Bimonthly newsletter of XML4Pharma,
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Happy New Year !

A happy new year to all the readers of our newsletter! Also in 2007 we will provide you with news about the use of XML in pharmaceutical research in general, and in clinical research in particular.

At this place we would like to thank all our customers of last year for their confidence in our services.

2006 was a pivotal year for CDISC. We now see that many companies do no longer hesitate with the implementation of CDISC standards, at it is now clear that CDISC is the way to go. This has of course also to do with the embracement of the CDISC standards by the FDA, especially SDTM and define.xml.

But we are not there yet! Submission data are still delivered as SAS Transport V files to the FDA, and there is no machine-readable implementation of the CDISC Protocol Standard yet.
The CDISC work groups will in 2007 work hard on an update of define.xml and SDTM, and on an XML-based format for the replacement of SAS Transport V. Also a machine-readable representation of the Protocol Standard is in progress.

Just before Christmas, CDISC published the ODM 1.3, which may be seen as one of the milestones of last year.

CDISC publishes ODM 1.3 Final

Just before Christmas, CDISC released the final version of the ODM 1.3 standard. Especially EDC vendors may see this as a Christmas present (although probably not meant so by CDISC), as the new version has very many new features for use in EDC, like a large number of new data types, internationalization at all levels of the metadata, and the conditional appearance of questions and groups of questions on eCRFs.
The new EDC features are so great that I dear to say that the ODM 1.3 should really become the standard for EDC.

As one of the co-authors of the new standard, XML4Pharma will of course provide all necessary services to pharma companies, CROs and EDC vendors to implement the ODM 1.3 Standard in their systems.

Furthermore, we are currently setting up a set of courses about the ODM 1.3.

DIA Basel November 2006

The Clinical DIA meeting is one of these yearly meetings that is important for anyone working on e-clinical. Also this year, the conference was very well visited, with many very interesting presentations, and a large vendor exhibition.

Although there was a separate CDISC track, the use of CDISC standards was mentioned in a good number of presentations outside this track, meaning that the use of CDISC standards is becoming normal practice and more and more widespread. Some presenters even made proposals for further extending the standards, e.g. for trial metrics.

In the CDISC stream itself, we gave a presentation "*From Protocol to Submission – The value of Using CDISC Standards: Experiences from a Long-Time Implementer*". In the presentation, emphasis was laid on strategies for implementing CDISC standards, on the cost of adapting existing systems to become CDISC compliant, and on new upcoming standards implementations (e.g.

a machine-readable Trial Design) from the CDISC organization.

A copy of our presentation can be obtained upon request.

Consolidation in the e-Clinical world ?

In our previous newsletter we reported on a number of mergers in the european pharma world. The ink wasn't dry yet, when ClinPhone, the eClinical service provider, announced the acquisition of DataLabs, the EDC vendor. Clinphone was more and more confronted with the request from customers to do EDC, but did not have the toolbox to do so. The logical next step was to acquire an EDC vendor.

DataLabs was one of the early adapters of CDISC standards in their systems, having CDISC import and export capabilities in their EDC system (DataLabsXC).

Under the agreement, DataLabs will keep selling its products as they are available at the moment, but ClinPhone stated it has already started integrating DataLabs technology into its existing solutions.

The overall company now has a workforce of over 700.

Business Case for CDISC Standards

CDISC, Gartner and PhRMA together published a report on the business case for CDISC standards. This report is available for CDISC members on the CDISC website (members-only section).
One of the major conclusions of the study is that especially at the start of the study very large savings in both time and money can be achieved through the use of CDISC standards. For example, study design and setup time can be reduced by a factor of 4 !
The literal text from the report:
"**Standards save time and money, especially when implemented in the study startup stage**".

Some "best practices" that were mentioned in the report (and which we already advocate for a long time) were:

- use ODM to collect data from various source
- use SDTM metadata to design CRF
- Annotate the CRF per SDTM so all the departments can see the variables in the context of the data flow

The report also lists a number of hurdles:

- Difficult to allocate resources to work on standards for the future while still continuing today's work
- Users do not want to make investments (to create tools themselves and to migrate) when vendor products do not support standards.
- Lack of expertise on XML and HL7

This is where XML4Pharma has its mission for already many years: to help companies in the industry with the implementation of CDISC standards, to develop tools and software, and to provide CDISC-XML knowledge through trainings, courses and consultancy.

XML4Pharma counts several EDC vendors among its customers helping them to implement the CDISC standards into their products.
Also our own tools are well known and widely used, and implemented at as well sponsors as CROs.

For us, the Gartner-PhRMA report confirms that we are on the right track, as still a lot is to do at many companies to have full implementations of the CDISC standards.

Sylva collins to join Kendle

Mid-November it became public that Sylva Collins, former VP Global Advanced Clinical Systems was appointed VP Global Biometrics at Kendle, the worldwide operating CRO.

In the past, dr. Collins was known as one of the pioneers of EDC, and the initiator and development leader of Novartis' own (home-build) EDC system.

Dr. Collins also served on the board of directors of CDISC starting from 2004.

IBM goes for XForms

It looks as IBM is getting heavily involved in further development, evangelization and implementation of XForms, the W3C standard for web forms. One of its senior product architects (John Boyer) is currently co-chair of the W3C XForms working group. Furthermore, IBM currently published a lot of technical articles on XForms on its DeveloperWorks website. IBM also provides the XForms support for the EHR-EDC integration demo planned for the HIMMS conference at the end February.

IBM seems to have opted for use of XForms using the Mozilla Firefox browser. This browser has an easy-to-install plugin allowing to work with XForms.

XForms for use in EDC and clinical research is one XML4Pharma's core competences, for which we started pioneering work already back in 2004.

XML4Pharma launches new EDC technology based on ODM 1.3 Standard

As the first technology provider, XML4Pharma has now developed new technology for use in EDC, based on the new CDISC ODM 1.3 standard.

The technology is based on as well the new ODM 1.3 standard, as on the XForms standard, which is the W3C standard for web forms. The new technology can be used for the automated generation of eCRFs starting from clinical study designs in ODM 1.3 format.

Many new features of the ODM 1.3 standard are supported. This includes many of the new data types and the enhanced internationalization. Especially interesting is the support for conditional appearance on the form of questions or groups of questions depending on the outcome of another question. For example, in the fully automatically generated form, all questions about smoking habits are blanked out when the investigator ticks that the subject is a non-smoker.

This new technology can already be tried out on our public application server (www.XML4PharmaServer.com): the user can submit an ODM 1.3 file with study definition (a sample file is provided on the website), and the eCRFs are automatically created for the language of choice (English, German, French, ...). The forms can then be tried out immediately in the browser, or can be downloaded to the PDA (DataMovil technology).

This technology will be made available to EDC vendors and other interested companies.
For more information about licensing, please send us an e-mail at info@XML4Pharma.com.

A screenshot of an automatically created eCRF can be found at the end of this newsletter.

XML4Pharma develops Java widgets based on ODM 1.3 for use in EDC

With the venue of the CDISC ODM 1.3 standard, many new great features have become available for the EDC community.

In order to help EDC vendors with the implementation of the new version of the standard, we have developed a set of new Java Swing widgets for the old and new data types that come with the ODM standard. These widgets make it considerably easier to develop EDC systems based on Java applets or Java applications.

An example of such a widget is given below. It shows the Swing widget that can be used for the new data type “IntervalDateTime”. This data type is meant to define an interval date/time. The latter can either be given using a start date and time and an end date/time, or using a start date/time and a duration, or using an end date/time and a negative duration.

The widgets are very intelligent. For example, for the shown widget, it is only possible to enter the month once the year has been entered (for the date/time part), so these widgets are self-validating, so that it is nearly impossible to submit invalid

data. Of course the widgets are also fully customizable. For example, the alignment of the different components can be changed.

More information about these Java widgets and their availability can be obtained on request.

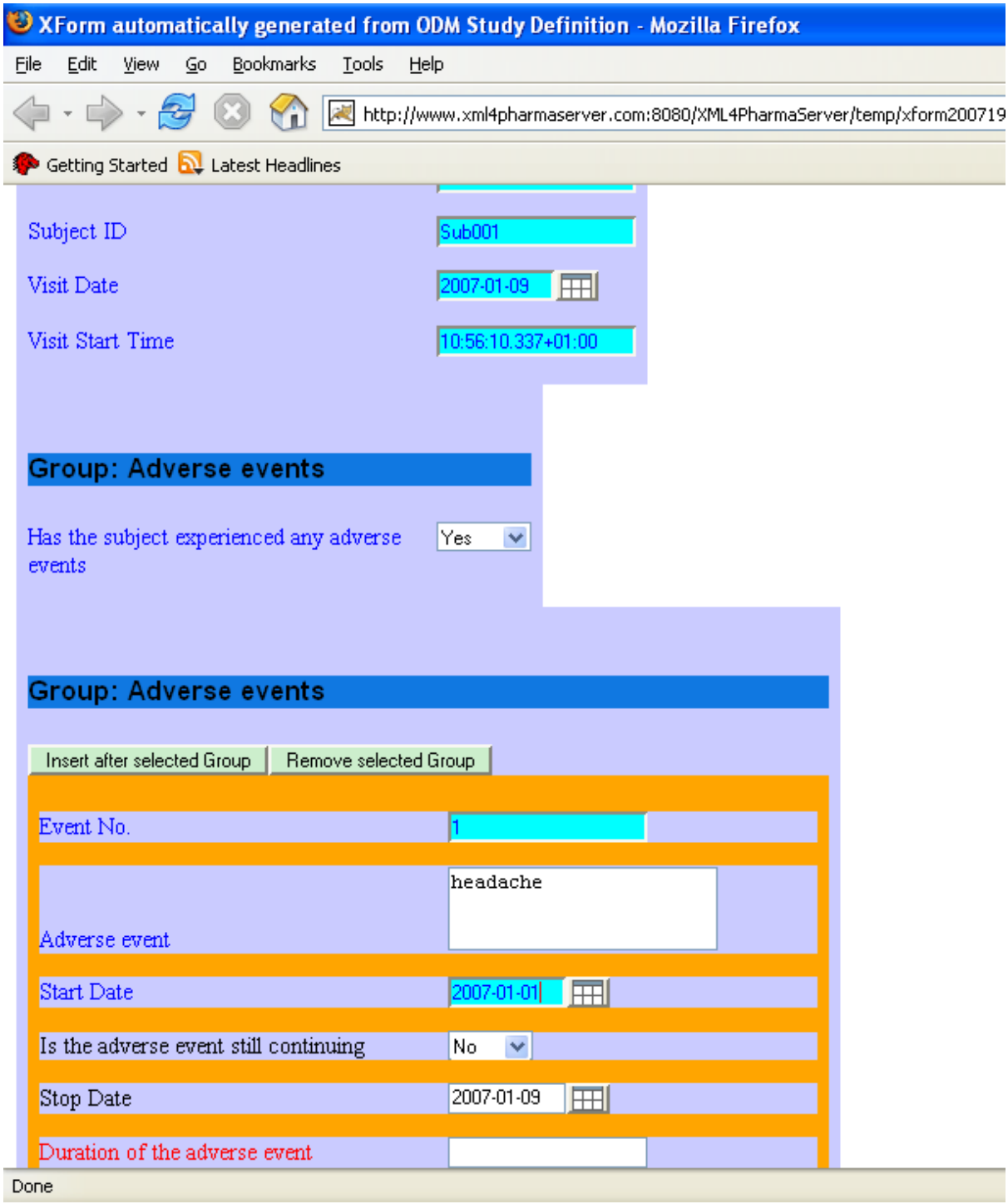

Fig.1: an eCRF automatically created from an ODM 1.3 file. Several adverse events can be added by clicking the “Insert” button. The questions on adverse events disappear when the user selects “No” on the question “Has the subject experienced any adverse events”. Similarly, the line “Stop Date” disappears when the user selects “Yes” on the question “Is the adverse event still continueing”.

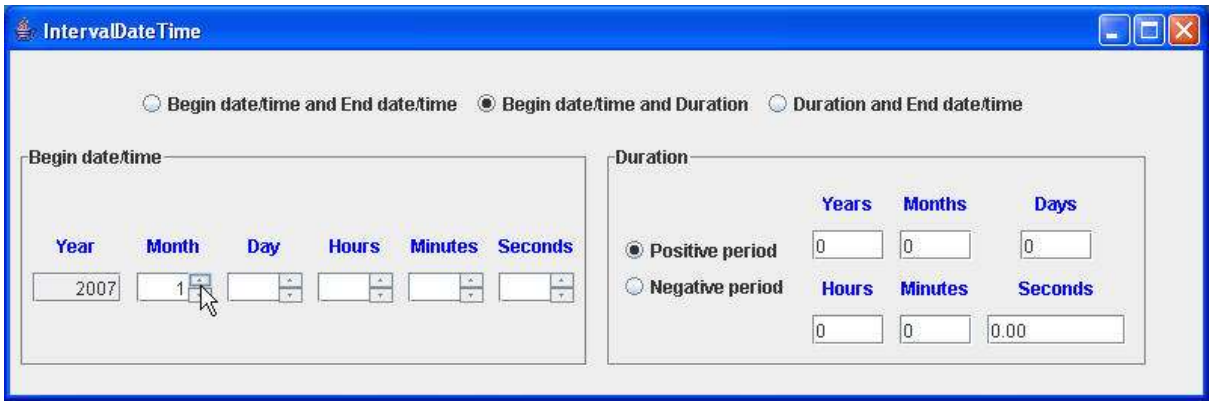

Fig.2: A Java Swing widget for the ODM 1.3 data type “IntervalDateTime”