Utilizing NIIMBL and ISA-88 Framework to Create a Proof of Concept Pharmaceutical Manufacturing Ontology

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Abstract

The NIIMBL Ontology serves as a semantic framework for understanding biopharmaceutical manufacturing processes. In this project we utilized NIIMBL Ontology and the industry standard ISA-88 framework to create a proof-of-concept knowledge graph that represents some of Merck's pharmaceutical manufacturing processes across different products, scales of production and production sites. By aligning on terminology and structure it has allowed us to visualize the pharmaceutical manufacturing processes in a more dynamic structure. From this we have gained insight into how these production processes are monitored and controlled, which can in turn facilitate tech transfer during the scale up production process as well as application to other manufacturing modalities.

Background and Objective

Ontologies provide a framework for understanding domain knowledge and its interconnectedness. This makes them an ideal base for modeling linked data. Ontologies allow us to describe concepts, as well as the relationships between these concepts creating a graph of knowledge rather than a document or a database. By defining a common set of terminologies, we can improve data interoperability between different manufacturing processes and across sites.

The National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL) Ontology serves as a framework for understanding biopharmaceutical manufacturing processes. NIIMBL uses BFO, IOF and QUDT as the backbone for the ontology with the ISA-88 manufacturing process laid over this backbone to maximize interoperability with other ontologies. We then layered Merck's manufacturing processes onto this framework. This layering enabled production of Conceptual and Logical Data Models (CDM and LDM, r2espectively) showing the relationships between key manufacturing steps, processes, machines, etc., along with a hierarchical ontology demonstrating key term relationships.

Data Modeling

The NIIMBL Ontology serves as a framework for understanding biopharmaceutical manufacturing processes. In this project, we utilized this ontology for creating a proof-of-concept ontology that represents some of Merck's manufacturing processes. Leveraging this ontology, we developed a conceptual data model (CDM) (Figure 1) and a logical data model (LDM) which is re-usable for multiple manufacturing modalities, using tablet compression as the pilot process. The data structure defined includes entity information, sample attributes, and valid predicates based on the NIIMBL and ISA-88 standards.

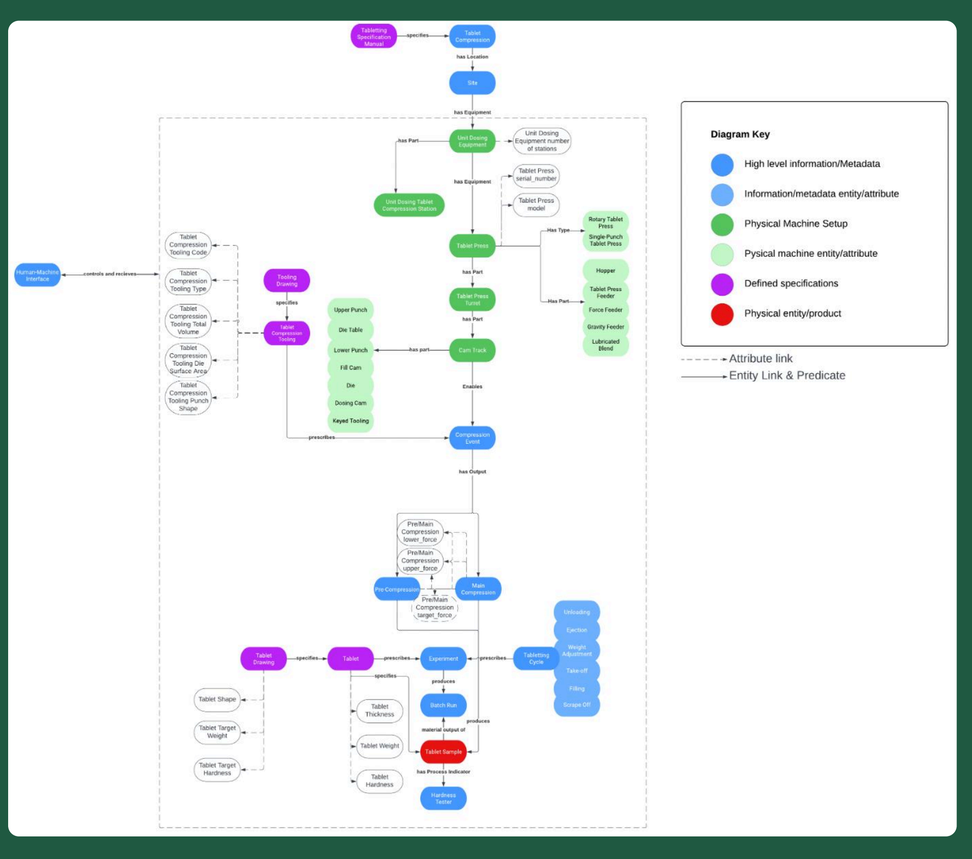

Figure 1 – Conceptual Data Model (CDM) of functional data structure. Leveraging the assembled ontology, this CDM represents an outline of a database to store manufacturing data inclusive of multiple modalities. This specific CDM represents the pilot work showing tablet compression manufacturing as a first link and includes multiple data types as well as entity and attribute level specifications.

Manufacturing Ontology

One of the primary challenges in ontology development is agreeing upon and defining a common set of terminologies to represent concepts in the lab. To accomplish this, we leveraged the generic NIIMBL parameter and ISA-88 process structures in the context of pharmaceutical manufacturing, including production equipment information, data storage, and human-machine interface definitions (Figure 2).

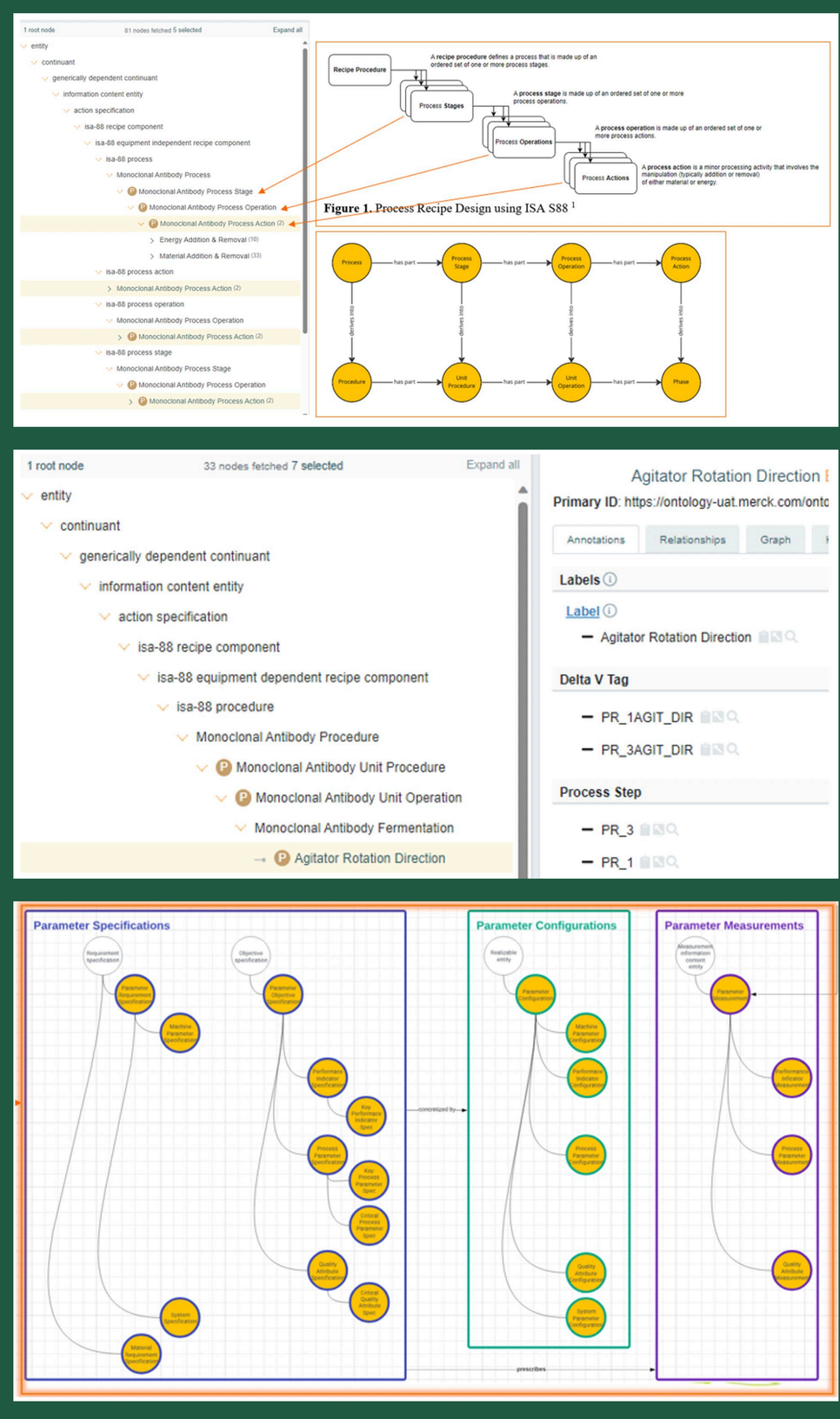

Figure 2 – Ontology structure and links to NIIMBL and ISA-88. The pharmaceutical manufacturing ontology hierarchy was assembled using existing NIIMBL and ISA-88 terminologies and structures. Primarily, parameter, process, and procedure hierarchies were adapted from NIIMBL to structure the manufacturing ontology.

Conclusions

- ISA-88 serves as a useful framework for understanding manufacturing processes.
- The NIIMBL ontology allows us to model these processes and make connections across different areas in the manufacturing domain.
- Much of the effort involved in building a data model and ontology entails agreeing upon and defining common language (standardized terminology) and data structures.
- This ontology helped us to identify, define and categorize key entities, attributes and relationships used on the development of the logical data model.
- The ontology serves as a functional structure to store and describe a myriad of manufacturing modalities and the relationships between them.
- The manufacturing ontology can be leveraged for data integrity and validation, semantic integration, inference and reasoning.

References

[1] NIIMBL Ontology Overview, by Crown Point Technologies, for the National Institute for Innovation in Manufacturing Biopharmaceuticals, Copyright 2022 Crown Point Technologies, LLC

[2] Pharmaceutical CMC Process Ontology Community Of Interest Meeting, Copyright Pistoia Alliance, Inc., 2024