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Welcome to the summer issue of our Newsletter. It contains the latest news about standards for data exchange in clinical research and how these are implemented in the industry.

### **New version of SDTM-ETL™ now available**

A new release (version 1.2) of our popular software for mapping between operational clinical data and CDISC-FDA submission data (SDTM) has now been released. The new version of the SDTM-ETL™ software has a lot of additional features for working with non-standard SDTM variables, and with sponsor-defined domains. Also a set of new script functions has been added, and advanced users can now also add their own script functions.

Also, CDISC ODM 1.3 as a data source is now fully supported.

More information about the new release is available on our [website](#).

The new release doesn't mean that we are sitting down and taking a rest. We already started working on the next version, which will implement SDTM 1.2 (SDTM-IG 3.1.2). We are expecting to release that new version in autumn, this although it is expected that the FDA will not be able to accept SDTM 1.2 submissions in the near future yet (they need to update their tools). However, we want our tools to be ready faster, so that our customers can already start preparing SDTM 1.2 submissions.

### **New version of the ODM Study Designer available – with CDASH**

We also released version 2009-R1 of our flagship offering, the [ODM Study Designer](#). The Designer now has extended support for define.xml, a cleaning up facility, and ... all CDASH forms included. So with a few clicks only, users can now add CDASH forms to their study design. These can then (but must not) be tailored ([CDASH](#) is a recommendation rather than a hard standard) to the needs and requirements of the study. An eCRF preview was already available, but in the new version, also a

number of different views of the “Schedule of visits” are possible.

Vendor extensions to the ODM standard often also make use of the “ref-def” mechanism. As this mechanism is not supported by XML-Schema (it will be in version 1.1 of XML-Schema), “ref-def” dependencies can also not be declared in vendor extension schemas. Therefore we added a new feature to the software, which allows to load the “ref-def” definitions for vendor extensions from a simple text file. This further enhances the functionality for working with ODM vendor extensions. By the way, our ODM Study Designer is the only designer software on the market allowing to work with any vendor extensions.

The ODM Study Designer is [fully certified by CDISC for compliance to the ODM standard](#) (versions 1.2 and 1.3).

A list of the new features can be downloaded [here](#). More information is of course available on our website.

The screenshot shows a software window titled 'Nachricht' with a sub-header 'Visit (StudyEvent)'. The main area is divided into two columns: 'Visit (StudyEvent)' and 'Forms'. The 'Visit (StudyEvent)' column contains details for 'Screening Visit -1 (EVT00001)' and 'Treatment Visit 1 (EVT00002)'. The 'Forms' column lists various forms with their IDs and mandatory status, such as '1. Comprehensive Hist, Phys & Vitals (FRM00001) - Mandatory' and '1. Electrocardiogram (FRM00003) - Mandatory'. A 'OK' button is visible at the bottom right of the window.

### **CDISC Intrachange**

At the time you are reading this, the CDISC [Intrachange](#) (not to be confused with the public Interchanges) is taking place. The Intrachange is a three-day face-to-face meeting of CDISC volunteers in order to work on (new versions of) the standards, and especially to do work on the integration of the standards. It's a great meeting with lots of discussions, new insights, new visions.

The only problem with this meeting (it takes place every half year) is that it must take place in Washington D.C.. The reason is that CDISC wants as many FDA representatives to be present, but as the FDA does not have any travel budgets for these people, CDISC is organizing the meeting in Washington each time. That this means that some volunteers must spend thousands of dollars (travel, hotel, missed income) does not seem to be a concern. So I asked CDISC whether it is not possible to broadcast the presentations live (that's what we have the internet for), but this does not seem to be possible technically, as the hotel where the meeting takes place does not have a very good IT infrastructure.

As said, it is a great meeting, though it is not a technical meeting. It is more about the contents of the standards, and the way they can be integrated with each other, than on the technical details. Therefore, it is my believe that we should also have “technathons”, just like [the “Connectathon” meetings of IHE](#). We could even try to make this a “virtual conference” as some other organizations have done.

Personally, I believe this kind of US-centricity of CDISC still makes it very hard to find more (technical) volunteers in (eastern) Europe, Asia, and other continents, and that is of course a pity.

### **XML-Schema 1.1 is coming**

The W3C XML-Schema working group has now published the “Candidate Recommendation” of [XML-Schema version 1.1](#). This new version of the schema language has many new features and removes many of the limitations of XML-Schema 1.0 (which was a huge improvement over DTD). In Schema 1.1, one can e.g. declare the conditions under which an attribute should be present or absent. I am currently following the very active [discussion forum](#), in order to be able to work with this great new technology as soon as possible. I know some people are working on [tutorials](#), and maybe someone is also already working on a book ...

Once “final” I want to start working on “updating” the XML-Schema for CDISC ODM to Schema version 1.1 (which by the way is 100% downward compatible). The reason is that there are many rules in the ODM standard that can currently (with Schema 1.0) only be expressed in words, so that they can always be interpreted differently by different persons. With Schema 1.1 however, they can be expressed in machine-readable language, so that the rules become more interpretation-free.

Schema-aware parsers for XML-Schema 1.1 are also already available. For example, one of the most popular parsers, [Saxon](#), has a lot of support for Schema 1.1 in its version 9.1 of the software.

### **DataSci versus Medidata (again)**

Back in 1995, I already used “online banking” over the internet. The browser based software allowed me to look into my bank account, and to execute payments. It even had some “intellency”, e.g. checking that an amount only consisted of numeric characters. I am sure it had a database backend.

A few years later, a company (named DataSci - it never ever released any EDC product itself) filed a patent exactly describing this functionality, but – for use in clinical trials. Surprisingly, the patent was accepted by the US patent office, and since then, DataSci (having become a “lawyer” company) has made big business by chasing EDC vendors and suing them for patent infringement.

Well, if this patent is valid, I should urgently file one claiming “the use of an automobile for driving to the mall”.

Also Medidata was a victim of DataSci. In 2007, Medidata settled with DataSci paying an amount of approximately \$2.2 million (PhaseForward paid about \$8 million). The exact details of the settlement were however not released. Now that Medidata has gone public, DataSci smelled a new opportunity to extract more money out of Medidata, and sued Medidata again (in Maryland), probably (but the details are not clear yet) for breaking the settlement agreement.

When reading such a news, I am thinking about the ultimate goal of doing clinical research: to obtain permission for bringing a drug or a therapy to the public that makes people healthy again. Therefore, even though business is business, I do not have an understanding for companies that hinder the accomplishment of such goals. Such practices make EDC considerably more expensive and slows down the implementation, ultimately meaning that people must wait longer for a new drug that can save their life. It is probably very hard to calculate, but I sometimes wonder how many lives DataSci has on its conscience.

### **Flexcipio and BioClinica obtain ODM certification**

Two software products obtained [CDISC ODM certification](#) in the last months. One is [BioClinica's](#) EDC system “BioClinica Express”, the other being [Flexcipio's](#) “eClinical Platform”.

BioClinica is a merger of the former companies Bio-Imaging Technologies and of Phoenix Data Systems. The latter was already pretty active in the CDISC community, so this certification does not come as a surprise. Flexcipio is a Belgian company, located near Waterloo (yes, where Napoleon was defeated by the English and the Prussians). It provides systems as well as software, especially for (but not limited to) clinical research.

With these new certifications, the number of products being certified for ODM compliance now has grown to 11, with some more being on the road to certification (I know, as I am helping a number of vendors to become CDISC compliant).

Essentially, the number of certifications clearly shows that the ODM standard has reached its goals: to become an industry standard for exchange of clinical research. In my personal opinion, e.g. EDC products that do not have support for ODM (import and/or export) have no future, and will surely lose market share.

### **CDISC-EHR integration – the next step**

Under the lead of Landen Bain, CDISC has, together with a number of volunteers from other organizations, clearly shown that integration of clinical research with electronic health records is possible. It demonstrated this several times, the last ones at the DIA Annual conference in San Diego, and at the CDISC Interchange in Budapest and at the [IHE Connectathon in Vienna](#).

Also, an interface between CDASH forms and electronic health records (EHRs) has recently been developed by a mixed CDISC-IHE team. For that project, [we delivered the XSLT technology](#) to transform EHR extracts (formatted as HL7-CDA) into CDISC-ODM format. We later extended this to [integration with EHRs in OpenEHR format](#).

During the project, we found out that a combination of XSLT and ODM (and not HL7-XML) is the best way to accomplish integration between EDC and

EHRs (and with hospital information systems in general). We also now starting providing services to our customers in this field.

As always, there is a next step. In order to better integrate clinical research with hospital systems, the latter need to understand (parts of) the trial protocol. Now that CDISC has published the [draft “Protocol Representation Model”](#) and will later publish an extension to the ODM standard (and XML-Schema), for this model, the opportunity arises to start working on things such as visit scheduling (and scheduling of other activities), not only in the EDC system, but also integrating it into the hospital information system.

I am currently keeping an eye on the [IHE profile “Retrieve Protocol for Execution”](#) and will later probably join this initiative. I do believe that the upcoming ODM-protocol-extension will be the ideal format for allowing such an integration, as it is easy to use with XSLT technology, which is unfortunately not the case with HL7-v3-XML messages. An HL7-XML implementation of the CDISC Protocol Model is also planned, but currently it is not further than a storyboard and some draft UML-diagrams. We estimate it will still take a few years before it really exists and is approved by HL7.

### **Roche chooses for Medidata (and for ODM?)**

The latest news (I just received it yesterday) is that Roche, one of the largest pharma companies in Europe, has selected Medidata Rave® as its enterprise-wide EDC system. The press release from Medidata can be found [here](#).

I presume that this also means that within Roche, the CDISC ODM standard obtains a giant opportunity, as Medidata's system fully supports the ODM Standard and is [fully certified](#) for it.

All together, this means a huge modernization step for Roche in EDC.

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