

EDC as Central Data Repository

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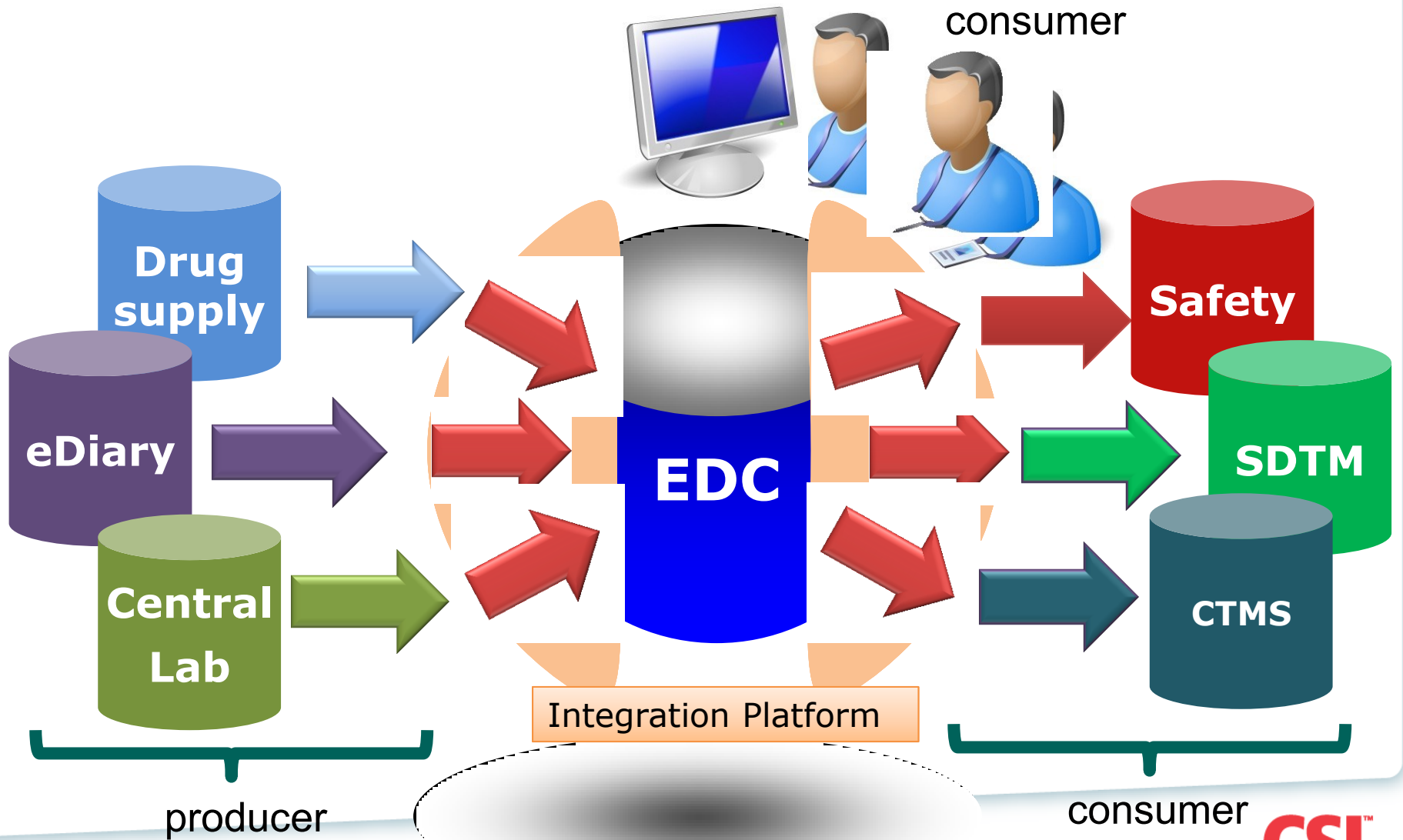
Integration Technology & Data Standards

EDC as Central Data Repository

- We have already:
 - Clinical Database or EDC
 - Single (proprietary) interface to data in single system
 - CDISC[®]

- We have not yet:
 - Connection to other 'electronic' source data
 - Single (open) interface to all data (sites, monitors, reviewers,...)
 - 'real-time' data
 - Standard metadata

EDC as Central Data Repository



What kind of producers/consumers?

- eDiary
 - Diary (home treatment, clinical events)
 - ePRO (Questionnaires, QoL,...)
 - Home diagnostic devices interface
- Interactive Voice/Web Response (IVR/IWR)
- Drug supply (RTSM)
- ECG, ...
- Central Lab
- ...
- Clinical Trial Management System (CTMS)
- Safety (reviewer, system)
- Medical monitor
- SDTM
- Statistics
- Pharmacokinetic (PK)
- Study Review Boards
- ...

Back to the 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



Back to the future (current)

- Multiple systems as data source
- Proprietary data structure
- No standard interface technology
- Data entry by the site
- Merge data after lock
- Review by listings and/or browsing in the database
- Nightmare for monitors
 - Multiple systems/paper sources

Back to the future (future)

- Multiple systems interconnected with a standard connection technology
- Cloud based, vendor independent, open user interface
- Standard metadata
- Common metadata repository



First steps towards the future

- Standard Metadata (CDASH/SDTM/...)
- Integration Platform
 - Standard interface language XML
 - CDISC[®] ODM
 - Standard Metadata conversion tool (XSLT)
- EDC as Central Data Repository
 - Single interface to data

Standard Metadata

- CDISC® CDASH/SDTM
- Standard eCRF forms
 - General medical
 - Therapeutic area (indication) specific
 - Commonly used
- Common terminology
- Standardised metadata

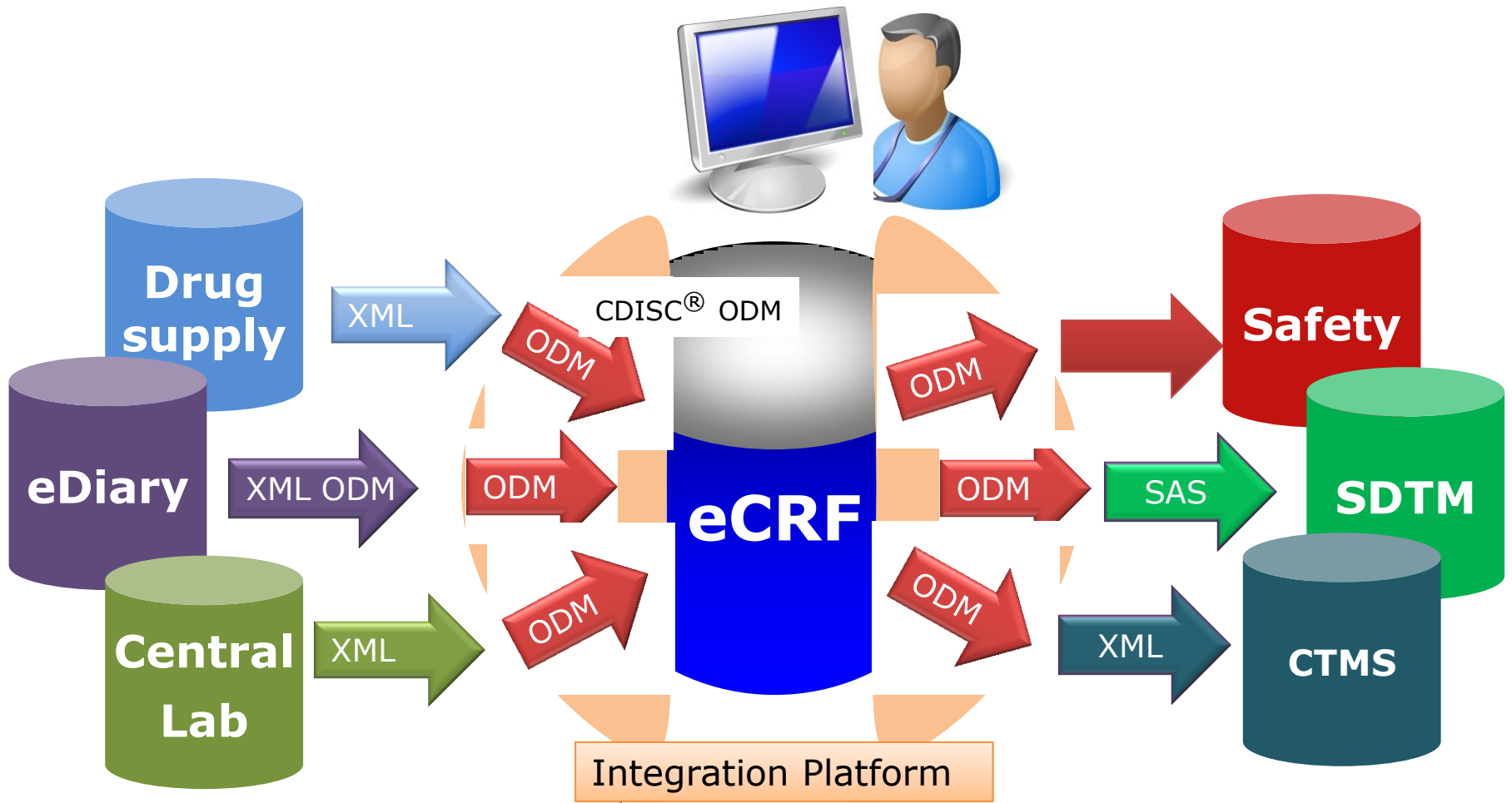
Standard Metadata: Benefits

- No multiple interpretations
- High re-usability
 - Design elements
 - Tools (reports,...)
- Less study specific training
- Straightforward SDTM mapping

Standard Metadata: Drawbacks

- Training of standards necessary
- CDISC standards
 - Multiple interpretable
 - Not always consistent
 - In continuous development
- Loss of necessary flexibility
- Study specific items are more labor intensive

Integration Platform



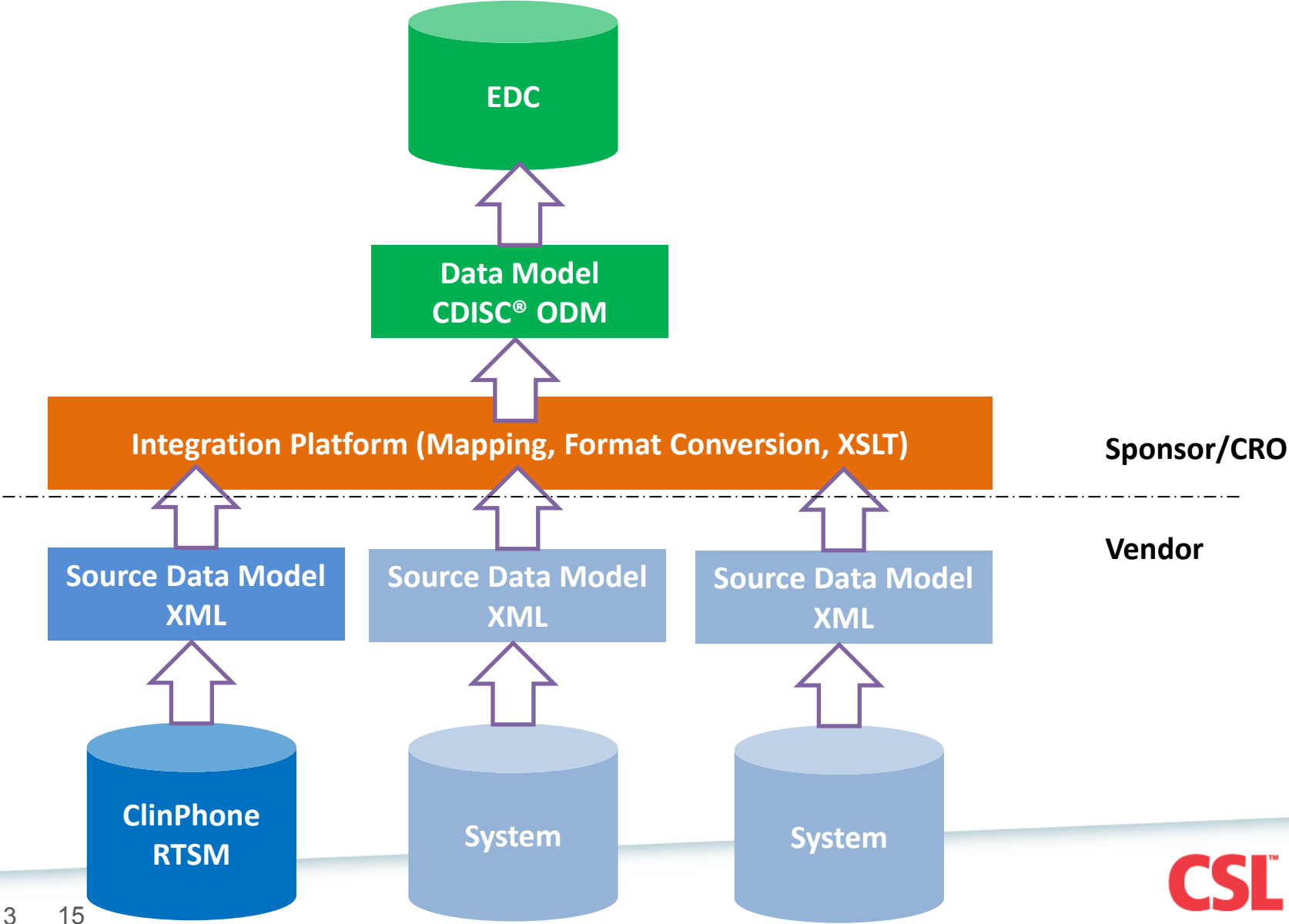
Integration Platform

- Integration Technology (XML ODM & XSLT)
- Type of integration and frequency (Cumulative, Incremental, Snapshot, Transactional)
- Users, Roles and authorizations
- Blinded / Unblinded
- Validation / Verification
- DCF handling (data; process)
- Error handling

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 (full, incremental, snapshot, transactional, ...)
- Users, Roles and authorizations
- Reconciliation and/or Validation
- Error handling and Correction
- DCF handling (data; process)
- Responsibilities (Vendor, CRO, DM, Integration Lead)

Integration Platform: Responsibilities



Example – Bleeding Event

Bleeding Event

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

▲ ▲ ▲
31 Jan 2007

▼ ▼ ▼

▲ ▲
11 : 59

▼ ▼

Back Next

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

Back Next

Bleeding Event

Please specify the TYPE of Bleeding Event:

Spontaneous

Traumatic

Post surgery

Back Next

Bleeding Event

Please add the locations of bleeding:

Most severe bleed location: [Computed] Add

Location 2: [Computed]

Location 3: [Computed]

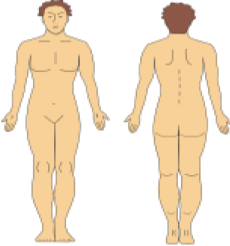
Location 4: [Computed]

Please select "Confirm" when ALL locations have been entered

Back Confirm

Bleeding Event

Please specify location of bleeding:



[Computed]

Tap here if "Other"

Back Next

Bleeding Event

Assessment of TREATMENT effectiveness:

Excellent ?

Good ?

Moderate ?

Poor/No response ?

Back Next

Bleeding Event

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

Yes

No

Back Next

Bleeding Event

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

Yes

No

Back Next

Bleeding Event

You have completed the bleeding event diary. To confirm, tap on "Confirm". To change information below, tap on "Back".

Start of bleed:

Type of bleed:

Bleed location 1:

Bleed location 2:

Bleed location 3:

Bleed location 4:

Study Medication:

Pain Medication:

Other Medication:

Back Confirm

Example – eCRF Bleeding Event

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: 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 (MMMYYYY)
Bleeding Start Date	Date	Yes	dd- <u>MMM</u> - 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- <u>MMM</u> - 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	Integer (1)	No	#REQ-BL-1	Bleeding Location 1			
Bleeding Location 2	Integer (1)	No	#REQ-BL-1	Bleeding Location 2			
Bleeding Location 3	Integer (1)	No	#REQ-BL-1	Bleeding Location 3			
Bleeding Location 4	Integer (1)	No	#REQ-BL-1	Bleeding Location 4			
Treatment Efficacy	Integer (1)	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	XBDMTC	DateTime	dd MMM yyyy hh:nn

#REQ-BT-1 Bleeding Type Code list

Value	Text
1	Spontaneous
2	Traumatic
3	Post surgery
4	Unknown

Bleeding Event
Please specify location of bleeding:

[Computed]

Tap here if "Other"

Back Next

- '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
- 'J' Selected -> Right Hand Front
- 'K' Selected -> Right Groin
- 'L' Selected -> Left Groin
- 'M' Selected -> Right Thigh
- 'N' Selected -> Left Thigh
- 'O' Selected -> Right Knee
- 'P' Selected -> Left Knee
- 'Q' Selected -> Lower Right Leg
- 'R' Selected -> Lower Left Leg
- 'S' Selected -> Right Foot
- 'T' Selected -> Left Shoulder
- 'U' Selected -> Upper Left Arm
- 'V' Selected -> Left Forearm
- 'W' Selected -> Left Elbow
- 'X' Selected -> Right Elbow
- 'Y' Selected -> Left Hand Front
- 'Z' Selected -> Left Hand Back
- 'A1' Selected -> Right Hand Back
- 'B1' Selected -> Right Gluteal muscle (buttocks)
- 'C1' Selected -> Left Gluteal muscle (buttocks)
- 'D1' Selected -> Right Ankle
- 'E1' Selected -> Left Hip/Left [Upper leg](#)
- 'F1' Selected -> Right Hip/ Right [Upper leg](#)
- 'G1' Selected -> Retroperitoneal



Example: Central Lab Upload Form

CRDSScratch | CSL Lab Loader Test | 00000001-0005 | Screening

Subject: 0000001-0005
Page: Central Laboratory Upload HEMATOLOGY - Screening

Date of Specimen Collection
Time of Specimen Collection
Specimen Accession Number
Specimen Type
Specimen Condition
Laboratory

#	ND	Report Test Name	Result	Unit	Lower Limit	Upper Limit	Upp			
1	<input type="checkbox"/>	Basophils (%)	1	%	0	2				
2	<input type="checkbox"/>	Basophils (Abs)	0.0	10 ⁹ /L	0.0	0.2				
3	<input type="checkbox"/>	Eosinophils (%)	2	%	0	7				
4	<input type="checkbox"/>	Eosinophils (Abs)	0.1	10 ⁹ /L	0.0	0.7				
5	<input type="checkbox"/>	Hemoglobin	150	g/L	135	175				
6	<input type="checkbox"/>	Hematocrit	0.51	L/L	0.40	0.52				
7	<input type="checkbox"/>	Total Lymphs (%)	46	%	20	44	HN		Entry Error	
<p>Clinically Significant ? Value is outside of range. Specify the clinical significance. Opened To Site from System (08 Nov 2012)</p>										
8	<input type="checkbox"/>	Total Lymphs (Abs)	1.9	10 ⁹ /L	1.0	4.0				
9	<input type="checkbox"/>	Monocytes (%)	7	%	3	10				
10	<input type="checkbox"/>	Monocytes (Abs)	0.3	10 ⁹ /L	0.1	0.9				

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

Projected administrative date
 22 Aug 2012 (DD MMM YYYY)
 12:00 (24 hr clock)
 204374 0018 100
 Blood
 Eurofins Medinet

Example: Central Lab Upload Form

Lab Report

Protocol No. CSLCT-HDL-10-70	CSL	PAREXEL #203857
<i>Mr. Test Contact EWA (9970097)</i>	<i>Neverland_NA</i>	<i>Fax : -979680</i>
Visit: Day 1 BEFORE dosing		
Subject ID: 99700970002	Process No: 9995	Fasting: Yes
Collection Date: 08-JAN-2012	Year of Birth: 1950	Weight: 90 Kg
Collection Time: 09:00	Gender: Male	

Central Lab Form

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

Example: Central Lab Upload Form

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 <input type="checkbox"/> No <input type="checkbox"/>
Hematocrit	1	%	L	40	- 52		Yes <input type="checkbox"/> No <input type="checkbox"/>
Reticulocytes (%)	1	%		0.7	- 2.5		
Red Cell Count	1	x10E6/uL	L	4.6	- 5.8		Yes <input type="checkbox"/> No <input type="checkbox"/>
MCV	1	fL	L	81	- 98		Yes <input type="checkbox"/> No <input type="checkbox"/>

Central Lab Form

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

Example: Central Lab Upload Form

Clinical Research Coordinator (view)

#	ND	Report Test Name	Result	Unit	Lower Limit	Upper Limit	Range Flag	Comment	CS/NCS	
1	<input type="checkbox"/>	Basophils (%)	1	%	0	2				  
2	<input type="checkbox"/>	Basophils (Abs)	0.0	10^9/L	0.0	0.2				  
3	<input type="checkbox"/>	Eosinophils (%)	1	%	0	7				  
4	<input type="checkbox"/>	Eosinophils (Abs)	0.1	10^9/L	0.0	0.7				  
5	<input type="checkbox"/>	Hemoglobin	140	g/L	120	160				  
6	<input type="checkbox"/>	Hematocrit	0.45	L/L	0.36	0.46				  
7	<input type="checkbox"/>	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	<input type="checkbox"/>	BASOLE	Basophils (%)	Basophils/Leukocytes	1	%	0	2				1	1	%	0	2		
2	<input type="checkbox"/>	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	<input type="checkbox"/>	EOSLE	Eosinophils (%)	Eosinophils/Leukocytes	1	%	0	7				1	1	%	0	7		
4	<input type="checkbox"/>	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	<input type="checkbox"/>	HGB	Hemoglobin	Hemoglobin	140	g/L	120	160				140	140	g/L	120	160		
6	<input type="checkbox"/>	HCT	Hematocrit	Hematocrit	0.45	L/L	0.36	0.46				0.45	0.45	L/L	0.36	0.46		
7	<input type="checkbox"/>	LYMLE	Total Lymphs (%)	Lymphocytes/Leukocytes	24	%	20	44				24	24	%	20	44		
8	<input type="checkbox"/>	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		

Example: Lab specification, analytes

Laboratory				LoMas		
Lab name		ResultID	Parameter	BaseBatteryName	TestCode	TestName
Eurofins	Chemistry		AST	Biochemistry	AST	AST
Eurofins	Chemistry		ALT	Biochemistry	ALT	ALT
Eurofins	Chemistry		Calcium	Biochemistry	CA	Calcium
Eurofins	Chemistry		CK	Biochemistry	CPK	CK
Eurofins	Chemistry		CK MB (electroph)	Biochemistry	CKMB	CK-MB
Eurofins	Chemistry		CK BB (electroph)	Biochemistry	CKBB	CK-BB
Eurofins	Chemistry		Creatinine	Biochemistry	CREA	Creatinine
Eurofins	Chemistry		C-Reactive Protein	Biochemistry	CRP	C-reactive Protein
Eurofins	Chemistry		Glucose	Biochemistry	GLU	Glucose
Eurofins	Chemistry		Potassium	Biochemistry	POT	Potassium
Eurofins	Chemistry		Sodium	Biochemistry	SOD	Sodium
Eurofins	Immunochemistry		Tropinin T hs	Biochemistry	ITROT	Troponin T
Eurofins	Chemistry		BUN (Urea)	Biochemistry	BUN	BUN (Urea)
Eurofins	Hematology		Hemoglobin	Hematology	HB	Hemoglobin
Eurofins	Hematology		Hematocrit	Hematology	HCT	Hematocrit

eCRF			SDTM		
LBCAT	LBTESTCD	LBTEST	LBCAT	LBTESTCD	LBTEST
	AST	Aspartate Aminotransferase (AST)	BIOCHEMISTRY	AST	Aspartate Aminotransferase
	ALT	Alanine Aminotransferase (ALT)	BIOCHEMISTRY	ALT	Alanine Aminotransferase
	CA	Calcium	BIOCHEMISTRY	CA	Calcium
	CK	Creatine Kinase	BIOCHEMISTRY	CK	Creatine Kinase
	CKMB	Creatine Kinase (Muscle)	BIOCHEMISTRY	CKMB	Creatine Kinase MB
	CKBB	Creatine Kinase (Brain)	BIOCHEMISTRY	CKBB	Creatine Kinase BB
	CREAT	Creatinine	BIOCHEMISTRY	CREAT	Creatinine
	CRP	C-reactive Protein	BIOCHEMISTRY	CRP	C Reactive Protein
	GLUC	Glucose	BIOCHEMISTRY	GLUC	Glucose
	K	Potassium	BIOCHEMISTRY	K	Potassium
	SODIUM	Sodium	BIOCHEMISTRY	SODIUM	Sodium
	PH	pH	BIOCHEMISTRY	PH	pH
	TROPONT	Troponin T	BIOCHEMISTRY	TROPONT	Troponin T

Integration Platform: Benefits

- All data in a central location
 - Simplified data management, review, monitoring
- All data “real time” available in EDC
- Interactions between datapoints possible
- Clear responsibility between vendor and EDC-developer
- Same technology for all integrations
 - Less dependent on vendor/system
 - Simplified documentation
 - UAT Testing is less complex

Integration Platform: 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
- Bug fixing is more complicated because of multiple systems involvement

Integration Platform: Future directions

- All interfaces in CDISC ODM format
- Standardized XSLT
- Error notification to “Integrations Lead”
- Single study setup team for all “data” systems
- Consistent use of originator of data in EDC
 - Distinguish between data to be entered and to be loaded
 - Patient related outcome data cannot be queried
- Integrate DCFs in EDC

EDC as Central Data Repository: Summary

- Awareness of importance of the integration platform
 - 'real-time' data of all sources
 - The term „source“ need to be redefined
- Develop tools (reports, consistency checks...)
- Training of producers/consumers is essential
 - Investigator as EDC user (producer and consumer)
 - Coders, medical reviewers, safety reviewers, data reviewers, statisticians, ... use EDC
- Less (critical) programming
- Standards are a prerequisite

EDC as Central Data Repository: Discussion

- Is EDC capable?
- Are we capable?
- or ...