Bimonthly newsletter of XML4Pharma, Schlossbergstrasse 20, DE-78224 Singen, Germany Phone: +49 7731 975044 Web : <u>www.XML4Pharma.com</u> Mail: <u>Info@XML4Pharma.com</u> November 2005



<u>A new tool for designing clinical studies</u> <u>in CDISC ODM format: the ODM</u> <u>Study Designer</u>

Setting up clinical studies in CDISC ODM format has many advantages. It allows to exchange the study setup information in a standardised, vendor-neutral format. Moreover, as CDISC ODM is based on XML, it allows automation of otherwise cumbersome and time consuming tasks like database creation, setting up the CDMS, design and generation of e-CRFs, etc..

Until now, a good, affordable software tool for setting up clinical studies in ODM format was not available. Some people used an XML Editor like XMLSpy to generate the Study setup in ODM format, others did not use the ODM at all and kept sending Study and Protocol information as Word documents or PDFs to the CRO, EDC company or other partner in the clinical process.

Therefore we developed the ODM Study Designer, which allows to set up clinical studies in ODM format without any knowledge of XML at all. The tool is very user-friendly, as it works with many dialogs and wizards, so that also users who are new to CDISC ODM can learn very quickly how to generate Study information in ODM format.

The tool has been developed so that Vendor Extensions based on ODM 1.2.1 are fully supported: the ODMDesigner reads the XML-Schema with the vendor extensions and base ODM XML-Schema and automatically creates all necessary tables and dialogs.Of course, also the upcoming ODM 1.3 standard is fully supported. The tool is SDTM-ready, which means that the user can add domain names and variable names from lists taken from the SDTM 1.1 (SDS 3.1) specification.

As the tool reads and writes ODM (no propriety formats are used), it eliminates software vendor-lock for designing clinical studies and eCRFs.

We expect that this tool will further boost the use of the ODM standard in setting up clinical studies: with this tool, there is no excuse anymore not to use the ODM standard right from the start of the clinical study process.

The reader can find some screenshots at the end of this newsletter.

Further information about the ODM Study Designer can be found on our website at:

www.xml4pharma.com/CDISC_Products/

<u>Four Worlds – One Vision:</u> <u>DIA Conference Prague</u>

The latest DIA conference in Prague was a very interesting one, as the "hot topic" of the conference was the use of EDC and its impact on Clinical Data Management and Regulatory.

Although there was a special e-Clinical stream, the EDC topic came back in almost every lecture of the other streams. Furthermore, a large number of EDC Vendors was present at the commercial exhibition.

Personally, I found a number of lectures about "mixed" trials, i.e. trials in which as well EDC as paper was used, very interesting.

There was a lot of discussion about the cost and ROI of EDC. Especially CROs keep having the feeling that EDC is not affordable. What was underexposed in my view, is that the use of (CDISC) standards in EDC can enormously reduce the costs. So maybe I should give a lecture on that topic at one of the next DIA conferences.

CDISC Lab Standard implementation

We heard it again at the last DIA meeting in Prague: CROs still believe that the use of the CDISC Lab standard is not affordable for small laboratories with which they cooperate. That is nonsense of course! Instead these CROs invest large amounts of money in systems that allow them to transform data from small laboratories into their own formats. This is an expensive exercise, as each of these small laboratories usually has its own, propriety formats, or have to maintain a large number of different formats of their customers.

A number of projects XML4Pharma executed sofar for CROs and small and mid-sized clinical labs clearly prove that the CDISC Lab standard can be implemented at an affordable cost, and that this investment quickly pays back.

An excellent article on the use of the CDISC Lab standard and its benefits was recently published in <u>Applied Clinical</u> <u>Trials</u>. The article states that the cost reduction of using the CDISC Lab standard is between 30 and 50%. This is considerable, as it has been estimated that 60-80% of clinical data originates in laboratories. Some centralized labs have even offered preferential pricing for customers that agree to receive the test data in CDISC Lab format. This, as the use of the standard saves them a large amount of time and money.

XML4Pharma is one of the pioneers in the development of tools for working with CDISC Lab files. A number of our tools can be tried online on our <u>free application</u> <u>server</u>. This includes a tool for checking CDISC Lab files in ASCII or in XML format against the standard, and a conversion tool that transforma CDISC Lab files in ASCII format to CDISC Lab files in XML format.

Other tools for generating Lab files or to work with CDISC Lab files have been

developed for some of our customers on project basis.

CDISC ODM 1.3: new features and enhancements

We are almost so far: the ODM team expects to be able to publish version 1.3 of the ODM standard for comment on the CDISC website before the end of the year.

Although 100% downwards compatible, version 1.3 has a good amount of new exciting features, especially for use in EDC and clinical data management. EDC vendors will especially appreciate further internationalization in Forms and the ability to use conditions for the use and occurrence of items, itemgroups, forms and even study events. For data transfer and archiving, the most interesting new features are the new data types, these e.g. allow to have binary data in an ODM file. Furthermore, the problem of partial and incomplete dates and times have now been solved using these new data types.

Automatic generation of e-CRFs from ODM study setups : technology now generally available.

A number of EDC vendors already do it: generating eCRFs directly from CDISC ODM files containing study setup information. With the new version 1.3 of the ODM standard, this will even become considerably easier (see previous topic). Most EDC vendors use propriety technology for performing the transformation from ODM to e-CRF, driving sponsors and CROs into an expensive vendor lock.

There is however good news: XML4Pharma has developed a technology, based on XForms, the open W3C standard for web-based and standalone forms, which enables to generate eCRFs on the fly at low cost. This XForms technology has now become so mature, and more and more XForms enabled browsers and PDA XForms software becomes available, that we decided to start offering this technology to sponsors, CROs and EDC vendors, based on a "technology transfer agreement". The use of W3C standardised XForms technology must so further enable to make EDC much more affordable, and eliminate vendor lock.

The technology can already be tried out at our <u>demo application server</u>: the user can submit a CDISC ODM file with Study information (samples are provided), and then gets a set of eCRFs back, which can be populated online and submitted. The end result is than presented in the form of a CDISC ODM ClinicalData file and a PDF file with the form data.

CDISC ODM Checker v.0.6 now available

In the last issue of our newsletter we announced v.0.6 of our CDISC ODM Checker, a conformity checking tool for CDISC ODM files. This new version has now become available.

The new version has a number of improvements against v.0.5, including support for vendor extensions based on ODM 1.2.1, the ability to save or print the results of a conformity check, and many small improvements for conformity checking of ODM 1.2 files with XML-schema.

The CDISC ODM Checker is freely available for CDISC member companies. Non-members can acquire a license.

Most recent new users of the CDISC ODM Checker are PRA International and Octagon Research.

IBM Releases XForms Generator

IBM recently released an update of its XForms Eclipse plugin. Using this software (which runs in the extremely popular Eclise Java IDE), it is possible to generate XForms from instance XML documents and their respective XMLschema. The generated XForms can then be rendered into a number of popular XForms browsers and renderers, including FormsPlayer, Chiba, X-Smiles, Novell, Mozilla Firefox and others.

Although the tool is not suitable to directly generate e-CRFs in XForms format from CDISC ODM files, it can be very helpful in making improvements (e.g. in the layout) of automatically generated eCRFs with our technology, and to test them in different browsers and XForms renderers.



The ODM Study Designer: screenshots

DDM Study Designer by XML4Pharma											
File Valida	te Options	Help									
				Global Stud	ly Variables		Basic Study Definiti	ons	Study M	etadata	
Includes	Protocols	Study Event Defin	nitions	Form Def	ininitions	ltem (Group Definitions	ltem D	efinitions	Codelists	Imp
	OID	Name	Da	taType	Lengt	h	SignificantDigits	SAS	FieldName	SDSVar	Name

The table templates, dialogs and wizards are generated from the ODM XML-schema

📕 ODM Study Designer by XML4Pharma									
File Validate Options Help Extra information for: ItemGroupDef ,with OID = IG.AE1									
😅 📑 🥵 🔹 🧿	ItemRef Alias								
	ItemOID OrderN	lumber Mandatory KeySequence ImputationMe	Bole RoleCodel ist						
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Includes Protocols Study Ever	IT.PNO 2	select a(n) Item	<u> </u>						
OID Nomo	IT.SCTRY 3	ItemOID +	ItemName						
Name Name	IT.F_STATUS 4		Normal/Abnormal/Not Done						
RQ IG AE2 Advarse Events	IT.LINE_NO 5	IT AFACTTRT	Actions taken re study drug						
Q IG AE3 Adverse Events		IT AECONTRT	Actions taken other						
SQ IG CONMED1 Concorn Mede		ITAEENDAY	Ston Day - Enter a value 1-31						
SQUG CONMED? Concorn Meds		ITAEENDT	Derived Ston Date						
S IG DEMOG Demography		ITAEENMON	Stop Month - Enter a value 1-12						
SQUG DRUG TRT Treatment Assi		ITAEENYB	Stop Year - Enter Four Digit Year						
S G PHARMO1 Pharmacokine		IT.AEOUT	Outcome						
G AIG PHYEX 1 Physical Exam		ITAEREL	Relationship to study drug						
G PHYEX 2 Physical Exam		IT.AESEV	Severity						
G G.REFSAMP Sample Refere		IT.AESTDAY	Start Day - Enter a value 1-31						
		IT.AESTDT	Derived Start Date						
		IT.AESTMON	Start Month - Enter a value 1-12						
		IT.AESTYR	Start Year - Enter Four Digit Year						
		IT.AETERM	Conmed Indication						
		IT.AE_RELAT	Taken for AE						
		IT.BODY_SYS	Physical Exam Body System						
		IT.COMMT1	Comment						
		IT.DOB	Date of Birth						
		IT.DOSEUNIT	Dose and Unit						
		IT.DRUG_TRT	Assigned Study Drug Treatment						
		IT.F_STATUS	Record status, 5 levels, internal use						
	Sort I	IT.HT	Height						
		IT.HTUNITS	Height Units						
	S	IT.INDIC	Conmed Indication						
	·	IT.LINE_NO	Line Number						
		IT.MEALDAY	Meal day - Enter a value 1-31						
		IT.MEALMON	Meal month - Enter a value 1-12						
		II.MEALTIM	lime of last meal						
		II.MEALYR	Meal year - Enter 4 digit year						
Add Row		II.MEAL_DI	Date of last meal						
Suggest Oli)s	ОК	Cancel						
Save to Libra	агу								

Many dialogs and wizards for fast generation and selection of Forms, ItemGroups, Items, Codelists and so on ...

The	ODM	Study	Designer:	screenshots
		•		

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Glob	al Study Varia	2	Domain Code	Domain Name Category A			
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ons 🛛 Form Defininitio		DS		Disposition	Events		
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peanity	No	DV		Protocol Deviations	Events		
	No	DA		Drug Accountability	Findings		
	No	EG		ECG Tests	Findings		
	No	IE	Inclusion/Exception Exceptio		Findings		
	No	LB		Laboratory Tests	Findings		
	No	MB		MicroBiology	Findings		
	No	QS		Questionnaires	Findings		
	No	PC		Pharmacokinetics Concentr	Findings		
	No	PP		Pharmacokinetics Paramet	Findings		
	No	PE		Physical Examinations	Findings		
	Voo	SC		Subjects Characteristics	Findings		
	Tes	VS		Vital Signs	Findings		
		СМ		Concomitant Medications	Interventions		
		EX		Exposure	Interventions		
		SU		Substance Use	Interventions		
DM			Demographics	Special-Purpose Domains			
		CO		Comments	Special-Purpose Domains		
		SUP	PQUAL	Supplemental Qualifiers	Special-Purpose Domains		
		REL	REC	Relate Records	Special-Purpose Domains		
		ОТН	R Other		Sponsor Defined Domain		
		TE		Trial Elements	Trial Design Domains		
		TA		Trial Arms	Trial Design Domains		
		TV		Trial Visits	Trial Design Domains		
		SE		Subject Elements	Trial Design Domains		
		SV		Subject Visits	Trial Design Domains		
		TI		Trial Inclusion/Exclusion Crit	Trial Design Domains		
TS			Trial Summary	Trial Design Domains			
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				OK Cancel			
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rary			Load from Library				

SDTM ready: a dialog to choose a Domain for an ItemGroup

Options	Help							
	Extra inf	ormation for: Protocol			2	3		
	?	StudyEventRef						
otocols	_	StudyEventOID SE.VISIT0 SE.VISIT1	OrderNumber	Mandatory Yes Yes	VisitDate 2005-12-12 2005-12-22	Methods Pr		
					Value is not of type date or	is an invalid date		
				1				
		Add Row Delete Selected Row						
		Sort by 0	rder Number					
		Save	to Library	Load				
	OK Cancel							

The ODM Study Designer: screenshots

Full and automatic support of Vendor Extensions: an example of a Vendor Extension allowing Visit Date Scheduling. The date 2005-12-32 is not a valid date.