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Towards a Single Data Exchange Standard for Use in Healthcare and in Clinical Research

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Abstract. Background: The development processes of data exchange standards for use in healthcare are very different from those used in clinical research. Healthcare data standards are traditionally developed by the Health Level 7 (HL7) organization, whereas those for use in clinical research are mostly developed by the Clinical Data Interchange Standards Consortium. No alignment of these standards has so far taken place. Objectives: Due to the increasing use of electronic health records as primary source in clinical research, it becomes necessary to align these standards, not only the semantic standards, but also the data exchange standards (formats) themselves. Methods: Mutual feature gaps between ODM and FHIR are investigated. Results: A transition path how the HL7-FHIR standard and the CDISC-ODM transport standard can grow into a single standard for use both in healthcare and in clinical research is presented.

Keywords. HL7, FHIR, CDISC, ODM, alignment.

1. Introduction

Information standards to be used in healthcare are traditionally developed by the "Health Level 7" (HL7) organization [1]. The first standard for data exchange was the HL7-v2 message standard, which is still very much used, especially for exchange of data within a single hospital or hospital organization. The use of these messages to exchange data between different organizations is however rare. The HL7-v3 standard was developed to overcome some of the limitations of HL7-v2, the most prominent one being the fact that HL7-v2 is only suitable for messages, and not for documents [2]. This was a huge problem, as care providers are used to exchange information with colleagues by means of "letters", i.e. documents. HL7-v3 however became only successful for documents, especially in the form of CDA (Clinical Document Architecture), which is also the basis of the interoperable health records system ELGA in Austria. Although a number of HL-v3 messages have been developed [3], they have never been very successful. This is probably due to the complexity of HL7-v3, which is based on the RIM (Reference Information Model), in which every piece of information need to be modelled either as an "act", a "participation", a "role", an "entity", an "actrelationship" or a "rolelink" or one of the subclasses of these. This made HL7-v3 hard to implement for IT people in software [4]. Therefore, a new standard "FHIR" (Fast Healthcare Interoperability Resources) [5] has been developed by HL7, encompassing both

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messages and documents, and using the most modern technologies such as RESTful web services [6] and different technical implementations such as JSON, XML and Turtle [7].

At the other side, CDISC developed the ODM (Operational Data Standard) for exchange of data within clinical research [8]. Its model is still mostly based on the paradigm of collection of data using paper forms (CRF: Case Report Form) during visits, or the electronic version of this (EDC: Electronic Data Capture) at the best. There is only one technical implementation (XML), which is not very suitable yet for exchange of data coming from wearables and other devices, nor for data originating from electronic health records, nor for remote trials in which there are essentially no visits. The latter are however recent evolutions, for which ODM was originally never designed for.

ODM has been very successful in the last 15-20 years, and is being used "end-to-end" [9], except for electronic submissions to the regulatory authorities. These still require data to be submitted in a very old binary format, the "SAS Transport 5" format [10], this although a variation of ODM (Dataset-XML) has exactly been developed for this use case [11].

2. Methods

Although HL7-FHIR and CDISC-ODM are rather different data exchange standards, there is a strong desire in specific parts of the CDISC as well as the HL7 organization to come to a single standard. The reason for that is that it is obvious that in future, large part of the data used in clinical research will either come from electronic health records, or will be shared between healthcare and research [12]. Coming to such a single standard is not easy, as not only technical issues need to be overcome, but also mental issues, such as a mutual understanding about the differences between healthcare and clinical research. For example, clinical research is "protocol driven" [13], meaning that is exactly predefined which tests need to be executed, which questions need to be asked to the patient. In healthcare, the treating physician in many cases acts "event driven", i.e. takes decisions about which tests to be performed, which treatment to be followed on basis on events that occur, such as an observation during a visit, an outcome of an earlier test, etc.

Also, the clinical research world is rather conservative, and the players in the field (pharma companies, Clinical Research Organizations (CROs), EDC vendors) are very reluctant to have any changes in the standards they use or need to use. Whereas the step from paper to EDC, and the use of the ODM standard was already a huge step for many (and which is still not completed), a move to FHIR (or FHIR-like) as a format, even if FHIR would completely be suitable for clinical research, would be another huge step. Thus, a transition path will be necessary in which FHIR and ODM evolve in the same direction and learn from each other to finally become a single standard. The time frame for this can only be estimated, but the author assumes this time frame will be 10 years or more.

HL7-FHIR resources are still in development, with different "STU"s (Standard for Trial Usage) as milestone stages [14]. Every developed FHIR resource has a "maturity level", ranging from 0 to 5 [15]. For example, the "Patient" resource currently has a maturity level 5 (the highest), whereas the "AdverseEvent" resource has the maturity level 0 (the lowest). This is interesting, as "adverse event" is one of the most important concepts in clinical research: the first requirement for a new drug of treatment is that it

is safe, i.e. that the number and kind of adverse events is low or very low and that the benefit / risk ratio is as high as possible.

In this paper, we report on our evaluations of both the FHIR and ODM standard, with a focus on the development of ODM Version 2 (ODMv2), which will in future replace the current ODM standard Version 1.3.2. ODMv2 will use a good number of concepts from FHIR, in an attempt to make a first step into the right direction with the long term goal that FHIR and ODM can become one single standard. We also report on a number of initiatives in the FHIR community to make FHIR more suitable for clinical research, as can be seen from a new category "public health and research" in FHIR STU3.

Table 1: Features supported by FHIR but absent or not supported in ODM

Feature	Description / Comment
Resources	ODM is not based on resources. However, when the content within a "Form" or "ItemGroupDef" logically belongs together, these can be compared to a "resource". For example, the CDASH forms [16] each describe logical grouping of terms belonging together and that can be compared to a "Resource". Example: CDASH form "Adverse Event" with FHIR resource "AdverseEvent". (also see "Profiles")
RESTful web services	Although a number of EDC vendors have developed RESTful web services for exchange of study metadata and data [17,18], unlike in FHIR [19], there is no standardized API.
Documents and Messages	CDISC ODM does not distinguish between messages and documents. A CDISC ODM file can both be used as a message or document. In FHIR, unlike in HL7-v2 and v3, the difference between a document and a message has become very small, both are "bundles" of resources [20] with either the type being "document" or "message". In the latter case, the first resource in the bundle must be "MessageHeader" whereas in the former case it must be "Composition".
Profiles	Specific use cases of FHIR resources can be described in "profiles" [21]. For example, a "vital signs profile" has been developed [22], describing a set of FHIR "Observation" instances, each defined by a LOINC [23] code. CDISC ODM has no such construct, as it has been regarded as out of the scope of ODM. However, CDISC-CDASH [16] defines semi-standardized forms such as a "vital signs form", describing the components of typical vital signs measurements such as systolic and diastolic blood pressure, body height and weight, pulse, etc. Unfortunately, CDASH does not provide LOINC codes for such measurements. The CDASH forms are however also available in ODM format. Furthermore, a number of people within the CDISC organization have developed "Biomedical concepts" (BCs) [24] which surely have a relationship with FHIR resources. For example, for the BC "systolic blood pressure" [25], it not only describes the test itself, but also the body position in which the measurement was taken (standing, sitting, supine), and the usual unit (mmHg). This compares very well to the "structure definition" of the component "systolic blood pressure" LOINC code 8480-6) in the FHIR profile "vital signs" [22]. Remark that currently, CDISC controlled terminology [26] does not allow the use of UCUM notation for units, whereas UCUM [27] is well established in the HL7 world. This kind of differences may become considerable hurdles when trying to come to a single standard.
Lack of semantics	ODM does not describe what needs to be done. It just describes the framework in which things can be done. The only semantics that is described by ODM is "study", "studyevent" (visit/encounter)", "form", "subform", "item/question", "skip condition"," code list" and "calculation method". ODM does not know what a "laboratory test" is, it only provides the framework to define one.
Different technical implementations	CDISC-ODM only has an XML implementation, whereas for HL7-FHIR, the standard can be implemented as XML, JSON or Turtle [7].
Distributed data	HL7-FHIR supports and promotes the use of distributed data. Single resources of a patient do not necessarily need to reside on the same server, but can be located on any FHIR server anywhere in the world. CDISC-ODM does not support this at all.

Table 2. Features supported by CDISC-ODM but absent or not supported in HL7-FHIR

Feature	Description / Comment
Multi-language support	From the start on, ODM contained multi-language support, and this feature was extended at each version update. The idea is that when a study is being developed, every important information point can be made available in any of the languages of the sites where the study will be conducted. This e.g. means that a single question or item like "systolic blood pressure" can also be defined in German ("systolischer Blutdruck") as sibling elements in the ODM. In FHIR, this would require a different instance of the resource "Questionnaire". Remark that in ODM, the identifier of the data point is independent from the language, so that data can be compared between languages. For example for "sex", the questions and enumerated answers may be in the local language, such as "Weiblich" and "Männlich" for the German language, but the captured values will be stored in a language-independent way in the database, such as "F" and "M".
Predefined data types	FHIR resources do not describe which data type for a data point is expected. This is logical as most FHIR resources describe data that was already captured, whereas the study definition part in ODM defines data that need to be captured. For example, a typical CDASH form definition in ODM [16] will define that the data point for "systolic blood pressure" is expected to be an integer. On the other hand, the data type of the captured data point will usually not appear in the ODM clinical data part of ODM, as it was already defined in the study definition part, where both are connected by a unique identifier within the study, the so-called "OID" which has a completely different structure and meaning than OIDs in healthcare [28]. In FHIR however, the data type appears in the resource itself as a variation of "value[x]", e.g. "valueQuantity", "valueString", "valueDatetime". There are 11 such "data types", whereas these are even more granular in ODM which counts 21 data types.
Audit records	CDISC ODM allows to describe data records that are fully 21 CFR Part 11 compliant by the use of "audit records" [9]. Audit records are however not described by FHIR. FHIR has an "AuditEvent" resource, but it has a different meaning. This is also very important for the ODM use case of archival [9].

3. Results

First, we made an inventory of differences in functionality between FHIR and ODM. Table 1 list a number of features that are found in FHIR but are not absent in ODM versions 1.3.2. Table 2 lists a number of features that are present in ODM but are not present or not supported in FHIR (STU3).

So, when trying to come to a single data exchange standard for as well healthcare as clinical research, it is clear that the best way to do so is to add features in ODM that are supported in FHIR, and add features to FHIR that are supported by ODM.

Leroux et al. made comparison and a mapping between CDISC-ODM and HL7-FHIR [29]. One of the statements in this paper is that "ODM is ill-suited for advancing the semantic interoperability solution". This is correct as ODM essentially describes a framework about "things" that are planned and "things" that happened according to that plan. CDISC did develop a large amount of controlled terminology [26], in first instance for electronic submissions to regulatory authorities, but this controlled terminology is mostly incompatible with what is used in healthcare informatics. For example, CDISC developed lists of as well laboratory tests, vital signs tests and even lists of microorganisms, but these are incompatible with LOINC and SNOMED. They are unfortunately also not mappable to these systems, as they are meant for post-coordination whereas most of the controlled terminology in healthcare informatics is pre-coordinated. When looking at the work done so far, especially the work of Leroux et al. [29] is of major importance. A summary of their mapping between FHIR and ODM is depicted in Table 3:

Table 3. Mapping between FHIR and ODM (summary) according to Leroux et al.

HL7-FHIR Resource	CDISC ODM Element	Comments
CarePlan	Study	Both the resources "CarePlan" and "Study" refer to things that are planned, but with different purposes. Plans of care can change during the treatment period, whereas studies are not meant to change during the study duration. In HL7-FHIR, plans of care can be nested, i.e. a care plan can consist of several sub-plans. This feature is not present in CDISC-ODM.
Questionnaire	FormDef / ItemGroupDef / ItemDef	The HL7-FHIR resource "Questionnaire" describes a list of questions to patients. Answers to these questions can be of several types, which match rather well with the data types in CDISC-ODM for "ItemDef". Both HL7-FHIR as well as ODM allow to define groupings of items. In CDISC-ODM however, "FormDef" is not limited to questions to patients, it is more a container for any kind of data that was captured in relation to the patient, directly or indirectly, during an encounter between a patient (subject) and an investigator. One important difference is that CDISC-ODM multi-language support: one and the same item/question can be translated into different languages for use at different sites in different countries and cultures. In HL7-FHIR, this requires several instances of "Questionnaire", one for each language.
Patient	SubjectData	In ODM, "SubjectData" is a container for all data points about a specific patient (traditionally designated as "subject"). ODM however itself does not define what these data points are. In HL7 however, the "Patient" resource exactly describes the primary properties of the patient such as date of birth, sex, etc..
ClinicalImpression	SubjectData	HL7 ClinicalImpression describes "A record of a clinical assessment performed to determine what problem(s) may affect the patient and before planning the treatments …". Part of the ODM "SubjectData" can indeed be mapped to this resource, when describing the state of the patient before study start.
EpisodeOfCare	StudyEventData	The HL7 resource "EpisodeOfCare" can be mapped to a set of encounters between a patient and a care provider. As such it can also be used to describe all clinical study data that were captured as a result of a number of encounters (ODM "StudyEvents") between a subject and an investigator.
QuestionnaireResponse	FormData	The HL7 "QuestionnaireResponse" is limited to answers of "questions" filled when responding to a questionnaire. ODM however does not distinguish between data that comes from questionnaires only, but also data that come from other sources, such as lab data. Originally, ODM "FormData" was indeed essentially meant for paper forms, but as more and more electronic data capture (EDC) became available, it was promoted to a container for data that belong together and that were captured in one way or another, directly or indirectly during an encounter between subject and investigator.

This list does not comprise any of the CDISC-ODM extensions, such as the "Study Design Model in XML" (SDM-XML) [30], where the Element "ActivityDef" nicely maps to the FHIR resource "ActivityDefinition". Other SDM-XML elements such as "Workflow" can also be mapped to FHIR resources from the "Workflow" resource group. Leroux et al. also proposed new FHIR resources: ClinicalStudyPlan and ClinicalStudyData [29], which are the FHIR equivalents of the ODM "Study" (study definition) and "ClinicalData" (captured data) elements. These two new proposed FHIR resources should make the mapping with CDISC ODM complete, at least at the semantic level.

Mappings are nice, but data transformations should be avoided whenever possible as they inherently lead to information loss and can easily lead to errors [31,32]. Therefore, it is a good idea to also let the ODM standard evolve towards the HL7-FHIR standard.

The CDISC ODM development team recently started working on a new generation ODM standard. The name of the project is "ODMv2". Requirements were developed and can be summarized as:

- Backwards compatibility as much as possible. If this cannot be guaranteed, an XSLT stylesheet should be delivered that transforms ODM version 1.x into ODM version 2
- Support for alternative formats such as JSON. This probably means that the XML implementation will remain "leading", as many of the rules of the standard are implemented by means of XML-Schema and Schematron.
- A standardized RESTful web services API. A number of vendors [33,17] already have developed RESTful web services for exchange of ODM data and metadata. A standardized RESTful web services based API would also allow to work with distributed data, i.e. that all the data points of a single subject do not necessarily need to reside on a single server, but can be obtained through a set of RESTful web service queries. This especially becomes important when data from electronic health records is used.
- More flexibility in study design. The HL7-ODM standard originates from the times that most of the data was captured on paper forms, or EDC "CRF screens" at the best. This paradigm is outdated. Not all data is collected in "forms" and during "visits". There is a strong tendency to "e-Source" where data can come directly from the hospital information system, from electronic health records (that can use FHIR resources) and from devices such as wearables. Even more, "virtual" or "remote trials" become more common [34] where the subject (almost) never visits the clinic or has encounters with the investigator. This means that the hierarchy "visit - form - item group - item" must be revised.
- Better support for multiple controlled terminologies. CDISC-ODM only has the concept of "codelist" and "external codelist". The former defines value lists defined by the designer of the study (e.g. sponsor-defined lists for possible answers to a question) or copied from CDISC controlled terminology [26], the latter to coding systems such as SNOMED-CT, LOINC and others. However, even the names of these external codelists is not standardized. HL7-FHIR has a better mechanism for this [35]. Also in ODM, it is currently not possible to create subsets of external codelists, for example stating that a SNOMED-CT term or code should be used, but only from a selection of these.

These requirements are such that it will not be possible to guarantee 100% backwards compatibility. This can however be overcome by providing an XSLT stylesheet that

allow to transform ODM v.1.x in ODM v2 documents. Support for JSON also means that "roundtripping", i.e. transforming an ODM document to JSON and then transforming it to XML again without any information loss, must be possible. Whereas FHIR had the advantage of starting from scratch and has a very good mechanism for this, this will not be so easy for ODM.

Within the scope of ODMv2, it will not yet be possible to make a complete move to "resources". The reason is that the clinical research world is very conservative, and vendors of EDC systems will highly probably not want to invest in data capture tools that use a completely different approach. However, in many cases, a resource can be implemented as an ODM "ItemGroup", by grouping items that logically belong together and annotating them with codes and designations from the healthcare world. For example, an ODM "ItemGroup" "blood pressure" or even "vital signs" essentially corresponds to HL7-FHIR profiles "blood pressure" [36] and "vital signs" [22]. So, by semantically "standardizing" concepts and putting them in a single ODM "ItemGroup" and/or "Form" and annotating them with codes from the healthcare world (in the case of "blood pressure" using LOINC) and/or CDISC controlled terminology codes, makes them resemble FHIR resources and profiles already, and allows to exchange definitions of "biomedical concepts" [24].

A major obstacle for coming to a single data standard however remains the difference in the semantic standards used. HL7-FHIR tries to use existing semantic standards as much as possible that are well accepted in healthcare, but that were not necessarily developed within HL7, such as SNOMED-CT and LOINC. These semantic standards usually are pre-coordinated, i.e. they combine different pieces of information into a single term or code. For example, the LOINC code 1751-7 describes the test "Albumin [Mass/volume] is Serum or Plasma". CDISC however only uses controlled terminology to be used in post-coordination. For example, the code "ALB" describes "Albumin", which then needs to be combined with other terms to come to a description of a quantitative albumin test in blood. The background of this is that it remains (unfortunately) very unusual to exactly describe test to be performed in clinical study protocols. Even the CDISC Therapeutic Area Guides (TAUGs) [37], describing best practices for performing clinical studies in specific therapeutic areas, do not exactly describe recommended specific tests to be performed. Instead, very unspecific wording is used such as "test glucose in urine". It is then up to the sponsor to translate this into more specific tests, but even then, LOINC and SNOMED-CT coding is very seldom used. Upon submission to the regulatory authorities, the information is then post-coordinated (categorized) using CDISC controlled terminology. This means that for each test, the sponsor assigns a group of codes to a single test, for example for the compound, the specimen type, the test method, etc. The CDISC standard for doing so is the Submission Data Tabulation Model (SDTM) [38], providing a transformed "tabular view" on the data, and containing as well derived data as having data redundancy: essentially moving the data from operational data (ODM) to SDTM is an Extract-Transform-Load (ETL) process. As stated, SDTM requires CDISC controlled terminology (post-coordinated) to be used which is incompatible with healthcare coding systems such as LOINC and SNOMED. Also a "decomposition" from LOINC and SNOMED-CT codes (among others) has been shown to be very problematic [39]. In SDTM, use of these healthcare codes is very limited, or even not allowed (e.g. UCUM notation for units). A further complication is that the regulatory authorities still require data to be submitted in a completely different, but outdated format, named SAS Transport 5 format (often referred to a "XPT format). This is a binary format from the era of mainframe computers.

It has severe limitations restricting variable names to 8 characters, labels to 40 characters and values to 200 characters [40]. Furthermore, it only allows ASCII characters. The CDISC-XML team developed an XML standard for such tabular data, named Dataset-XML [41] but it is still not accepted by the regulatory authorities. This seriously delays the acceptance of XML as a technology within the clinical research world. Unfortunately, SDTM as a semantic standard is strongly influenced by the constraints of the XPT format, such as variable names to be constraint to 8 characters. HL7-FHIR does not have any such restrictions. Dataset-XML as a format does not have these constraints either, but for some of the information, instance files still need to implement these constraints for data when the dataset is for an SDTM submission. As long as these constraints exist, integration with healthcare data may remain difficult, if not impossible.

4. Discussion

This article describes some of the differences between the HL7-FHIR standard for exchange of data in the healthcare world with the CDISC-ODM standard for exchange of data in the clinical research world. Recent efforts to create new FHIR resources for use in clinical research are described, as well as the current efforts of the CDISC-ODM development team to modernize the ODM standard and add a number of features that are already supported by HL7-FHIR or even form the basis of HL7-FHIR. Unifying HL7 FHIR and CDISC ODM does not seem to be possible at this moment, but due to serious efforts of volunteers both from the HL7 side as from the CDISC side, such a unification may well be possible in not too far future.

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