

EDC integrations

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Integration Technology & Data Standards

Past, Present and Future

- Past (10 years back)
- Few sources, all on paper
- Source data copied on paper CRF
- Data entry from CRF to clinical database
- Programming creates listings for review
- Data clean and locked -> generate extracts for analysis

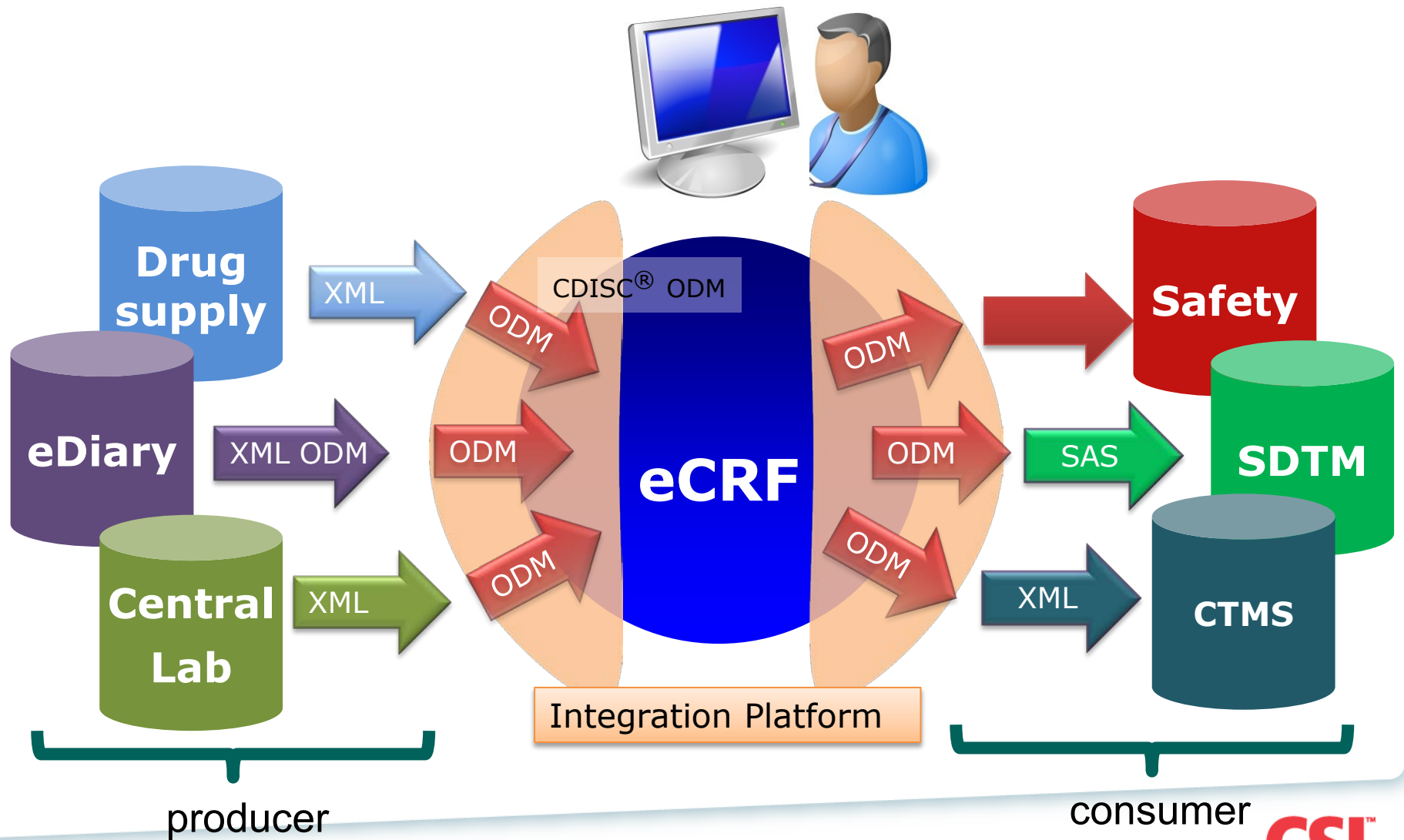
Past, Present and Future

- Multiple systems and paper as data source
 - (nightmare for sites, monitors, data management,)
 - No standard user interface
- Proprietary metadata
- Data entry by the site
- SDV and/or data reconciliation
- Review by listings and reports
- Merge data after database lock
- Lag time of data

Past, Present and Future

- Multiple systems interconnected with a standard connection technology (EDC integration)
- Single (open) interface to all data (sites, monitors, reviewers,)
- Standard (EDC) metadata
- 'real-time' data

EDC Integration Platform



Producers and Consumers

Producers

- eCOA
 - eDiary (home treatment, clinical events)
 - ePRO (Questionnaires, QoL,)
 - Home diagnostic devices interface
- Interactive Voice Technology (IRT)
- Trial Drug Supply (RTSM)
- ECG,
- Central Lab
-

Consumers

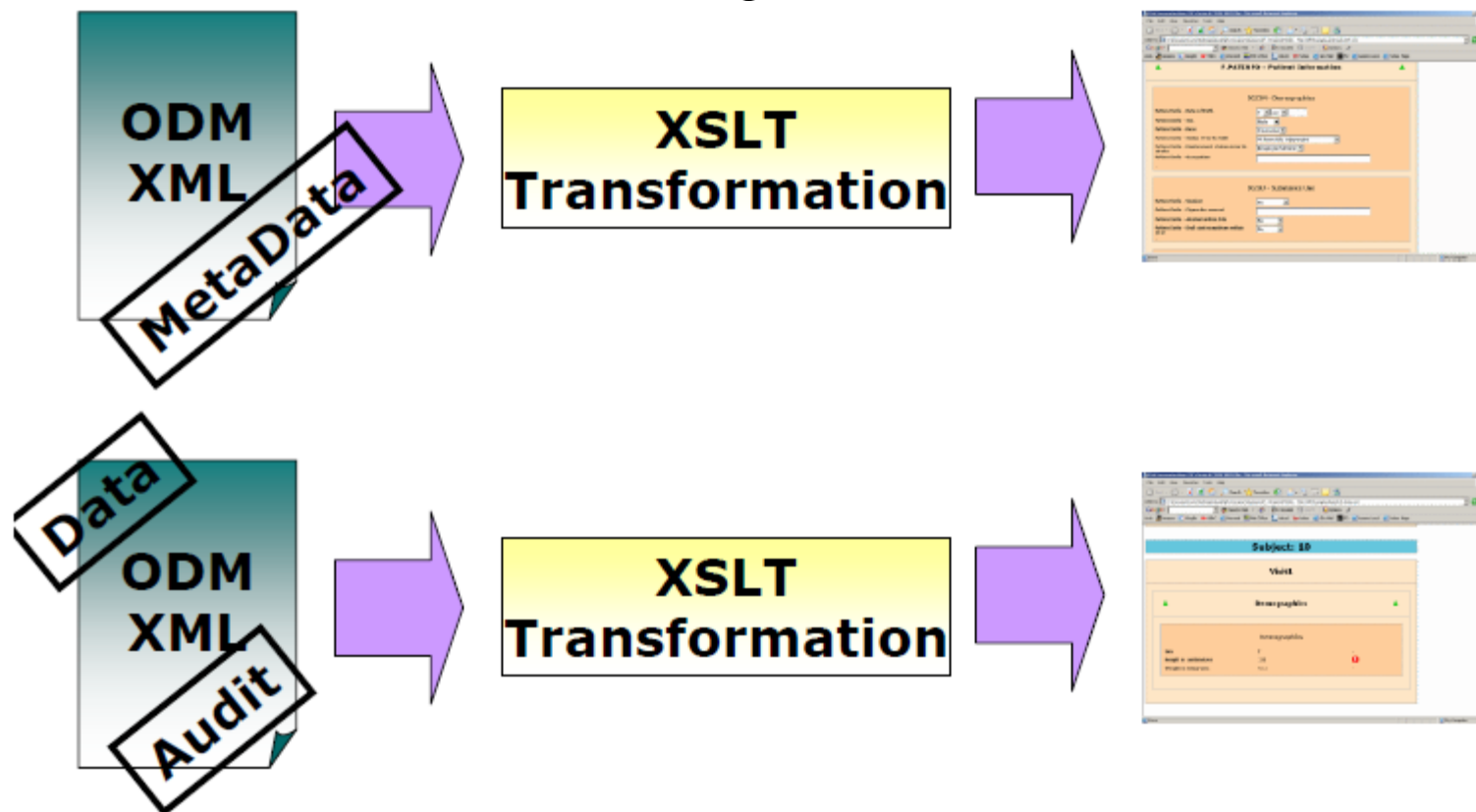
- Clinical Trial Management System (CTMS)
- Pharmacovigilance system
- Safety reviewer
- Medical monitor
- SDTM
- Statistics
- Pharmacokinetic (PK/PD)
- Study Review Boards
-

Integration Platform

- **Integration Technology (XML ODM & XSLT)**
- Data model (source -> target) transfer specification
 - (Model specification, Mapping, Transform metadata)
- Transfer technology (Webservices, file upload,)
- Frequency and Mode (time or event driven, snapshot or transactional)
- Users, Roles and authorizations
- Reconciliation and/or Validation
- Error handling and Correction
- DCF handling (data; process)
- Responsibilities (Vendor, CRO, Data Management, Integration Lead)

Integration Platform: Technology

ODM for transferring data to EDC



Introduction to the Operational Data Model (ODM)

CDISC European Italian-Speaking User Group Meeting, Milano, 16 November 2007

Dr. Philippe Verplancke, XClinical GmbH

Integration Platform: eCRF+

- Multiple views (sites, medical monitors,)
- Additional variables
 - SDTM (--CAT, --METHOD,)
 - Data validation checking
 - Compliance information
- Audit trail
- “real-time” data

Process: Frequency and Mode

- Depends on the modality and system capabilities
- Event driven -> transactional
 - When new data becomes available
 - Incremental
- Time driven
 - Every x hours/days
 - Incremental or snapshot

Process: Error handling

- Extracting errors
- Conversion errors
- Loading errors
 - System availability
 - Authentication
 - Conflicts (locked data points, inactivated data points,)
 - Changed system specs (source or target system)
- Resolve, reload and correct

Example 1: Bleeding Event (eDiary screens)

Bleeding Event

Please enter the START date and time of the bleeding event:

▲▲▲

31 Jan 2007

▼▼▼

▲▲

11 : 59

▼▼

BackNext

Bleeding Event

Please enter the END date and time of the bleeding event:

▲▲▲

31 Jan 2007

▼▼▼

▲▲

11 : 59

▼▼

☐ Tap here if the END date and time is Unknown
☐ Tap here if you are still bleeding

BackNext

Bleeding Event

Please specify the TYPE of Bleeding Event:

Spontaneous

Traumatic

Post surgery

BackNext

Bleeding Event

Please add the locations of bleeding:

Most severe bleed location: [Computed] Add

Location 2: [Computed]

Location 3: [Computed]

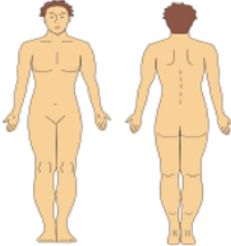
Location 4: [Computed]

Please select "Confirm" when ALL locations have been entered

BackConfirm

Bleeding Event

Please specify location of bleeding:



[Computed]

☐ Tap here if "Other"

BackNext

Bleeding Event

Assessment of TREATMENT effectiveness:

Excellent?

Good?

Moderate?

Poor/No response?

BackNext

Bleeding Event

Was there any PAIN MEDICATION taken due to the Bleeding Event?

Yes

No

BackNext

Bleeding Event

Was there any OTHER MEDICATION taken to treat the Bleeding Event?

Yes

No

BackNext

Example 1: Bleeding Event (eCRF)

Page: Bleeding Event (eDiary) - eDiary?



#	Visit Month	Start Date	Start Time	End Date	End Time	Ongoing	End time link	Nature of Bleed	Location #1	Location #2	Location #3	Location #4	Location Type #1	Location Type #2	Location Type #3	Location Type #4	Treatment Efficacy	Study Med	Pain Med	Other Med	Form Save Time
1	MAY2012	26 May 2012	16:00	26 May 2012	16:08			Spontaneous	Other				Other				Excellent	Yes	N	N	26 May 2012 16:10
2	MAY2012	31 May 2012	06:00				Y	Spontaneous	Right Foot				Joint				Good	Yes	N	N	01 Jun 2012 21:30
3	JUN2012	04 Jun 2012	13:00	04 Jun 2012	13:45			Spontaneous	Oral				Other				Excellent	Yes	N	N	04 Jun 2012 13:58
4	JUN2012	08 Jun 2012	16:30	09 Jun 2012	09:25			Traumatic	Right Hand Back				Other				Good	Yes	Y	N	09 Jun 2012 09:27
5	JUN2012	12 Jun 2012	18:10				Y	Traumatic	Left Elbow				Joint				Good	Yes	N	N	12 Jun 2012 18:30
6	JUN2012	12 Jun 2012	18:00	12 Jun 2012	18:30			Traumatic	Left Elbow				Joint				Good	Yes	N	N	13 Jun 2012 18:56

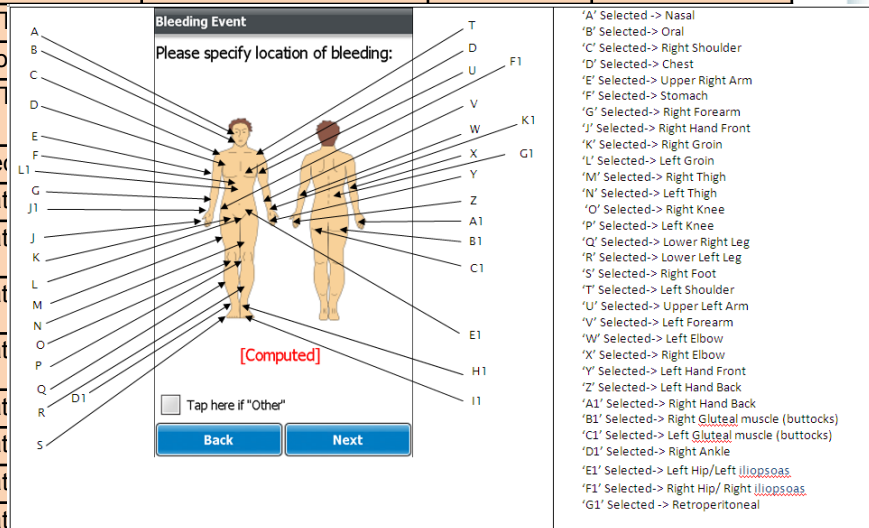
Example 1: Bleeding Event (Transfer specification)

Question/Label name	Data type (length)	Required	Format	Field Label	Field OID	Data type	Format
Visit Month	Text (7)	Yes	MMMyyyy	Visit Month	NS_VISMON	Text	\$30 (MMMMYYYY)
Bleeding Start Date	Date	Yes	dd-MMM-yyyy	Bleeding Start Date	XBSTDAT	Date	dd MMM yyyy
Bleeding Start Time	Time	Yes	HH:mm:ss	Bleeding Start Time	XBSTTIM	Time	HH:nn
Bleeding End Date	Date	No	dd-MMM-yyyy	Bleeding End Date	XBENDAT	Date	dd MMM yyyy
Bleeding End Time	Time	No	HH:mm:ss	Bleeding End Time			
Bleeding Ongoing	Integer (1)	No	#REQ-BLN-1	Bleeding Ongoing			
Bleeding End Date Time Unknown	Integer (1)	No	#REQ-BLN-1	Bleeding End Date Time Unknown			
Bleeding Type	Integer (1)	Yes	#REQ-BT-1	Nature of Bleeding			
Bleeding Type Location 1	Integer (1)	Yes	#REQ-BTL-1	Bleeding Location 1			
Bleeding Type Location 2	Integer (1)	No	#REQ-BTL-1	Bleeding Location 2			
Bleeding Type Location 3	Integer (1)	No	#REQ-BTL-1	Bleeding Location 3			
Bleeding Type Location 4	Integer (1)	No	#REQ-BTL-1	Bleeding Location 4			
Bleeding Location 1	Text (10)	No	#REQ-BL-1	Bleeding Location 1			
Bleeding Location 2	Text (10)	No	#REQ-BL-1	Bleeding Location 2			
Bleeding Location 3	Text (10)	No	#REQ-BL-1	Bleeding Location 3			
Bleeding Location 4	Text (10)	No	#REQ-BL-1	Bleeding Location 4			
Treatment Efficacy	Text (10)	No	#REQ-EFC-1	Subject Assessment of Hemostatic Efficacy	SUPPXB_XBTRTEFF	Decode Text	\$50
Study Medication Taken	Integer (1)	Yes	#REQ-BLN-1	Study Medication Taken	SUPPXB_XBTRTNY	Decode Text	\$3
Pain Medication Taken	Integer (1)	Yes	#REQ-BLN-1	Pain Medication Taken	SUPPXB_XBCMPAYN	Decode Text	\$3
Other Medication Taken	Integer (1)	Yes	#REQ-BLN-1	Other Medication Taken	SUPPXB_XBCMOTYN	Decode Text	\$3
CREATETIME				Form Save Time	XBDBC	DateTime	dd MMM yyyy hh:nn

#REQ-BT-1 Bleeding Type Code list

Value	Text
1	Spontaneous
2	Traumatic
3	Post surgery
4	Unknown

'A' Selected -> Nasal
'B' Selected-> Oral
'C' Selected-> Right Shoulder
'D' Selected-> Chest
'E' Selected-> Upper Right Arm
'F' Selected-> Stomach
'G' Selected-> Right Forearm
'H' Selected-> Right Hand Front
'I' Selected-> Right Groin
'J' Selected-> Left Groin
'K' Selected-> Right Thigh
'L' Selected-> Left Thigh
'M' Selected-> Right Knee
'N' Selected-> Left Knee
'O' Selected-> Left Knee
'P' Selected-> Lower Right Leg
'Q' Selected-> Lower Left Leg
'R' Selected-> Upper Left Arm
'S' Selected-> Upper Right Arm
'T' Selected-> Left Shoulder
'U' Selected-> Left Forearm
'V' Selected-> Left Elbow
'W' Selected-> Left Hand Front
'X' Selected-> Left Hand Back
'Y' Selected-> Left Hand Back
'Z' Selected-> Left Hand Back
'A1' Selected-> Right Gluteal muscle
'B1' Selected-> Right Gluteal muscle
'C1' Selected-> Left Gluteal muscle
'D1' Selected-> Right Ankle
'E1' Selected-> Left Hip/Left iliopectineal muscle
'F1' Selected-> Right Hip/ Right iliopectineal muscle
'G1' Selected-> Retroperitoneal



Example 2: Central Lab Form (lab report, eCRF)

Lab Report

Protocol No. IgPro20_3003	CSL Behring	PAREXEL #203735
<i>Dr. Suraj Muley (8400173)</i>	<i>United States</i>	<i>Fax : +16024066698</i>
Visit: Screening Up to two weeks		
Subject ID: 84001730002	Collection Date: 11-JUN-2013	Year of Birth: 1949
Process No: 52	Collection Time: 12:45	Gender: Male

Central Lab Form

Subject	0000001-0006									
Page: Central Laboratory Upload HEMATOLOGY - Screening										
Date of Specimen Collection	3 Sep 2012 (DD MMM YYYY)	✓ ✕ 🗑								
Time of Specimen Collection	12:02 (24 hr clock)	✓ ✕ 🗑								
Specimen Accession Number	2043740038100	✓ ✕ 🗑								
Specimen Type	Blood	✓ ✕ 🗑								
Specimen Condition		✓ ✕ 🗑								
Laboratory	Eurofins Medinet	✓ ✕ 🗑								
#	ND	Report Test Name	Result	Unit	Lower Limit	Upper Limit	Range Flag	Comment	CS/NCS	
1	☐	Basophils (%)	1	%	0	2				○ ✕ 🗑
2	☐	Basophils (Abs)	0.0	10^9/L	0.0	0.2				○ ✕ 🗑

Example 2: Central Lab Form (lab report, eCRF)

Lab Report

				Normal Ranges					Clinical Significance
Parameter	Result	Unit	H/L	Low		High	Comment		
Hematology									
Hemoglobin	1	g/dL	L	13.5	-	17.5			Yes ☐ ¹ No ☐
Hematocrit	1	%	L	40	-	52			Yes ☐ ¹ No ☐
Reticulocytes (%)	1	%		0.7	-	2.5			
Red Cell Count	1	x10E6/uL	L	4.6	-	5.8			Yes ☐ ¹ No ☐
MCV	1	fL	L	81	-	98			Yes ☐ ¹ No ☐

Central Lab Form

#	ND	Report Test Name	Result	Unit	Lower Limit	Upper Limit	Range Flag	Comment	CS/NCS	
1	☐	Basophils (%)	1	%	0	2				☒ ☐ ☐
2	☐	Basophils (Abs)	0.0	10^9/L	0.0	0.2				☒ ☐ ☐
3	☐	Eosinophils (%)	1	%	0	7				☒ ☐ ☐
4	☐	Eosinophils (Abs)	0.1	10^9/L	0.0	0.7				☒ ☐ ☐
5	☐	Hemoglobin	140	g/L	120	160				☒ ☐ ☐
6	☐	Hematocrit	0.45	L/L	0.36	0.46				☒ ☐ ☐
7	☐	Total Lymphs (%)	24	%	20	44				☒ ☐ ☐

Central Laboratory Upload BIOCHEMISTRY

Central Laboratory Upload HEMATOLOGY

Central Laboratory Upload THROMBOPHILIA

Central Laboratory Upload COAGULATION

Central Laboratory Upload VIRAL SAFETY

Central Laboratory Upload URINALYSIS

Clinically Significant

#	ND	Report Test Name	Result	Unit	Lower Limit	Upper Limit	Value	Units	Comments	Status	Action
1	☐	Basophils (%)	1	%	0	2				OK	[Icon]
2	☐	Basophils (Abs)	0.0	10 ⁹ /L	0.0	0.2				OK	[Icon]
3	☐	Eosinophils (%)	2	%	0	7				OK	[Icon]
4	☐	Eosinophils (Abs)	0.1	10 ⁹ /L	0.0	0.7				OK	[Icon]
5	☐	Hemoglobin	150	g/L	135	175				OK	[Icon]
6	☐	Hematocrit	0.51	L/L	0.40	0.52				OK	[Icon]
7	☐	Total Lymphs (%)	46	%	20	44	HN		Entry Error	Warning	[Icon]
8	☐	Total Lymphs (Abs)	1.9	10 ⁹ /L	1.0	4.0				OK	[Icon]
9	☐	Monocytes (%)	7	%	3	10				OK	[Icon]
10	☐	Monocytes (Abs)	0.3	10 ⁹ /L	0.1	0.9				OK	[Icon]

Example 2: Central Lab Form (multiple views)

Clinical Research Coordinator (view)

#	ND	Report Test Name	Result	Unit	Lower Limit	Upper Limit	Range Flag	Comment	CS/NCS	
1	☐	Basophils (%)	1	%	0	2				  
2	☐	Basophils (Abs)	0.0	10 ⁹ /L	0.0	0.2				  
3	☐	Eosinophils (%)	1	%	0	7				  
4	☐	Eosinophils (Abs)	0.1	10 ⁹ /L	0.0	0.7				  
5	☐	Hemoglobin	140	g/L	120	160				  
6	☐	Hematocrit	0.45	L/L	0.36	0.46				  
7	☐	Total Lymphs (%)	24	%	20	44				  

Data Manager (view)

#	ND	Parameter Code	Report Test Name	Parameter Name	Result	Unit	Lower Limit	Upper Limit	Range Flag	Comment	CS/NCS	Char. Result (Std.Units)	Num. Result (Std.Units)	Standard Units	Lower Limit (Std.Units)	Upper Limit (Std.Units)	Reason Test Not Done	Completion Status
1	☐	BASOLE	Basophils (%)	Basophils/Leukocytes	1	%	0	2				1	1	%	0	2		
2	☐	BASO	Basophils (Abs)	Basophils	0.0	10 ⁹ /L	0.0	0.2				0.0	0.0	10 ⁹ /L	0.0	0.2		
3	☐	EOSLE	Eosinophils (%)	Eosinophils/Leukocytes	1	%	0	7				1	1	%	0	7		
4	☐	EOS	Eosinophils (Abs)	Eosinophils	0.1	10 ⁹ /L	0.0	0.7				0.1	0.1	10 ⁹ /L	0.0	0.7		
5	☐	HGB	Hemoglobin	Hemoglobin	140	g/L	120	160				140	140	g/L	120	160		
6	☐	HCT	Hematocrit	Hematocrit	0.45	L/L	0.36	0.46				0.45	0.45	L/L	0.36	0.46		
7	☐	LYMLE	Total Lymphs (%)	Lymphocytes/Leukocytes	24	%	20	44				24	24	%	20	44		
8	☐	LYM	Total Lymphs (Abs)	Lymphocytes	1.9	10 ⁹ /L	1.0	4.0				1.9	1.9	10 ⁹ /L	1.0	4.0		

EDC Integration: Benefits

- All data in a central location
 - Eliminates the need to log in to multiple systems
 - Eliminating redundant data capture
 - Central audit trail of activity
 - Simplified data management, review, monitoring
 - Less (critical) programming
- “real-time” access to various forms of clinical data
 - Interactions between datapoints possible
 - Improvement of data quality and reliability
- Uniform technology for all integrations
 - Less dependent on vendor/system
 - Simplified documentation

EDC Integration: Drawbacks

- eCRF Study development is more complex
 - Additional documentation
 - Study setup involves multiple systems/vendors
 - Multiple teams and multiple timelines
- Negative experience/attitude to new roles (consumers)
- Error handling is new and is more complicated because of multiple systems involvement

EDC integration: To do list

- Improvement of integration platform
 - 'real-time' data of all sources
 - Error handling
 - Developing of tools (reports, consistency checks)
- Training of producers/consumers
 - Investigator as EDC user (producer and consumer)
 - Coders, medical reviewers, safety reviewers, data reviewers, statisticians, use EDC
 - The term „source“ need to be redefined