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FDA: No HL7-XML for SDTM submissions for the foreseeable future

Though there were some signs before that some things are changing within the FDA, the message still came as a surprise: during a [meeting with the top of CDISC](#), FDA-CBER and CDER announced that they are not going to implement HL7-XML for electronic submissions for the “foreseeable future”. Literally: *“For the foreseeable future CDISC standards (SDTM and ADaM) will be accepted in SASXPT with Define.xml”*, followed by: *“Before moving to HL7 transport, this method of submission will need to be tested, approved and “net better” than what they are receiving now and for the foreseeable future, in SASXPT with Define.xml”*.

Essentially this means that the FDA radically changes its opinion from “HL7-XML at any price” to “HL7-XML only when proved to be better”.

As our regular readers know, we have always strongly opposed against HL7-XML for SDTM and ADaM submissions ([see our previous newsletters](#)), for many reasons. Luckily, as one of my US colleagues stated “there seems to be a new sheriff in town”, and this stupid idea has now been put on ice, at least for the next few years.

So should we “declare victory”?

Not at all, as the same CDISC publication also states that SAS Transport 5 format (XPT) will remain the transport mechanism for the next years. SAS XPT is a very old format from the era of the IBM mainframe (the eighties) and has very many disadvantages¹. Essentially one can say that it is not

very compatible with modern computers and software. Furthermore, we realize the FDA did not give up the development of HL7-XML. CBER and CDER only stated they will not use it in the foreseeable future.

So, should the FDA stick to this “computer-stone-age” format for the next 5-10 years? We don't think so.

In our opinion, it is high time that we (CDISC?) start developing a modern, easy-to-use, format for SDTM and ADaM submissions based on define.xml. Such a format is already being used by at least 4 vendors internally in their software for generating SDTM datasets: only in the last step the SDTM-XML datasets are transformed (“downgraded”) into the legacy SAS Transport 5 format.

CDISC has supported the idea for HL7-XML for submissions to the FDA for about 3 years . So we now need to convince CDISC first to leave this trail and to give support to the development of a format based on define.xml. If we can convince CDISC, then there is also a good chance that we can convince the FDA at the end.

This new, easy-to-use format can be developed within a year by the same group of people that developed define.xml. Convincing the FDA will take more time, but we hope we could do so by providing the agency with viewing stylesheets, and maybe even with user-friendly software.

Currently, we use 30 year old technology for electronic submissions to the FDA. We should avoid that in ten years from now, we need to confess that we are using 40 year old technology for electronic submissions.

¹ The most catastrophic one being that important submission information is ending in Supplemental Qualifier domains.

CDISC publishes draft pharmacogenomics domains

CDISC has just published a first draft for two new SDTM domains: the Pharmacogenomics (PG) domain and the Pharmacogenomics Findings (PF) domain. The [distribution](#) can be found in the “Members only” section of the CDISC website.

We are currently reviewing the draft, and also have already implemented it into the newest version of SDTM-ETL (see further on). Existing customers of the software can therefore obtain an updated template containing these two new draft domains. They do however need to understand that these are still in draft and thus subject to change.

XML4Pharma at the CDISC European Interchange

The CDISC European Interchange 2010 is rapidly approaching. It is taking place in the week of 26 to 30 April in London. The program and all other necessary information can be found [here](#).

For us, the Interchange will start with a short “[German User Group Meeting](#)” on Tuesday evening. A reception together with the other european user groups is planned later the same evening.

On the second day of the conference itself, I will be giving a presentation titled “Towards a Fully Machine-Readable Protocol: The New ODM Extension for Trial Design / Protocol”. This presentation will deal with the ODM-extension that is currently being developed by the “XML Technology Team”, and that includes features such as Inclusion/Exclusion Criteria, Arms, Epochs and Study Segments, Study Activities, Workflow and Timings between Activities.

We will also have a booth at the exhibition (booth #11), where we will give demonstrations of new releases of our software offerings (see further).

New at the Interchange are the “User Discussion Groups”. We have been asked to help moderating the ODM discussion group which is planned for Wednesday early afternoon.

On Friday, I will give a small contribution to the course “Healthcare Link Training: How to use an EHR for Clinical Data Capture”, including recent work that has been done at the interface between ODM and hospital information and planning systems.

If you have not registered for the European Interchange, do now – it will be a great event!

SDTM-ETL v.1.4

Also at the European Interchange, we will present a new release of our popular SDTM-ETL software for defining mappings between operational data (ODM format²) and the SDTM standard, and for executing these mappings and generate the SDTM datasets according to the SDTM Implementation Guides.

Some of the new features are (a detailed overview can be obtained upon request) are:

- partial support for ADaM datasets
- support for ODM “Alias” containing SDTM and CDASH annotations
- fast mapping for CDASH forms
- faster access to user-defined functions
- extended HTML view of the underlying define.xml
- mapping completeness report
- logging with timestamps
- integration of the [OpenCDISC-Validator](#)
- even more support for sponsor-defined domains and for non-standard variables

We will publish full details during the next few days on [our website](#), where you also will be able to download the “new features” document.

Also remember that we published a number of instruction movies on the usage of SDTM-ETL for generation of SDTM datasets from operational data. You can find these movies at:

www.xml4pharmaserver.com/SDTM-ETL

SDTM-ETL Light

Why spend very large amounts of money for doing something relatively simple as generating SDTM datasets?

We recently had the issue that one of our potential customers decided to not use SDTM-ETL. Reason was they had the requirement that the software “must generate SAS macros so that our partners can also generate the SDTM datasets based on our mappings”.

This of course supposes that the partner has the same (expensive) statistical software available.

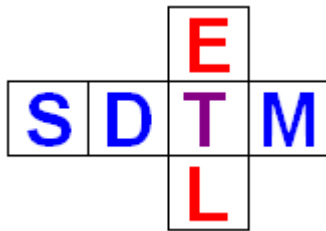
So to make the usage of the SDTM-ETL software even more easy (and cost-effective) we decided to develop a “light” version of the software which only allows to execute existing mappings (which are

² CDISC-ODM can now be exported from almost any modern EDC system

stored within the define.xml file), but not to develop new mappings.

This “light” version of the software is especially interesting for partner companies of existing (or new) users of the SDTM-ETL software that require a low-cost, easy-to-use solution for generating SDTM datasets from existing mappings.

The license cost of SDTM-ETL “Light” will be a fraction of what needs to be paid for a license of the base version of a statistical software package.



OpenCDISC 1.0 released

Our colleagues at OpenDISC (www.OpenCDISC.org) recently released final version 1.0 of their “OpenCDISC Validator”.

The validator implements all SDTM and Janus rules as implemented in WebSDM™, and is thus a very good alternative. Even more, the OpenCDISC Validator is not only free-of-charge - it is also “Open Source”!

The Validator uses the most modern XML technologies. All validation rules are being defined as XML (including [Schematron](#)). This means that the rules are both human- as machine-readable.

Defining validation rules as XML is surely the future. The great advantages are:

- the validation rules are unambiguous (no interpretation discussions)
- everyone (including regulatory agencies) uses the same rules
- computers can validate the rules and generate standardized error messages
- the rules can be displayed in a human-friendly format using a viewing stylesheet
- sponsor defined rules (for internal usage) can be added and flagged as such.

What OpenCDISC has realized already implements for a good part what we think should be the future of SDTM (and ADaM) submissions, i.e. that submission datasets should come as XML (based on define.xml instead of as SAS Transport 5), with the SDTM rules being defined as XML rules (e.g. using Schematron), allowing unambiguous validation using inexpensive software.

Congratulations to OpenCDISC – this is a great achievement !

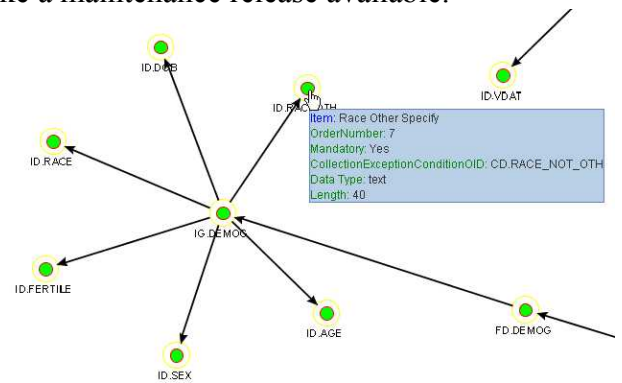
CDISC ODM Designer Release 2010

At the CDISC European Interchange we will also present the new release of the ODM Designer.

Release 2010 has a number of new features available such as:

- “star” and “web” view of the full study design
- full HTML view of the full study design including annotated CRFs. The HTML can be saved to file and/or transformed to PDF
- individually annotated CRFs as PDF (Swing)
- much faster navigation for insertion of new forms, itemgroups, items, codelists etc..
- further improved “schedule of visits” in table or grid form.

We did already have a CDASH implementation in our ODM Designer. Once the official ODM templates for CDASH are published by CDISC (expected in May) we will also implement these and make a maintenance release available.



“Star” view of the study design

Annotated CRF as PDF

Height
V\$ORRES
Alias: SDTM_V\$ORRES where V\$TESTCD=HEIGHT

Weight
V\$ORRES
Alias: SDTM_V\$ORRES where V\$TESTCD=HEIGHT

Systolic blood pressure
V\$ORRES
Alias: SDTM_V\$ORRES where V\$TESTCD=SYSBP

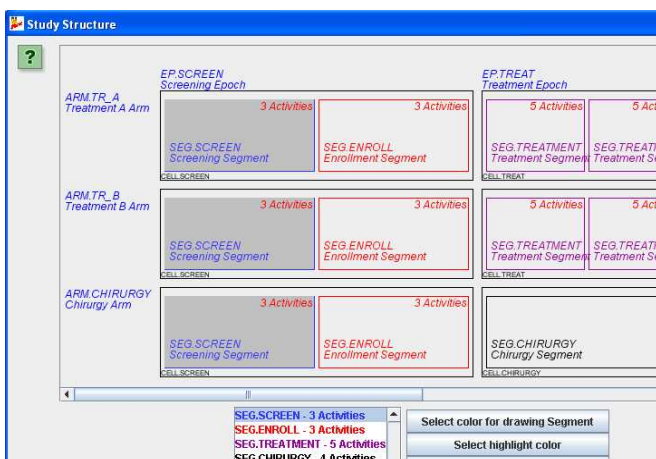
Diastolic blood pressure
V\$ORRES
Alias: SDTM_V\$ORRES where V\$TESTCD=DIASP

Blood pressure ratio
@SDVName Not Set
Method: Systolic blood pressure divided by diastolic blood pressure

Does the subject feel dizzy when standing up from a sitting position
@SDVName Not Set
Skip condition: Needs not be collected when the diastolic blood pressure is 0 or higher.

Annotated CRF as HTML

Furthermore, we are experimenting with the upcoming ODM-extension for trial design, where one can also define Arms, Epochs, Segments, Activities, and where one can define workflows and timings between them. As soon as the ODM-extension becomes publicly available, users will obtain a free maintenance release.



Study structure, defining Arms, Epochs, Segments and associated Activities.

Chiba XForms is now BetterForm

It has been a bit silent around Chiba, the server-side implementation of XForms, which you can also [test out \(using CDASH forms\) on our website](#).

Until very recently, when I found out that Chiba now rebranded to “BetterForm” and just released version 3.0 of the software which is a successor the Chiba-3.0.

As usual, BetterForm is also open-source, and can be freely downloaded from the [BetterForm](#) website.

I had a first try with BetterForm, and am currently implementing some of the CDASH forms. My first impression is that this is excellent web software, only the styling (so not the contents nor the functionality) is a bit more difficult to implement (it uses CSS and the [Dojo toolkit](#))

XForms has (surprisingly) not been accepted very well yet for eCRFs in the (conservative) clinical research community. What we are now observing however, is that more and more companies that are piloting in integration between electronic health records and clinical research are implementing XForms, as it is “first choice” (i.e. very easy to implement) when it comes to prepopulate eCRFs with information from other sources such as electronic health records.

XForms was already used in the first effort in this field (the [IHE RFD profile](#)) to which also CDISC was a contributor. It also showed to be a key enabler in our **demo application** [which you can test out online](#) on integration between hospital information systems and clinical research.

Group: Physical examination: Base

Height* [Red Box] The height value should be below 220 cm

Weight* [Red Box] The weight value should be below 150 kg

Systolic BP 132

Diastolic BP* 80

Does the subject feel dizzy when standing up from a sitting position* No

Prepopulated (from an EHR) eCRF rendered using XForms

Also see our presentation at the 2009 European CDISC interchange which can be downloaded from [our website on EHR-CDISC integration](#).

BetterForms as a company has also grown. Whereas the company first started (still as Chibacon) with the internet and XForms pioneers Joern Turner and Lars Windauer, the company now employs two more people. As the software itself is open-source, the company lives from professional services and support and from implementation of large (XForms) projects, with customers coming from the banking world, from aeronautics IT, and from ... healthcare.

OpenXData: a mobile solution for clinical research?

I recently also became aware of [OpenXData](#), an open-source technology for collection of data using forms on low-cost mobile devices (i.e. cell phones).

The technology consists of a web application server (using e.g. Tomcat), a MySQL database, and Java-based client software for the mobile phone. The client itself uses XForms technology.

The technology seems to be very successful for in-the-field healthcare in developing countries (a

number of movies is available on their website). I also came into contact with one implementor who uses the technology for non-profit clinical research in developing countries, this in combination with [OpenClinica](#) (see our [November 2009 Newsletter](#)). This organization is also interested in ODM as the standard for exchange of clinical data and metadata.

In the past, we have already developed technology for transformation of CRF definitions in ODM into XForms forms ([you can try it out using our demo application server](#)) and we are now discussing with this non-profit organization to make this technology available to them for free. By doing so we hope to be able to make a small contribution to improvement of healthcare in developing countries.



OpenXData: scanning a barcode of a vaccine bottle using the mobile phone



Meet us at the European CDISC Interchange:

- German User Group Meeting on Tuesday evening
- Presentation “Towards a Fully Machine-Readable Protocol: The New ODMExtension for Trial Design / Protocol”
- Booth Nr. 11 during the exhibition
- Presentation during the course “Healthcare Link Training: How to use an EHR for Clinical Data Capture”

Not registered yet ?

Do so at: <http://www.cdisc.org/interchange>

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