Digitalization in the metrology quality infrastructure – perspectives from Novo Nordisk

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Abstract. This paper presents our experiences and challenges with implementing the (DCR) Digital Calibration Request and (DCC) Digital Calibration Certificates initiative in our metrology process at Novo Nordisk, a Danish pharmaceutical company producing medication for chronic diseases. We have a strategic goal to remove all manual transfer of data from our calibration activities, as well as to gain insight by trending on calibration results. Currently, we specify calibration tasks to our suppliers manually, using our IT system, and receive calibration certificates from them mostly as digitally signed PDF-files. We then must manually enter the calibration records into our IT system, which is time-consuming and prone to errors. The DCR/DCC initiative offers a great opportunity to automate both processes companywide, by using standardized and machine-readable formats for exchanging calibration information. Novo Nordisk is actively involved in this initiative, by running pilot projects with several metrology institutes to test the generation and reception of both DCRs and DCCs. However, we have also encountered some data integrity challenges, due to the flexibility of the DCR and DCC schemas. We have realized that, to ensure a robust and reliable transfer process between DCRs, DCCs and our IT system, all these elements must adhere to the ALCOA++ principles, which are a set of criteria for ensuring data quality and traceability in a highly regulated industry.

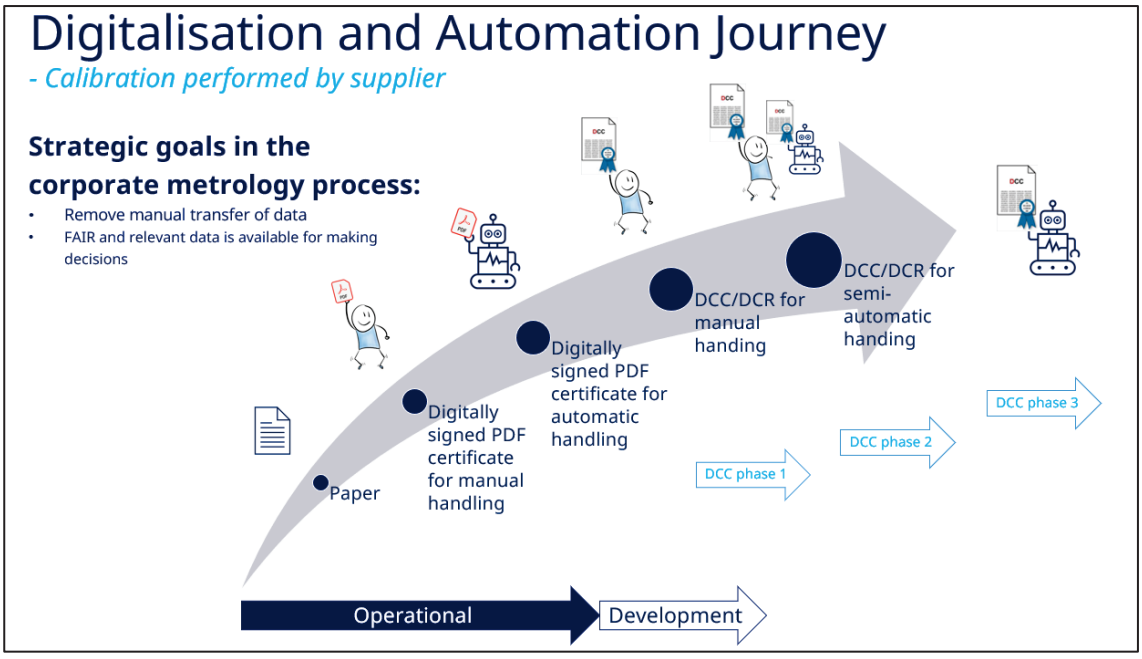

Fig. 1. Digitalisation and automation journey.

1. Introduction

Novo Nordisk, founded in 1923 and based in Denmark, is a global healthcare company focused on providing medication for chronic diseases. Operations are managed through process management across the organizational structure, with the corporate metrology process ensuring reliable and traceable measurements for critical processes. This paper outlines two strategic goals within the corporate metrology process: eliminating manual data transfer and ensuring that data is Findable, Accessible, Interoperable, and Reusable (FAIR) as well as relevant, to support informed decision-making. Pilots are being conducted to implement Digital Calibration Certificates (DCC) and Digital Calibration Requests (DCR).

1.1 Calibration program

The calibration program begins by defining measurement parameters and identifying requirements for these parameters. Calibration requirements for measuring equipment are derived from measurand requirements.

Calibration intervals are determined based on a risk assessment, which considers:
- The impact on Novo Nordisk if measuring equipment does not meet calibration requirements.
- The likelihood of measuring equipment failing to meet calibration requirements.
- Mitigations such as intermediate checks, adjustment limits, and the length of the calibration interval.

A corporate IT system evaluates whether calibration results pass or fail, with the final decision made by a qualified Novo Nordisk employee. If measuring equipment fails to comply with calibration requirements, an investigation is conducted to assess the potential impact on product quality and patient safety since the last successful calibration.

While Novo Nordisk can outsource the execution of calibrations, ultimate responsibility is retained; thus, conformity statements in calibration certificates are not required. All calibration certificates must be delivered to Novo Nordisk.

2. Digitalisation and automation journey

A project has been undertaken to digitize calibration certificates from suppliers in the corporate metrology process. Annually, approximately 20,000 external calibrations are managed, performed by various suppliers across different countries. The digitization process began with the creation of a system for receiving digitally signed PDF certificates for manual handling. Later, the receipt and archiving of these digitally signed PDF certificates were automated. This process is depicted in Figure 1.

2.1 Testing the three-step process

We are testing a three-step process for DCCs and DCRs:
- Manual handling
- Semi-automatic handling
- Fully automated handling

Achieving full automation in our regulated industry is challenging.

2.1.1 Digitally Signed PDF Certificates for Manual Handling

Our metrology process involves receiving digitally signed PDF certificates, verifying data integrity, and archiving. Our records management process specifies the requirements for exchanging these documents with external partners. We have contracts with thirteen suppliers for these certificates. A qualified Novo Nordisk employee verifies the signatures against a root certificate using the Adobe Approved Trust List (AATL) and ensure no changes were made after signing.

2.1.2 Digitally Signed PDF Certificates for Automatic Handling

Ensuring data integrity verification presents challenges for some employees. While it is straightforward to train those who manage digitally signed PDF certificates daily, maintaining competence is more difficult for individuals who handle them infrequently.

In collaboration with the corporate automation department, the corporate metrology process has developed a Robotic Process Automation (RPA) solution for receiving and archiving digitally signed PDF certificates.

The process flow is as follows:
- The supplier sends an email to the software application (BOT).
- The BOT opens the email and reads the email body text, which must adhere to specific syntax requirements.
- The BOT conducts data integrity verification before archiving the certificate(s) in Novo Nordisk's document database.
- Once the certificate(s) are uploaded, the BOT sends a notification to the relevant Novo Nordisk employee with a hyperlink to the certificate in the document database.
- The employee can then review and evaluate the calibration certificate(s) and decide to release or reject the measuring equipment for use.

The syntax requirements in step 2 are necessary due to the lack of machine readability of PDF certificates. Therefore, machine-readable metadata must be included in the email body to facilitate the processing of the PDF certificates.

2.1.3 Manual Handling of DCCs/DCRs

Handling DCCs/DCRs involves logging into Novo Nordisk's IT system, opening the calibration work order, and using middleware to create the DCR. After calibration by a supplier, the employee logs in again, extracts data with middleware, and transfers it back to the IT system. The employee verifies the transfer and signs off the work order. A second person confirms the accuracy and signs for review.

2.1.4 Semi-automatic Handling of DCCs/DCRs

An employee logs into the Novo Nordisk IT system to initiate a calibration work order, generating and sending a DCR to the supplier. After calibration and receipt of the DCC, the data is transferred to the IT system. The employee then verifies and signs off on the data transfer.

2.1.5 Fully Automated Handling of DCCs/DCRs

Fully automated handling functions in a manner like semi-automatic handling as described in section above; however, it does include automation of the work order review process.

3. Development – phase 1: manual handling of dcc/dcr

In the first phase of the DCC pilot (see figure 1), we will apply insights gained from the digitally signed PDF calibration certificate. The DCC in XML format will be embedded into the PDF while maintaining the human-readable PDF for inspections and audits. The PDF will also

act as a manual backup if automation fails. This pilot is being conducted with Danish suppliers, including DFM, TI, and FORCE.

3.1 Mapping of Data Flow from Novo Nordisk IT System to DCR

To generate a DCR, it is crucial that data in the Novo Nordisk IT system is FAIR, ensuring retrievability. Analysing all aspects of the calibration request process, including unwritten practices between customer and supplier, identifies three groups of information for the DCR:

Data transferred from the Novo Nordisk IT System:
- Equipment ID number
- Calibration work order
- Requirements for calibration method, environmental conditions, sensor connection, calibration point direction, units for DUT, standard, and expanded uncertainty, and adjustment if limits are exceeded

Standard text describing fundamental requirements:
- Calibration must be performed according to ISO 17025 or a Metrology Quality Agreement between Novo Nordisk and the supplier
- Only one measuring equipment per certificate
- As found and as left calibrations must be in separate certificates
- Consistent units for DUT, standard, and uncertainty
- No conformity statements in the certificate

Manually collected information:
- Contact person (name, initials, email, phone)
- Return address for equipment and certificate

Figure 2 shows an example of mapping data flow from the Novo Nordisk IT System.

3.2 Mapping of Data Flow from DCC to Novo Nordisk IT System

When handling automatic data transfer, it is important to ensure unique data identification in both systems. In the Novo Nordisk IT system, each calibration point has a unique ID, as shown in figure 3. Here, a Device Under Test is referred to as a Unit Under Test (UUT). The first calibration point is labelled 01UUT, the second 02UUT, and so forth. Calibration standards used by suppliers are labelled in a similar manner; for example, 01PRT01 indicates the first point reading, and 02PRT01 the second. Calibration result uncertainties are marked as 01U, 02U, etc.

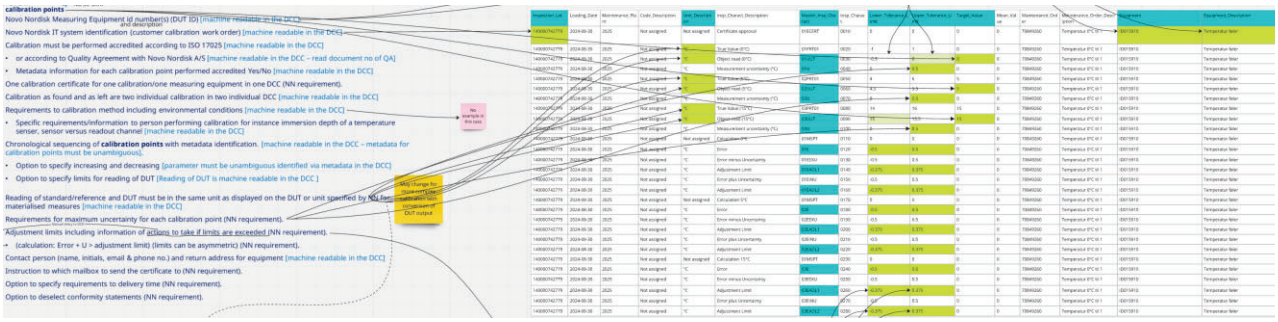

Fig. 2. Illustration of mapping of data for IT system

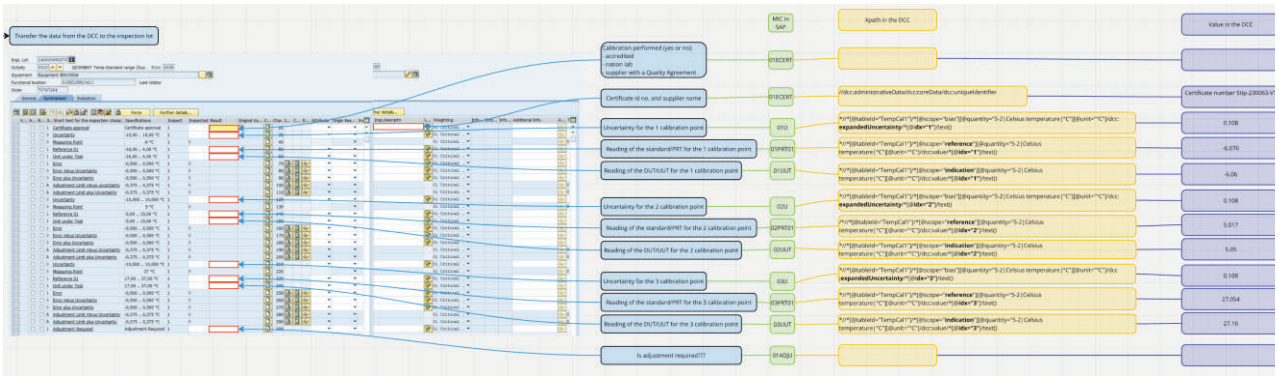

Fig. 3. Illustration of unique data identification.

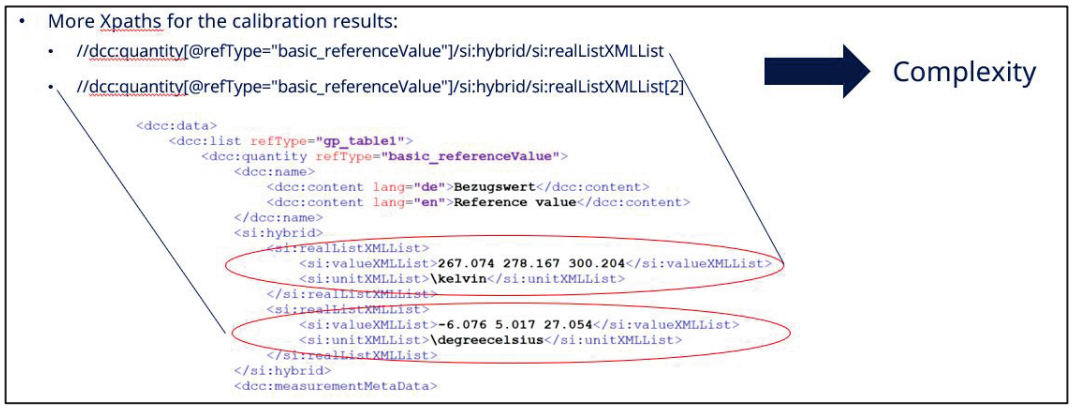

Fig. 4. Illustration of an XPath resulting in multiple query results.

3.3 Ensuring accurate data transfer

To ensure accurate data transfer and reduce transcription errors, calibration results within the DCC must be uniquely identifiable, as specified in section 9.4 of [1].

XPath is used to query XML files. Queries in DCCs should follow consistent, well-defined, and objective XPaths as specified in section 5.5.3 of [1]. XPaths producing multiple results, as seen in figure 4, increase middleware complexity and risk of failure.

While humans can easily distinguish between temperatures in kelvin and Celsius, developing middleware to handle this complicates IT risk assessments, which must validate all potential data transfer issues. Robust XPaths enhance DCC reliability, so the design should simplify creating robust XPaths.

3.3.1 Regulatory Requirements to a Record (ALCOA+)

In the healthcare industry, documentation including calibration certificates are required to meet various regulatory requirements. At Novo Nordisk, the corporate record management process ensures compliance with these standards. Both electronic and paper calibration certificates adhere to the same rules. The ALCOA+ (Attributable, Legible, Contemporaneous, Original, Accurate) principles help ensure that regulatory expectations are met.

Attributable in [1] is ensured by having a clear identification of the individual performing a calibration task and the date or date range for when the calibration was performed. We expect the calibration certificate to be locked for editing with a trusted signature and in a way so it can be verified that the document has not been altered after the last signature was applied.

Legible in [1] covers the record being readable and unambiguous for it to be understandable and usable. This is where the unambiguous identification of calibration data described in section 3.1 becomes important.

Contemporaneous in [1] is covered by section 7.8.1.2 in [2] and is a requirement that specifies that recording of calibration data must be documented when the calibration takes place. By requesting an accredited calibration, the accreditation ensures that the result of the calibration is accurate, clear, unambiguous, and objective.

Original in [1] is also covered by section 7.8.1.2 in [2] and is a requirement to ensure the first capture of calibration results.

Accurate in [1] is a requirement to ensure that the calibration results are a truthful representation of fact which is the intent of [2].

Complete in [1] is a requirement to ensure that all critical information to understand the calibration is captured to ensure that all relevant metadata is available in the DCC and that the information is not deleted or lost.

Consistent in [1] is requirement to help control or standardise the DCC. We need an international standard for the DCC.

Enduring in [1] is a requirement to ensure that the calibration certificate is readable and reliable in the retention period. In Novo Nordisk the retention period for a calibration certificate is ten years. From our experience with digitally signed PDF calibration certificates, we know that the root certificate has an expiry date after typically three years. By uploading the certificates to the Novo Nordisk database upon receival and at the same time ensuring the data integrity we protect the certificates in the entire retention period.

Available in [1] is a requirement to ensure that the calibration certificate is available for Novo Nordisk employees.

3.3.2 Further risk reduction

Section 5.5.3 in [1] gives good practice guidance in reducing risk by having a simple process which is consistent, well defined, and objective. Complex or inconsistent processes with open ends and subjective outcomes lead to increased risk. At Novo Nordisk we prefer simplicity.

4. Why digitalize

At Novo Nordisk, most measuring equipment is calibrated in situ and documented within a corporate IT system. Calibration requirements are accessible to employees via calibration work orders. The readings of the Unit Under Test (UUT) and the standard are directly recorded in the IT system, which then calculates and evaluates whether the calibration has passed or failed to assist the employee in making the final determination. This calibration process is

paperless and environmentally friendly, with the capability to trend calibration data as outlined in [3].

Calibrations outsourced to suppliers are also managed within the same IT system, although the digital maturity level is lower. Calibration requirements are available in the IT system for the employee requesting the calibration; however, data covering the calibration requirements, such as calibration points and accuracy requirements, is manually transferred to a letter that is sent to the supplier along with the equipment. After calibration, some departments transfer the calibration result data into the IT system, where it is verified by a second person. Other departments do not transfer this data. The IT system only evaluates calibration data once it has been transferred, and trending on the data is possible only if data transfer occurs. Presently, approximately 25% of all calibration certificates received by Novo Nordisk are digitally signed PDF certificates, indicating progress towards a fully paperless process.

On average, it takes 20 minutes to transfer data from a certificate to the IT system and for a second person to verify the data transfer accuracy. It typically takes 25 minutes to transfer calibration requirements from the IT system to a letter. Additionally, 5% of all revised calibration certificates are due to errors in Novo Nordisk's calibration requests.

The successful transfer of data is just one aspect; true success is achieved when calibration data is used to trend the performance of measuring equipment, build leading indicators, and gain valuable insights for proactive action, as described in [3].

5. Conclusions

The establishment of an international standard for Digital Calibration Certificates (DCC) and Digital Calibration Requests (DCR) is pivotal for successful global implementation. Such a standard ensures that all aspects of DCC and DCR comply with a unified framework, promoting smoother operations across various countries and suppliers. Maintaining data integrity is essential to guarantee trustworthy and reliable information, which is the cornerstone of effective implementation.

A phased implementation approach simplifies change management by breaking down the process into manageable stages. This method allows for thorough planning, monitoring, and adjustment at each phase, thereby reducing the risk of errors and ensuring a seamless transition. Furthermore, being a pioneer comes with challenges and the potential for rework. It is thus crucial to select the right collaboration partner who shares your vision and can offer the expertise and support required for successful implementation.

In conclusion, adhering to international standards, ensuring data integrity, adopting a phased implementation strategy, and partnering with the appropriate collaborators are critical factors for achieving a successful global implementation.

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