This year, we will try to send out our newsletter regularly again (i.e. bimonthly) as we did in the past. The eClinical and XML world are rapidly evolving (the former sometimes less rapidly than we desire), so we really need to keep our customers informed on a regular basis about new evolutions and new technologies.

This newsletter already contains a good number of news items about what has been happening on the eClinical and XML front during the last months

CDASH is out and hot !

The CDISC CDASH (short for "Clinical Data Acquisition Standards Harmonization") team has released version 1.0 in October last year.
The document can be found here.
CDASH essentially describes a set of standardized forms for use in data acquisition that are as close as possible to what needs to be submitted to the FDA in an SDTM submission. As such, CDASH is really the bridge between data acquisition and SDTM.
Already before the final document was published, CDASH was very "hot": EDC vendors published press releases that their products would fully support CDASH.
We have also extended our "ODM Study Designer" software so that users can now include (and edit) CDASH forms in their study design. This will be only one of the new features of the software in the next release (see further).
Currently, a mixed CDASH-ODM team is preparing to publish ODM files that implement CDASH. This will enable any system that can read CDISC-ODM to directly incorporate the CDASH forms into the system.

CDASH and EHR Integration

CDASH and its integration with EHR systems is also a theme of the next IHE Connectathons in Chicago and Vienna. At these meetings for e-Health "integration geeks", a number of vendors of Electronic Health Record systems and EDC vendors will demonstrate the interconnectivity of

electronic health records and EDC systems: they will demonstrate how CDASH forms can be prepopulated with information from the EHR system.

e-Health integration geeks at work at the 2008 Connectathon

XML4Pharma has been contributing to this project by helping to define a format (based on ODM) that is produced from the EHR (in this case, an HL7 "Continuity of Care Document" - CCD). The EHR data in this format can be read by the EDC system to prepopulate the CDASH forms. Also we contributed to the development of the XSLT stylesheet that executes the transformation from the CCD to the intermediate format (see diagram at the end of this newsletter).

We are currently also developing technology (especially XSLT stylesheets) to do the same for electronic records from OpenEHR systems, which is a competing "standard" to HL7-v3-XML, and which is more popular in Europe and Australia. OpenEHR is also the only system that complies to the European norm CEN 13606, which may become the norm for all EHR systems in Europe in the future.

We hope to give a demo of this OpenEHR – CDASH integration at the next EU Interchange in Budapest in April.

CDISC-EHR Integration: first commercial system goes life

I just received the latest e-Newsletter from CDISC, which contains a link to a very interesting article by Landen Bain, CDISCs liason to Healthcare.

The article is about the first commercial implementation of RFD, the profile for CDISC-EHR integration, in a commercial product from Greenway Medical. In their EHR application, forms being served from an EDC system can be selected and displayed, as if were that the eCRF were part of the EHR system – the user even doesn't notice that it isn't. The eCRF is even prepopulated with data from the EHR system, according to the article for 75%.

With this kind of integrated systems, it becomes much easier for investigators to do clinical research, as they can do everything within one system. As such, it is hoped that many more physicians and hospitals can be engaged in clinical research.

CDISC European Interchange 2009

XML4Pharma will be present at the next European CDISC Interchange in Budapest (April 20-25). We will have a booth at the commercial exhibition, and will also give a presentation with the title "Integration of EHR with CDISC, CDASH and ODM – a European initiative".

Furthermore, I will be the co-trainer at the SDTM training course, which is expected to take place on Monday and Tuesday.

We will also announce and demonstrate major updates of two of our products. First of all, the newest version of the ODM Study Designer will be shown, containing major improvements such as incorporation of and full support for CDASH forms. Secondly, we will show the newest version of the SDTM-ETL software for mapping between ODM and SDTM, and for the automated generation of define.xml and SDTM datasets from CDMS and EDC systems that can export to ODM.

CDISC German-speaking User Group Meeting, February 19, Berlin

For those wanting to know what is happening with CDISC implementation in Germany, Switzerland and Austria (or just do not want to await the Budapest Interchange), I can recommend to attend the German-speaking User Group Meeting in Berlin on February 19th. The meeting will be hosted by Parexel.

If you would like to attend this meeting and haven't received an invitation yet, please have a look at the announcement on the CDISC website.

The main topic of the meeting will be (just guess ...) "CDASH". There will be a CDASH tutorial by Elke Sennewald (Kendle) and presentations about integration with ODM and mapping to SDTM.

In the afternoon, the different workstreams will meet. These workstream meetings are ideal, not only to discuss the standard of your choice, but also to meet some of the people that drive these standards in German-speaking countries.

Schematron and XML-Schema version 1.1

Also the XML world is evolving. One relative new XML-technology is especially worth mentioning here, as it will also have its impact on CDISC standards like the ODM.

More and more, we see that standards that have an XML implementation (such as CDISC-ODM) that rely on an XML-Schema for validating instance documents, are not only published with the XML-Schema, but also with a so-called "Schematron".

Schematron is an XML-technology that allows to define complicated rules that cannot be defined in an XML-Schema. Examples in the world of ODM are dependencies between attributes (e.g. when the value of the "Archival" attribute is "Yes", the value of the value of the attribute "FileType" must be "Transactional") or the **"Reference-Definition" mechanism** in ODM Study design (when referencing a Form in a StudyEvent, the Form must be defined using a FormDef element).

Schematron rules can be incorporated in XML-Schemas using the "appinfo" element, or can be defined in separate Schematron files. They are based on assertions using XPath expressions, also allowing to define dynamic error messages to be given when the rule is violated.

A first (for us) relevant example is the draft XML-Schema for the ISO-21090 datatypes which in future should become the "core" data types for use in e-Health in general and for EHR records in particular. These ISO-21090 datatypes have been developed (as a compromise) as the current HL7-v3 data types have been found unacceptable by the European Union (CEN). This upcoming standard may eventually lead to a worldwide standard for EHRs that is acceptable as well in Europe as in the US as in the rest of the world. A very interesting

background article and presentation can be found here.

I am currently also working on a Schematron for the ODM 1.3 standard, and made good progress. It will be discussed within the ODM team before being published.

In my personal opinion, a Schematron should also become part of the XML-Schema for a future ODM 1.4 standard.

Another interesting evolution is the work of a W3C working group on **XML-Schema 1.1** (the current standard is 1.0). Although XML-Schema is pretty powerful and an enormous improvement relative to the "Document Type Definition" (DTD), which is e.g. still used by the eCTD standard, XML-Schema does have its limitations. These can be taken care of by Schematron, but of course it is better to improve and extend the XML-Schema specification itself.

Although the work on XML-Schema 1.1 is not complete yet, and the standard has not been released by W3C, the IBM DeveloperWorks website has published a series of very interesting articles on the technical aspects of XML-Schema 1.1. These articles also contain many working examples.

Another interesting short presentation by XML-guru Michael Kay from Saxonica can be found here.

Of course before using XML-Schema 1.1 in CDISC standards such as the ODM, we will need to ensure that there is sufficient tool support, in the form of XML editors and validating parsers (e.g. for C#, Java, Perl, etc..). So, the real use of XML-Schema 1.1 will probably first start in 2-3 years.

Initiative for an ODM extension for ePRO

"Vendor" extensions to the ODM standard are very practical at one side, but they limit portability on the other side. Many vendors, including ePRO vendors have generated extensions to the ODM standard to allow to define features that are not supported by the ODM standard. One must realize that the ODM standard is a "consensus" standard, i.e. it is a common denominator. As in any consensus process, there are always things that the working team could not agree on, and thus have not come into the standard. This has also been recognized by the ODM team, so they designed an extension mechanism, so that any implementor can extend the standard. Of course, vendor extensions also mean reduction of portability. The ODM team has always encouraged vendors to submit their extensions to the team "for possible future standardization", and several have indeed done this.

Also several ePRO vendors have developed ODM extensions. As ODM is also becoming more and more important in ePRO, I think the time is right to start working on a "standardized" ePRO extension to the ODM.

As a first step, we will setup a discussion web site (i.e. a forum) where ePRO vendors can submit their ideas about what should go into such an extension and what shouldn't. Essentially, an inventory of the needs and requirements.

I hope that after some time, this will lead to a new CDISC team, with a somewhat more formal process of teleconferences and "real work".

HL7-v3-XML messages for SDTM submissions

Our article "Ten good reasons why an HL7-XML message is not always the best solution as a format for a CDISC standard (and especially not for submission data)" (which you can find here) has not gone undiscovered in the internet world. Several blogs and articles about the XML-technical problems with HL7-v3-XML have referenced and discussed it.

The real discussion about whether HL7-v3-XML is a complete overkill for submission of two-dimensional tables to the FDA, has however not really started yet. It is still my personal opinion that an HL7-v3-XML message for SDTM submissions will be extremely difficult to implement (due to the overcomplexity of HL7-v3-XML) and thus cost the industry a enormous amount of money.

This is very painful, as there is already an open standard for exchange of clinical data (submission is also a form of exchange ;-)): the CDISC ODM standard.

All that is needed is a small extensions to the ODM (which some volunteers have already available). Such an extension would also ensure that submission data can easily be validated against define.xml.

The argument from the FDA that an HL7-v3-XML message is needed for future integration with EHRs is nonsense, as we recently experienced in our work on integration of EHRs with CDASH. Essentially, the FDA argument reduces to that you need a car to build a car. In reality, in order to build a car, you need materials, tools, robots. The materials are there: CCD, CDA, ODM, CDASH. In the XML world the tools are named XSLT and the robots XML parsers. XSLT can itself be generated by relative simple software, unlike instances of another overcomplicated HL7-v3-XML message.
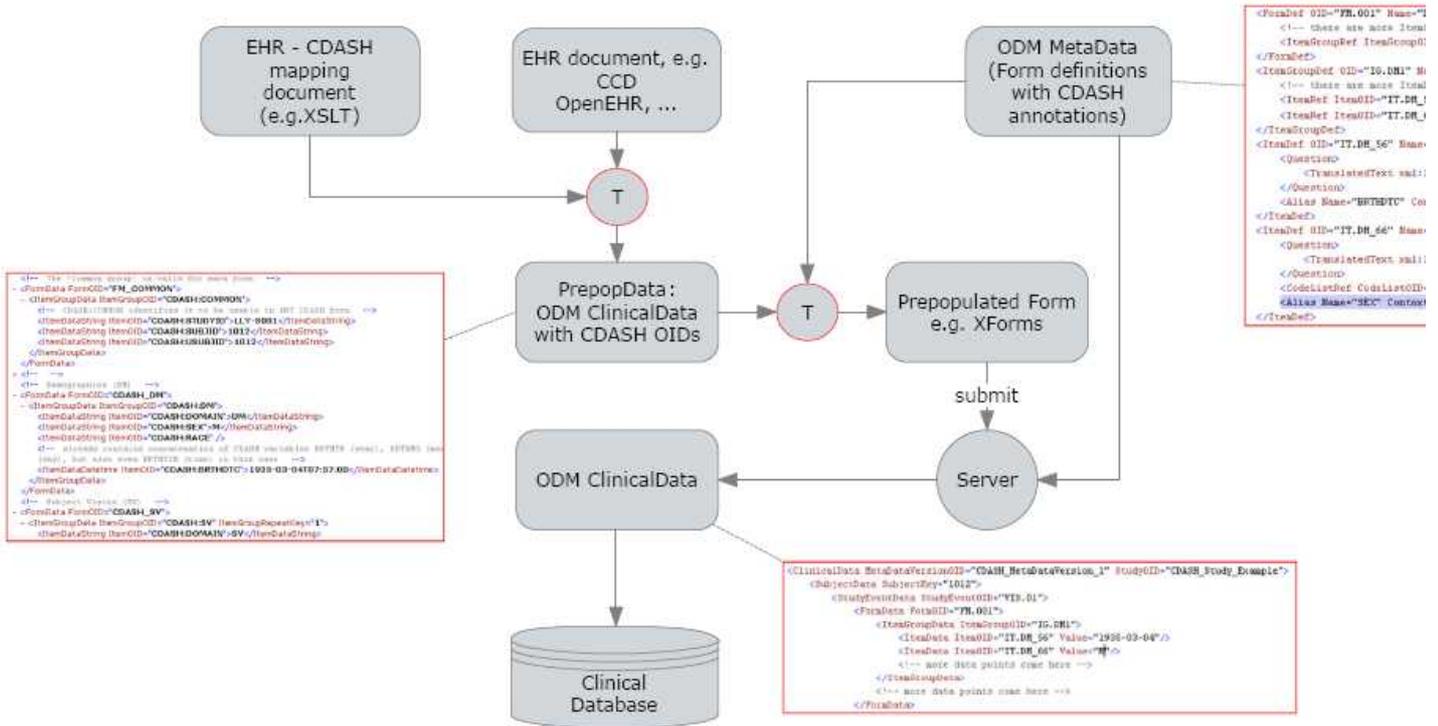
Integration of CDISC-ODM and CDASH with EHR
Flowchart of the mechanism