplete or if additional risks are identified by the Quality review, the CCR will be rejected and sent back to the initiator with an explanation.

8.2.2 If the CCR is rejected, the initiator may discuss options with the Medical/Program Director and/or the QSU, as applicable for further guidance.

8.2.3 The initiator of the CCR is notified via MasterControl when the CCR plan is approved.

8.2.4 Final Approval to Implement Change (Section IV)

8.2.4.1 A second routing is required to document all requirements have been met before implementation of the change occurs.

8.2.4.2 The CCR routes back to the initiator after initial CCR plan approval.
8.2.4.3 The initiator reviews Sections II and III and performs all requirements attaching, when feasible, relevant documentation to the CCR form (e.g., validations).

8.2.4.4 When all required actions are completed, the initiator will submit for final approval to implement change.

8.2.4.5 QA reviews the CCR to ensure all requirements have been met.

8.2.4.5.1 If QA approves, the initiator may implement the change (Ex. put equipment into use, make document effective).

8.2.4.5.2 If QA rejects, the CCR will be sent back to the initiator with a comment explaining why the change cannot be implemented. The initiator will collaborate with QA to determine a plan to move forward.

8.2.4.6 For COMM-QA-019 FRM2 Change Control Request (No Effectiveness Check) FRM2, this is the final step in the CCR process. The CCR is complete.

8.2.4.7 For COMM-QA-019 FRM1 Change Control Request (Effectiveness Check) FRM1, The CCR routes back to the initiator to hold until the EC is completed.

8.3 Effectiveness Check of Change (Section VI)

8.3.1 A third routing of the COMM-QA-019 FRM1 Change Control Request FRM1 is required to document an effectiveness check of the change after implementation.

8.3.2 An effectiveness check is required only for changes graded as high risk, or, medium risk as determined by initiator and QSU, per Impact and Risk Assessment section detailed above. The method of the effectiveness check is approved in the initial routing of the form in Section V Effectiveness Check Requirements.

8.3.3 The Effectiveness Check Completion section of the COMM-QA-019 FRM1 Change Control Request (Effectiveness Check) FRM1 will be completed by the initiator documenting the outcome of the check. Upon completion of the Effectiveness Check activities, the target timeline for routing of this form by the initiator is 30 days.

8.3.4 The change is determined to be satisfactory if it meets the desired outcome.

8.3.4.1 If the change is satisfactory, the CCR is closed and no further action is required.

8.3.4.2 If the change is not satisfactory, the initiator will document a plan of action of how to proceed. A new CCR may be initiated if a new change is required.
8.3.4.2.1 The Medical director and QSU will review the plan of action. If rejected, a comment is added providing explanation. The initiator and QSU will collaborate to determine next steps. The CCR is closed once an approved plan is reached.

8.4 Handling Controlled Document Changes Involving EMMES

8.4.1 When an author develops a new EMMES form or identifies changes required to an existing form located in EMMES, a CCR must be submitted and approved in MasterControl.

8.4.2 The CCR must include detail in the description of change section of the CCR form; e.g., form change; verification required. Additionally, select “Other, Explain” and note generation of STCL-FORM-034 Data Verification Form on the Impact and Risk Assessment Section.

8.4.3 When the parallel document is final in MasterControl, and prior to release, the author or designated initiator, must initiate the STCL-FORM-034 Data Verification Form.

8.4.4 The completed STCL-FORM-034 Data Verification Form with any supporting documentation, is provided to the QSU for review and approval and is scanned and attached to the associated CCR by MasterControl Document Control Operations.

8.5 Handling Emergency Change Requests

8.5.1 Emergency change requests will be allowed when SQIPP is compromised.

8.5.2 The person making the emergency request must consult with the Medical/Program Director, QSU and RA, if applicable, for consideration of how to proceed.

8.5.3 A CCR is submitted in MasterControl for documentation of the emergency approval and for tracking purposes.

8.5.4 Review by the Medical/Program Director and RA, if applicable and approval by the QSU are required prior to implementation of the emergency request.

8.6 The Supervisor/Manager is responsible for ongoing assessment and evaluation of the effectiveness of implemented changes by reviewing the change(s) and improving any area(s) not working as expected.

9 RELATED DOCUMENTS/FORMS

9.1 COMM-QA-019 FRM1 Change Control Request (Effectiveness Check)
9.2 COMM-QA-019 FRM2 Change Control Request (No Effectiveness Check)
9.3 COMM-QA-069 Job Codes – Roles and Users within Job Codes
9.4 STCL-FORM-034 Data Verification Form
9.5 COMM-QA-076 FRM1 CAPA Report
9.6 COMM-QA-042 Deviations and Investigations

10 REFERENCES


10.3 21 CFR 211.22(c) The quality control unit shall have the responsibility for approving or rejecting all procedures or specifications impacting on the identity, strength, quality, and purity of the drug product.

11 REVISION HISTORY

<table>
<thead>
<tr>
<th>Revision No.</th>
<th>Author</th>
<th>Description of Change(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>06</td>
<td>B. Shen</td>
<td>Updated procedure throughout to reflect new detailed CCR forms with additional routing steps. Changes include the addition of implementation approval and effectiveness checks.</td>
</tr>
</tbody>
</table>
Appendix I
CHANGE CONTROL REVIEW PROCESS FRM1 (Effectiveness Check)

<table>
<thead>
<tr>
<th>INITIATOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Submits CCR</td>
</tr>
</tbody>
</table>

**CCR PLAN REVIEW ROUTE**

<table>
<thead>
<tr>
<th>MEDICAL/PROGRAM DIRECTOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completes initial review to ensure program alignment.</td>
</tr>
<tr>
<td><strong>Approve</strong></td>
</tr>
<tr>
<td><strong>Reject</strong></td>
</tr>
<tr>
<td>Documents reason for rejection. Discusses options with Initiator.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>REGULATORY AFFAIRS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reviews certain CCRs related STCL. Documents comments and classification of change.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>QSU</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Approve CCR Plan</strong></td>
</tr>
<tr>
<td>CCR routes back to Initiator for post plan approval activities, followed by Implementation Approval Route</td>
</tr>
<tr>
<td><strong>Reject</strong></td>
</tr>
<tr>
<td>Requests further review or information. Discuss options with Initiator.</td>
</tr>
</tbody>
</table>

**POST CCR PLAN APPROVAL ACTIVITIES (As needed)**

<table>
<thead>
<tr>
<th>SUPERVISOR/MANAGER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completes required validations or qualifications.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TRAINING COORDINATOR (As Needed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identifies potential training needs.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>EMMES VERIFICATION (As Needed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completed verification documents attached to associated CCR by DCO.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SUPERVISOR/MANAGER, QSU, RA, TRAINING COORDINATOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collaboration on implementation/effective date.</td>
</tr>
</tbody>
</table>
IMPLEMENTATION APPROVAL ROUTE

**INTIATOR**
Submits CCR for Implementation

**QSU**

<table>
<thead>
<tr>
<th>Approve to Implement</th>
<th>Reject</th>
</tr>
</thead>
<tbody>
<tr>
<td>(CCR routes back to Initiator until EC is complete)</td>
<td>Requests further review or information. Discuss options with Initiator.</td>
</tr>
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</table>

EFFECTIVENESS CHECK REVIEW ROUTE

**Initiator**
Documents the outcome of the effectiveness check.

**MEDICAL/PROGRAM DIRECTOR**
Completes initial review to ensure program alignment.

<table>
<thead>
<tr>
<th>Approve</th>
<th>Reject</th>
</tr>
</thead>
<tbody>
<tr>
<td>Documents reason for rejection. Discusses options with Initiator.</td>
<td></td>
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**QSU**

<table>
<thead>
<tr>
<th>Final Approval</th>
<th>Reject</th>
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<tbody>
<tr>
<td>Form is closed in MasterControl</td>
<td>Requests further review or information. Discuss options with Initiator.</td>
</tr>
</tbody>
</table>
Appendix II
CHANGE CONTROL REVIEW PROCESS FRM2 (No Effectiveness check)

INITIATOR
Submits CCR

CCR PLAN REVIEW ROUTE

REGULATORY AFFAIRS
Reviews some CCRs related to STCL.
Documents comments and classification of change.

<table>
<thead>
<tr>
<th>Approve CCR Plan</th>
<th>Reject</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCR routes back to Initiator for post plan approval activities, followed by Implementation Approval Route</td>
<td>Requests further review or information. Discuss options with Initiator.</td>
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</table>

POST CCR PLAN APPROVAL ACTIVITIES (As needed)

SUPERVISOR/MANAGER
Completes required validations or qualifications.

TRAINING COORDINATOR (As Needed)
Identifies potential training needs.

EMMES VERIFICATION (As Needed)
Completed verification documents attached to associated CCR by DCO.

SUPERVISOR/MANAGER, QSU, RA, TRAINING COORDINATOR
Collaboration on implementation/effective date.
IMPLEMENTATION APPROVAL ROUTE

<table>
<thead>
<tr>
<th>INITIATOR</th>
<th>Submits CCR for Implementation</th>
</tr>
</thead>
<tbody>
<tr>
<td>QSU</td>
<td></td>
</tr>
<tr>
<td><strong>Approve to Implement</strong></td>
<td><strong>Reject</strong></td>
</tr>
<tr>
<td>Form is closed in MasterControl</td>
<td>Requests further review or information. Discuss options with Initiator.</td>
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## Signature Manifest

**Document Number:** COMM-PAS-004  
**Revision:** 06  
**Effective Date:** 20 May 2019  
All dates and times are in Eastern Time.

### COMM-PAS-004 Change Control

### Author

<table>
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<tr>
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<th>Date</th>
<th>Meaning/Reason</th>
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<tr>
<td>Patrick Killela (PK37)</td>
<td></td>
<td>16 May 2019, 01:45:21 PM</td>
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### Medical Director

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<tr>
<td>Joanne Kurtzberg (KURTZ001)</td>
<td></td>
<td>16 May 2019, 03:39:01 PM</td>
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### Quality

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<tr>
<td>Lisa Eddinger (LE42)</td>
<td></td>
<td></td>
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<tr>
<td>Taylor Orr (TSO4)</td>
<td></td>
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<tr>
<td>Richard Bryant (RB232)</td>
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<td>16 May 2019, 03:47:16 PM</td>
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### Document Release

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<tr>
<td>Sandy Mulligan (MULL1026)</td>
<td></td>
<td>16 May 2019, 05:46:25 PM</td>
<td>Approved</td>
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