**Document approval**

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# Purpose

According to the rules for Good Manufacturing Practice (GMP), documents are an important part of a Quality Management System (QMS). A Good Documentation Practice (GDocP) enables proper documentation and correction of information entries.

# Scope

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

# Responsibilities

Responsible for the content of this SOP is the Head of Quality Organization.

|  |  |
| --- | --- |
| **Role** | **Definition/Task** |
| Head of Quality Organization | System and Content Owner; responsible for creation, life cycle, archiving, training and adherence to this SOP |
| Line Managers | Support implementation and supervision of this SOP |
| All Employees | Compliance to this SOP |

# Definitions, terms and abbreviations

|  |  |
| --- | --- |
| **Term/abbreviation** | **Definition at NBE-Therapeutics** |
| ALCOA | attributable, legible, contemporaneous, original and accurate |
| SOP | Standard Operating Procedure |
| GDocP | Good Documentation Practice |
| Quality Record | A document (for example, data sheet, form, table) that contains objective evidence to demonstrate how quality requirements are met. |

# Workflow

Documents must be error-free and available in writing. For this reason, appropriate controls exist, to ensure the exactness, correctness, availability and legibility of the documents.

## Requirements for GDocP

Documentation following a GDocP must be follow **ALCOA**

* + - **A**ttributable (to a person or system generating the data, or who modified the data with linkage to the source)
    - **L**egible (readable and permanent, accessible throughout the data lifecycle)
    - **C**ontemporaneous (recorded at the time of activity performance)
    - **O**riginal (original data is the first recording, or a true copy conserving this data)
    - **A**ccurate (free of error)

Additionally, the following points must be adhered to, to fall under GDocP:

* + - Documents are only valid if they contain all the required signatures.
    - The content of the documents must be unambiguous; the title and purpose of the document must be clearly indicated.
    - The documents must be clearly structured.
    - Measures must be taken to prevent the use of an outdated, obsolete version.
    - Records (e.g., batch records) must be created or completed at the time of the actual process to ensure traceability of all important activities relating to the product. The documentation of an individual step of a procedure must reflect the task that was actually carried out. It must be done promptly by the person who carried out the task.
    - Documents must never be backdated and predated (with the only exception of contracts and Effective date of Main Documents).

## Handwritten entries

* + - Sufficient space must be provided for handwritten entries.
    - Handwritten entries must follow ALCOA
    - Any handwritten changes and adjustments made to an approved document must me indicated by Initials of the changing person and date of the change
    - All handwritten entries must be carried out using an indelible blue pen (e.g., ballpoint pen) Pencils and similar writing instruments are not permitted.
    - The use of indelible stamps, e.g., for entering data information, is possible with approval of the Head of Quality Organization.

## Printouts

If printouts are used for documentation, it must be ensured that the print is permanent and will remain legible in the long term. This requirement is not fulfilled by thermal paper, for example. If the printouts available are not permanent, they must be copied on normal paper and the copies used and stored together with the original for documentation purposes.

Printouts which are attached for documentation purposes (e.g., attachments to a report, extracted raw data) must be labelled properly to ensure they can be clearly identified. Originals and original printouts bond or glued to a document must be marked by an employee in such a way that their Initials and the date are half on the printout and half on the paper that the printout is attached.

## Copies

If copies of original documents (MDs, SOPs, WIs and their appendices) are used as working copies, it is important to ensure that this does not lead to errors. The created copies must be legible. Only copies that have been created by Quality Organization or responsible Line Manager according to **SOP-01 Documentation Management** shall be used as working copies.

All other copies, e.g., test reports as attachments to deviations, must be marked as a uncontrolled copy, and be dated and initialed.

Non-authorized copies should never be used, to prevent the use of versions that are not valid.

## Corrections

Every correction of an entry in a document must be signed and dated. The corrected original information must remain legible. The original content of an entry may not be made illegible by crossing it out or by using any other method. In addition, aids such as “Tipp-Ex” or “ink eraser” may not be used. Pasting over the original content is also not permitted. Corrections are carried out as follows:

* + - An incorrect entry is invalidated by crossing it out with a single line. The original entry must remain legible.
    - The correct entry should be written next to, above or under the incorrect entry and include Initials, date and a brief explanation.
    - The following terms or abbreviations are acceptable to use for explanations:
      * RE: Reading Error
      * WB: Wrong Check Box
      * CE: Calculation Error
      * FE: False Entry
      * SSI: Stamp Setting Incorrect
      * WS: Wrong Stamp
      * TE: Transcription Error
      * SE: Spelling Error

Expected correction is explained and demonstrated in ***Table 1.***

|  |  |  |  |
| --- | --- | --- | --- |
| Cross out incorrect entry so that it is still legible | Make correction | Reason | Voiding |
| ~~209 g~~ | 290 g | TE  (Transcription Error) | Date, Initials,Signature |

***Table 1:*** *Example of a QMS-compliant correction*

## Date and time formatting conventions

The date format used must be unambiguous. The following format is required for writing dates:

**DD.MM.YYYY** or **DD/MM/YYYY**, where

* **DD** represents the day (two digits),
* dot or slash,
* **MM** represents the month (two digits),
* dot or slash, and
* **YYYY** represents the year (four digits).

e.g., 28.01.2022 or 28/01/2022 for the 28th of January 2022.

The time shall be formatted at using the military time (24-hour clock) as follows:

* hour two (2) digits,
* colon, and
* minute two (2) digits

e.g., 08:30 for eight thirty a.m. and 20:30 for 08:30 p.m.

Any exceptions, for example, for batch related records shall be described and explained in the corresponding Main Documents.

## Formatting conventions for numbers

The rounding up or down of numbers, as well as the number of digits after a decimal place used to carry out calculations, is as follows:

* + - For rounding to a whole number, the digit after the decimal is taken into consideration. With values between 1 and 4, the number is rounded down; with values between 5 and 9 the number is rounded up.
    - For rounding the first, second or third digit after the decimal, the value of the next digit is taken into consideration and rounded as described above.

Exceptions are described in applicable Finance & Accounting procedures.

**At NBE-Therapeutics, specifications are written with a maximum of three (3) decimal places.**

* + - All manual calculations must be clearly shown in an understandable way in the documentation.
    - All significant decimal places must be included in the calculation, as set forth in the relevant specification.
    - Rounding is only permitted in the last step of ascertaining results. Here the requirements of the valid test documents must be followed, pertaining to the relevant fractional digits.
    - All calculations, including traceability of the used values, must be checked and initialed by a second person.

***[Table 2](#_bookmark15)*** shows several examples of correct rounding.

|  |  |  |  |
| --- | --- | --- | --- |
| **Product related specification based on SOP** | **Calculated result (unrounded value)** | **Calculated result (rounded value)** | **Compliant with specification** |
| ≥ 50% | 48.99% | 49% | no |
| 49.49% | 49% | no |
| 49.50% | 50% | yes |
| 49.51% | 50% | yes |
| ≤ 25 EU/mL | 0.05 | 0 | yes |
| 12.25 | 12 | yes |
| 24.50 | 25 | yes |
| 26.23 | 26 | no |
| ≥ 2 | 1.49 | 1 | no |
| 1.50 | 2 | yes |
| 1.75 | 2 | yes |
| 2.3 | 2 | yes |

***Table 2:*** *Several examples of correct rounding of numerical values at NBE-Therapeutics.*

## Signing requirements

First name, Last name, signature, time (date or date/time) are required in order to identify acting persons. Typically, full signatures are required for the final signing of documents. Initials, on the other hand, are used when several independent process steps or work procedures can be documented individually.

For written amendments or changes in already approved documents, e.g., in protocols, the purpose of the signature or Initials should be explained, e.g., with the following additions:

* added,
* confirmed,
* recalculated,
* changed in consultation with …,
* verified or controlled.

Documents must only be used after they have been brought into effect. Signatures and Name must always appear with the date. Entries made by multiple persons must be signed in such a way that it is clear who made which entry and when.

## Signatures

The meaning of a specific signature must always be explicitly stated:

* + - * for the person signing, so that the scope of the signature is clear, and
      * for later readers.

In all documents this information must be given directly in the signature field and applies for all corresponding appendices. Examples include (but not limited to):

* + - * executed,
      * verified/reviewed for content,
      * checked for completeness,
      * verified on-site (= double verification principle),
      * created,
      * approved,
      * confirmed,
      * implemented, or
      * read and understood.

Names and signatures are always in connection with the current date.

## Signing as substitute

A signature can only be given by the person executing the procedure. If the executing person cannot sign in person due to absence and a procedure is conducted by the substitute, the substitute sign with the addition „O/B”. The addition „O/B” signifies the act “on behalf” of the absent person using their own name. The prerequisite for this is that the authorization as substitute is documented in writing in the Job Description and carried out by a qualified employee.

The signature must make clear that the executing person acts on behalf of another.

## Voiding empty fields

Empty fields must be unambiguously voided, e.g. by crossing it out or entering “n/a = not applicable“.

Date and Initials are not required when a signature field is available on the same page.

Date and Initials are required when no signature field is available on the same page.

## Double verification principle

For quality or process-critical steps the execution and verification using the double verification principle is required. First person confirms the correct execution of the step or operation with date, name, signature. A second person present at the place of action checks that the execution was done correctly and confirms this by entering the date, name, signature. Both signing individuals carry responsibility for the execution (e.g., weighed portions, dilutions, calculations during the execution). The necessity of performing a doublecheck on-site is explained in division-specific documents.

## Second signature for review

Second person also verifies the correct calculation and/or execution according to records and confirms the verification by entering the date and Initials or signature.

This second signature may also be provided at a later time, if necessary,

The second person does not need to be on place for checking during execution. Examples: calculation, checking for completeness of records.

# Applicable documents

MD-01 Quality Manual

SOP-02 Good Documentation Practice

SOP-10 Training Management

SOP-16 Archiving

# Appendices

n/a

# Document revision history

|  |  |  |  |
| --- | --- | --- | --- |
| **Version** | **Valid from** | **Description of the revision** | **Reason for the revision** |
| 1 | See header | Initial SOP introduction | QMS implementation |