**Document approval**

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# Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe the Change Management process at NBE-Therapeutics.

# Scope

This SOP is valid at NBE-Therapeutics for all Organization. The respective training shall be given in accordance with **SOP-10 Training Management***.*

Within Scope are the following possible key areas:

|  |  |
| --- | --- |
| **Key application areas** | |
| * Manufacturing process * Manufacturing equipment * Product formulation * Raw Materials, starting materials, Excipients intermediates, Auxiliaries * Stability (transport, storage, shelf-life) | * Analytical equipment * Analytical methods * Analytical specifications * Pharmacopeias * In-process controls |
| * Primary Packaging * Suppliers /Third Parties * GMP documentation * Computerized Systems | * Manufacturing Site * Facility and Utilities * HVAC systems * Water Systems * Cleaning and sanitization |

# Responsibilities

Responsible for the content of this SOP is Quality Management Director.

| **Role** | **Definition/Task** |
| --- | --- |
| Change Owner /Change Requestor | Initiates and monitors the Change. |
| Regulatory Affairs Head | Checks for filing implications and authority communication requirements |
| SMEs | assess for the potential impact in their domain of expertise, document the outcome and initiate appropriate actions. |
| Quality Organization | * assesses for GxP compliance * defines related impacted Departments for further change evaluation and implementation * ensures action plan is sound and complete * reviews of submitted documentation |

# Definitions, terms, and abbreviations

| **Term/abbreviation** | **Definition at NBE-Therapeutics** |
| --- | --- |
| Change Management | A formal system by which qualified representatives of appropriate disciplines review proposed or actual changes that might affect the validated status of facilities, systems, equipment or processes. The intent is to determine the need for action to ensure and document that the system is maintained in a validated state. |
| Change Request | Documented request from any stakeholder for change in facilities, systems, equipment, or processes that might affect their validated status. |

# Workflow

## General

A change must be initiated according to **Change Form** and submitted for new, ongoing or termination of any change under an appropriate Change Management system, that might affect the validated status of facilities, systems, equipment or processes.

The Change Owner / Initiator for each Change Request is responsible for promoting the change, and arranging for the provision of additional information, if necessary. The Change Owner / Initiator is responsible for controlling change to ensure timely completion of the process and acceptance of appropriate action in the event of a delay.

Common Change Control categories (areas) are reflected in ***Figure 1***.

Diagram

Description automatically generated

***Figure 1: Change Control categories (areas)***

### Product/process changes include but are not limited to:

* process upscale for a commercial product,
* process flow,
* process parameters,
* manufacturing capacity,
* packaging materials,
* storage conditions,
* shelf-life,
* holding time,
* specification limits,
* analytical procedures.

### General changes

General changes include but are not limited to:

* changes to the bill of materials,
* suppliers, vendors,
* product distribution,
* marketing authorization,
* service providers,
* QMS changes,
* product launch,
* product discontinuation,
* documents revision (SOP, WI, Specifications, etc.),
* system/equipment modifications.

### Asset Changes

Asset Changes include but are not limited to:

* new equipment (production or lab),
* manufacturing,
* storage facilities,
* infrastructure.

## General

The Change Control lifecycle is shown in ***Figure 2****.*

***Figure 2: Change Management lifecycle***

Change Requests must be submitted for new, ongoing or termination of any activity under an appropriate change control management system.

The change request holder for each change request shall be responsible for promoting the change, and arranging for the provision of additional information, if necessary. He shall be responsible for controlling change to ensure timely completion of the process and acceptance of appropriate action in the event of a delay.

### Preparation

Change Owner / Initiator shall collect and assess all available data and define purpose for particular change: improvement, alignment with other documents, standards, requirements, approach review, etc. Pre-and post-change state should be clearly reflected for further evaluation.

### Initiation

Change Owner / Initiator requests potential change according to **Change Form**. Quality Organization defines related impacted Departments for further change evaluation and implementation according to **Change impact assessment SMEs Matrix Appendix**. Respective Department Heads / Line Managers provide relevant support in proposed change documentation, evaluation, execution, implementation.

### Evaluation

All potential impact aspects on business, compliance and risk are assessed. Potential implications on the following are included:

* Safety and ecology
* Bioequivalence/ bioavailability / stability
* Qualification and Validation status
* Specification and sampling plans
* Quality profile and Quality System impact
* Marketing Authorization and authority communication requirements.

If changes in the production process or product are being considered, the hold and idle times must also be taken into account. Assessment of the change and its potential impact should be documented as part of the Change Request.

Upon completion of the assessment, the Change Owner prepares an implementation plan according to **Change Form** ***section C***, based on a summary of the assessment results and input from SMEs. It includes relevant action items to be executed for successful Change Management.

The execution of the change may not proceed until final implementation plan approval has been obtained.

### Execution

The respective Responsible Department / Team designated representatives perform the tasks (action items) as outlined in the implementation plan and provide evidence for the completion.

### Implementation

The implementation is closely monitored by the Change Owner. A summary statement of the successful implementation and revision of respective documents must be provided to conclude the implementation.

### Closure

A change is considered successfully closed when all assigned action items are completed. All deviations from implementation plan (timelines, completeness, supported evidences, correctness) shall be investigated and addressed (if applicable) according to   
**SOP-06 Deviation and Nonconformance Management**.

## Cancellation

In case of change cancellation where particular action items were already successfully implemented, those action items can be leveraged in the new Change Request by referencing the previous Change reference number. The decision to cancel the change must also take into account the need to reverse particular action items (recovery) if an implemented action item could have a negative impact after Change cancellation.

## Tracking

Change Controls are reported and reviewed periodically according to **Changes Tracker Form**. The following Key Performance Indicators are tracked:

* Number of opened Changes (i.e., under evaluation, planning, implementation)
* Number of outstanding Changes (i.e., after plan approval)
* Number of overdue Changes
* Action items and their completion

Each particular Change is assigned a number CC/XXX, where XXX is a subsequent number that starts with 001.

Each particular Change action item has number CC/XXX/YY, where XXX is the subsequent Change number, and YY is the particular action item subsequent number that starts with 01.

When a Change Request exceeds 90 days from the Request date it should be reported monthly.

# Applicable documents

MD-01 Quality Manual

SOP-01 Documentation Management

SOP-06 Deviation and Nonconformance Management

SOP-10 Training Management

# Appendices

The following appendix(ces) is/are integral part of this SOP:

Appendix Change Form

Appendix Change impact assessment SMEs Matrix Appendix

Appendix Changes Tracker Form

# Document revision history

|  |  |  |  |
| --- | --- | --- | --- |
| **Version** | **Valid from** | **Description of the revision** | **Reason for the revision** |
| 1 | See header | Document created | QMS implementation |