# Leveraging the USDM Standard in OpenStudyBuilder for Enhanced Data Exchange

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ABSTRACT

The OpenStudyBuilder (OSB) Metadata Repository (MDR) and Study Metadata Repository (SDR) serve as pivotal components in Novo Nordisk's comprehensive approach to digitizing the entire clinical process. This encompassing digital transformation commences with the Protocol and extends to the Trial Files and Listings (TFL), facilitated by the Schedule of Activity. The OSB leverages these repositories to drive the production of the Case Report Form and specify the Tabulation of Metadata. Central to this process is the Activity concept, which orchestrates the interconnection of metadata elements through a Graph database provided by Neo4j. A recent milestone achieved by the OSB is the capability to extract Protocol metadata within the Unified Study Definition Model (USDM), enabling the generation of a Novo Nordisk protocol but at the same time, an ICH - M11 one, by leveraging shared metadata.
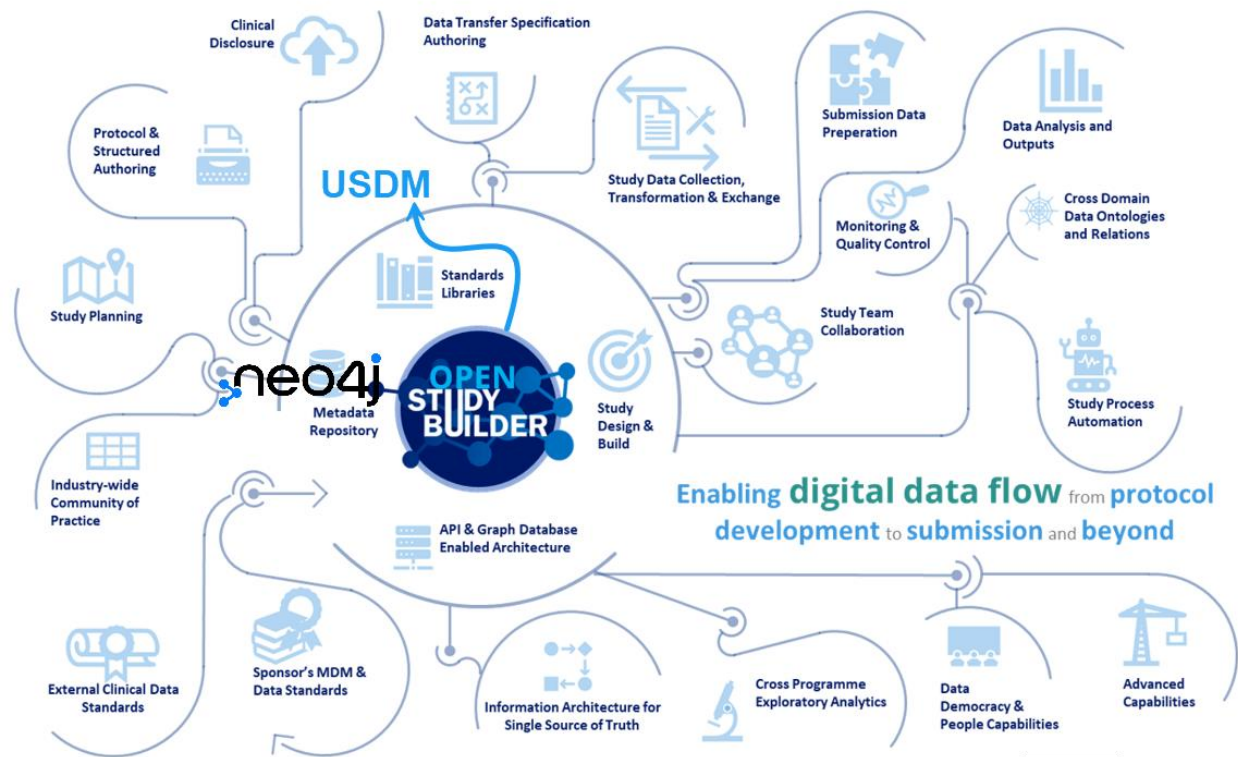
INTRODUCTION

In the realm of clinical research, the digitization of processes has become paramount in enhancing efficiency, accuracy, and overall management of trials. For Novo Nordisk, this digital transformation begins at the very foundation of clinical studies, the Protocol, and extends throughout the entire lifecycle, encompassing Trial Files and Listings (TFL). The Schedule of Activity is driving the specification of the Case Report Form but also of the tabulation to SDTM for example. This interconnected ecosystem is further empowered by the Activity concept, which intricately binds various metadata elements with the aid of a Graph database. Notably, a recent advancement in this framework allows the OpenStudyBuilder to extract Protocol metadata within the Unified Study Definition Model (USDM), thereby facilitating the generation of protocols compliant with the ICH - M11 standard, as Sponsor version through the utilization of shared metadata. This introduction sets the stage for understanding the critical role played by the OSB MDR and SDR in driving Novo Nordisk's comprehensive approach to digitizing the clinical process from end to end.

WHAT IS THE OPENSTUDYBUILDER ?

The OpenStudyBuilder (OSB) is an open-source project for clinical study specifications. This tool is a new approach for working with studies that once fully implemented will drive end-to-end consistency and more efficient processes - all the way from protocol development and CRF design - to creation of datasets, analysis, reporting, submission to health authorities and public disclosure of study information.

The heart is the Metadata Repository using a graph database containing a biomedical concept. This allows for FAIR data, semantics, traceability and automation. Then there is the Application itself where all data can be browsed, entered, updated and managed. And finally, there is a very powerful API which provides the complete functionality through a standard interface!
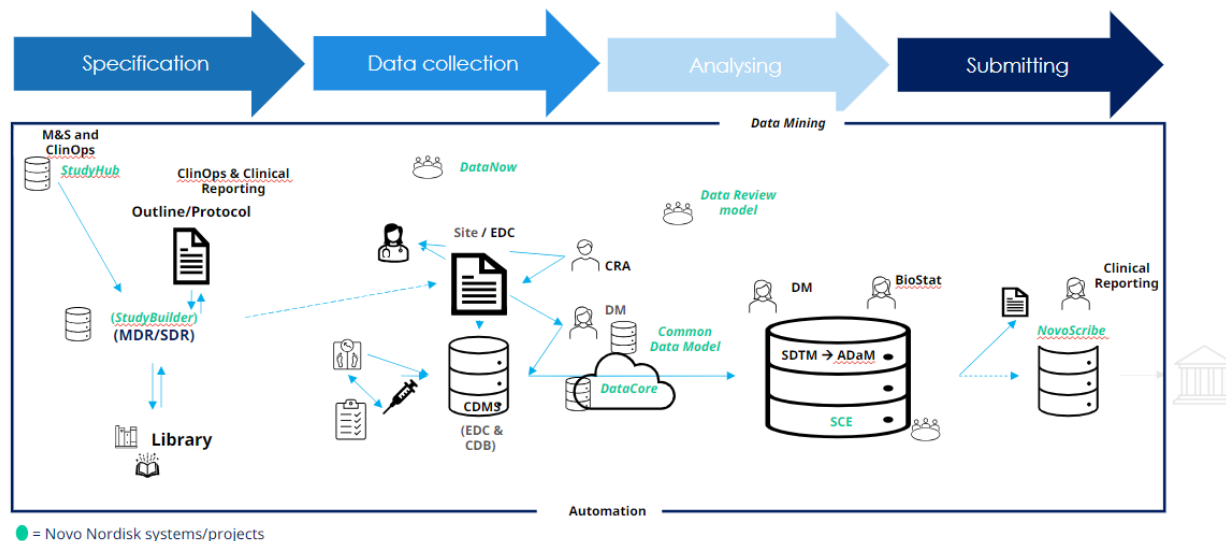

Figure 1: Global integration of the OpenStudyBuilder / Neo4j database in the ecosystem at Novo Nordisk

THE LIBRARY

In the library section you can browse all kinds of standards, like for CDISC the SDTM, ADAM, SEND, CDASH and many more. Also, other dictionaries like SNOMED, LOINC, UCUM is available - MedDRA could be loaded as well of course. Want to see differences of different SDTM versions? No Problem with the OpenStudyBuilder! As everything is FAIR, concepts can be created and maintained, so these can easily be reused. A core feature is the usage of syntax templates, for example for objectives and endpoints. Here general standard wordings and types are defined, which can then be instantiated with a concrete compound or comparator.

THE STUDY AREA

All study-related content which is needed for the protocol and Trial Domains can be managed in the study area. Objectives, endpoints, study design, population - whatever is needed can be entered. There is also a nice protocol flowchart. Lately, we were adding here, a Unified Study Definition Model (USDM) API converting our metadata into a full JSON file following the specification.

THE API

The API provides a standard interface which is very powerful. The application itself uses the API to update the database. Everything could also be done by using the API in a different fashion. Notable is also the USDM API Adapter which supports the TransCelerate Digital Data Flow (DDF) connections.

THE DATABASE

The data model to support this tool is very densely connected and must have a high level of flexibility because it is still growing and will keep growing for years as we extend it. It also includes versioning and auditing of all manipulated metadata, which increases the complexity and connectedness of the model.

This is why we chose a graph database (Neo4j) over other database types, because it is the only technology that can cater for such levels of connectedness.

WHAT IS THE DDF – USDM ?

The TransCelerate Digital Data Flow project (DDF) aims to a future state of fully automated, dynamic, study start-up readiness. This automated end-to-end process is also the goal of the OpenStudyBuilder. In the context of the DDF, the OpenStudyBuilder can be seen as an SDR (Study Definition Repository), but with more capabilities than what DDF is containing in its first version.

The main advantage of DDF is the standard API which allows the connection of very different up- and downstream systems. All tools which support the DDF project through their standard APIs should also be usable with the OpenStudyBuilder, which supports the same APIs.

THE API – USDM ENDPOINT

The OSB provide a dedicated API endpoint that is only requesting the reference of the Study and will return a complete USDM JSON file based on the version 3 of the DDF definition (see figure 2).

Figure 2: DDF api endpoint showing the USDM JSON extraction for a dedicated study

THE USDM IN THE FRONT APPLICATION

With the utilization of USDM version 3, the front end of the OpenStudyBuilder now boasts the capability to display the JSON view within the Study level section, allowing for direct file download through a dedicated button. Once the minimum set of metadata is established for a specific study, users can seamlessly access the USDM viewer by navigating to the View Specification menu, as illustrated in Figure 3.

Figure 3: USDM view inside the OpenStudyBuilder application

EXPORT FEATURE BUT LOOKING FOR IMPORTING

The Open Source team looking to enhancing the capabilities of the OpenStudyBuilder is willing to integrate a USDM importer endpoint. This strategic initiative aims to streamline and fortify the platform's functionality by enabling seamless integration of data aligned with the Unified Study Definition Model (USDM). With the addition of this importer endpoint, users will gain the ability to effortlessly incorporate USDM-compliant data into the OpenStudyBuilder ecosystem, further solidifying its position as a versatile and adaptable solution for managing clinical research processes.

INTEGRATION OF A M11 TEMPLATE

The incorporation of an ICH - M11 template within the OpenStudyBuilder would represent a significant advancement, as it leverages the USDM JSON metadata to seamlessly generate an HTML version of the M11 protocol that will be converted into a PDF doc. By harnessing the power of USDM-aligned data, this functionality enables the production of M11 documents that align with industry standards, providing a parallel reference alongside the Sponsor version. This integration not only enhances efficiency and accuracy but also ensures compliance with regulatory requirements, thereby empowering researchers and stakeholders with a comprehensive and standardized view of the protocol within the clinical research landscape.

Figure 4: ICH – M11 Template to be integrated into the OpenStudyBuilder

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The implementation of the ICH - M11 template within the OpenStudyBuilder not only streamlines protocol generation but also paves the way for seamless sharing with regulatory agencies in a straightforward and standardized manner. By leveraging the USDM-aligned data to produce compliant HTML versions of the M11 protocol, this functionality ensures that sharing protocols with regulatory bodies becomes an easy and generic process, thereby enhancing transparency, compliance, and efficiency in regulatory interactions.

CONCLUSION

The successful generation of JSON aligned with the Unified Study Definition Model (USDM) underscores the efficacy of the OpenStudyBuilder's approach in managing complex metadata. This achievement underscores the pivotal role of the Neo4j Graph database in orchestrating the intricate interconnections within our metadata ecosystem. As we look to the future, our focus will center on integrating an M11 display to further strengthen our capacity to produce protocols compliant with industry standards. Furthermore, the planned incorporation of a USDM import function represents a pivotal next step, promising to enhance our ability to seamlessly integrate and leverage USDM-aligned data within our ecosystem.
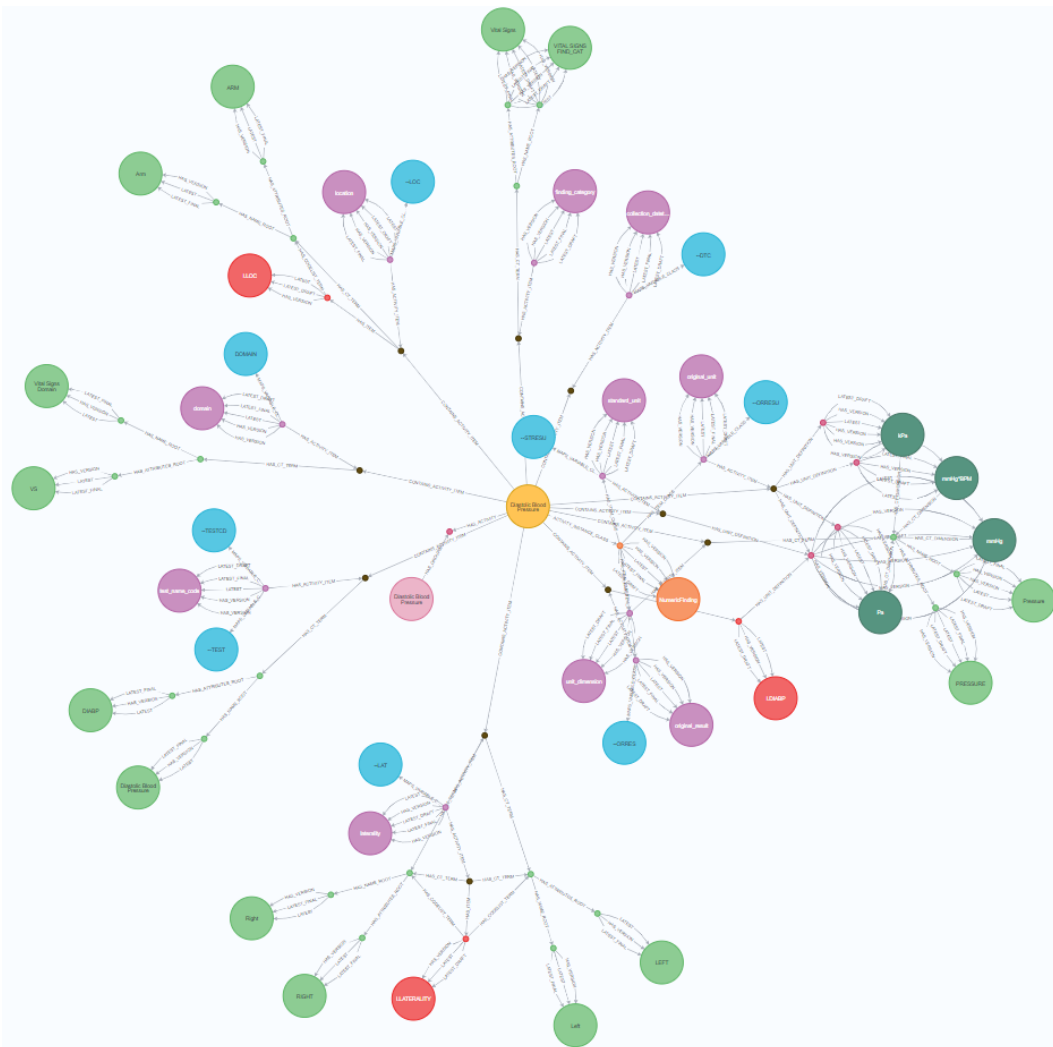

Figure 5: View of the Activity Concept Model inside the graph database – Heart of the USDM conversion

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