Clinical study oversight: different approaches and starter pack

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AGENDA

- *Introduction*
- *Outsourcing and Oversight models*
- *Starter Pack*
- *Questions*

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Common concerns when outsourcing

- ? Is my CRO collecting the right data?
- ? Will my data be fit for a regulatory submission?
- ? My CRO delivers CDISC, so I guess that's good enough?
- ? Will I be able to compare data between different trials?
- ? Am I giving the right information to the CRO?
- ? How do I check the CRO deliverables?
- ? I am keeping my study data on my server, I guess that's ok?

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- *Outsourcing and Oversight models*
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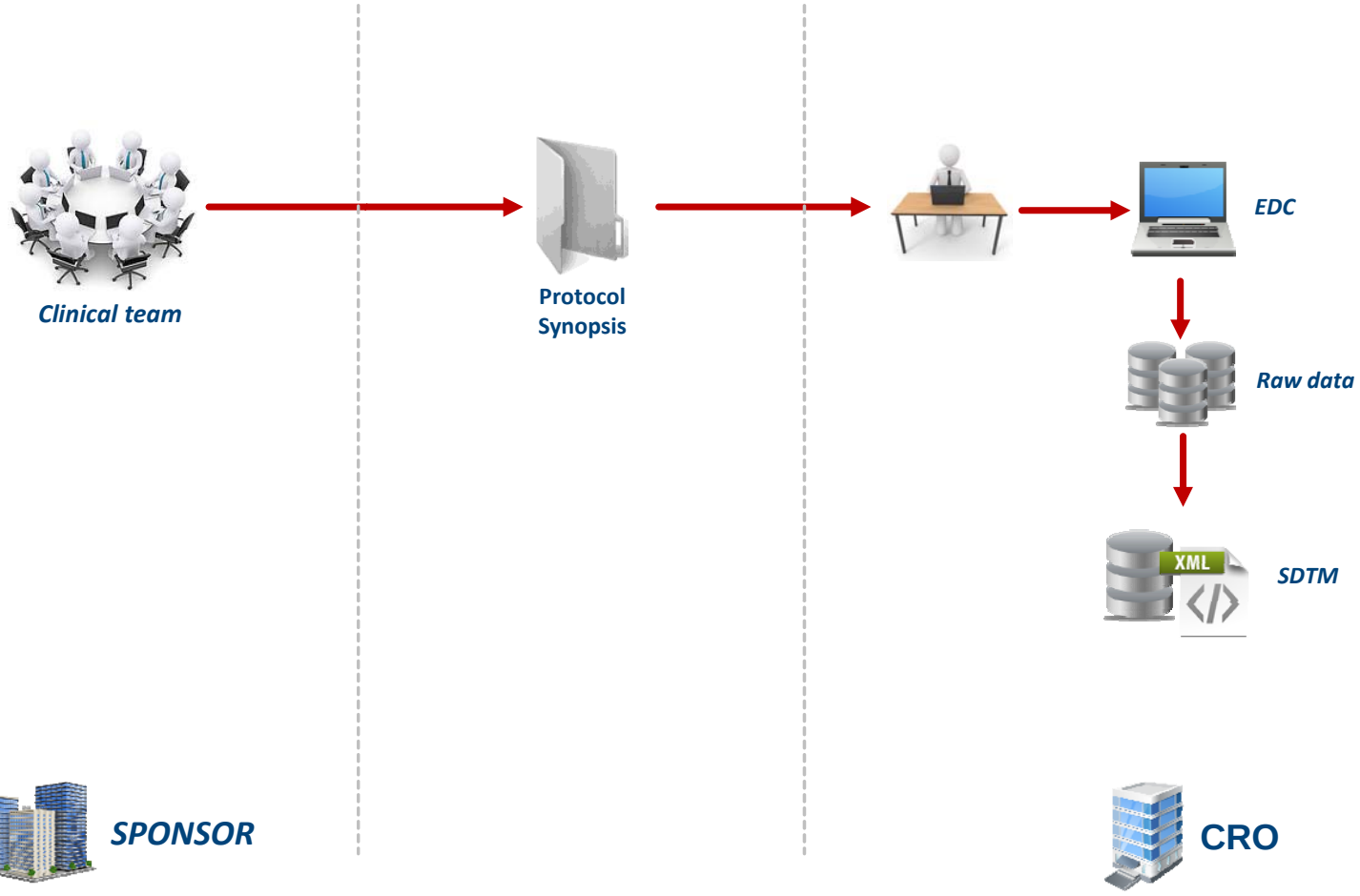
Outsourcing Model I: Let the CRO decide



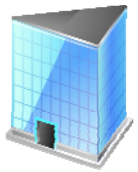
What will you get back?

CRO A

STUDYID	DOMAIN	USUBJID	SUBJID	RFSTDTC	…	SITEID
ABC	DM	ABC-CAN1-001	001	2017-04-09		CAN1

RFSTDTC = date of informed consent

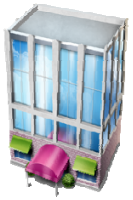
CRO B



STUDYID	DOMAIN	USUBJID	SUBJID	RFSTDTC	…	SITEID
DEF	DM	DEFCAN1001	001	2017-04-12		CAN1

RFSTDTC = date of first visit

CRO C



STUDYID	DOMAIN	USUBJID	SUBJID	RFSTDTC	…	SITEID
GHI	DM	GHI-CAN1-01001	01001	2017-04-15		CAN1

RFSTDTC = date of first dosing

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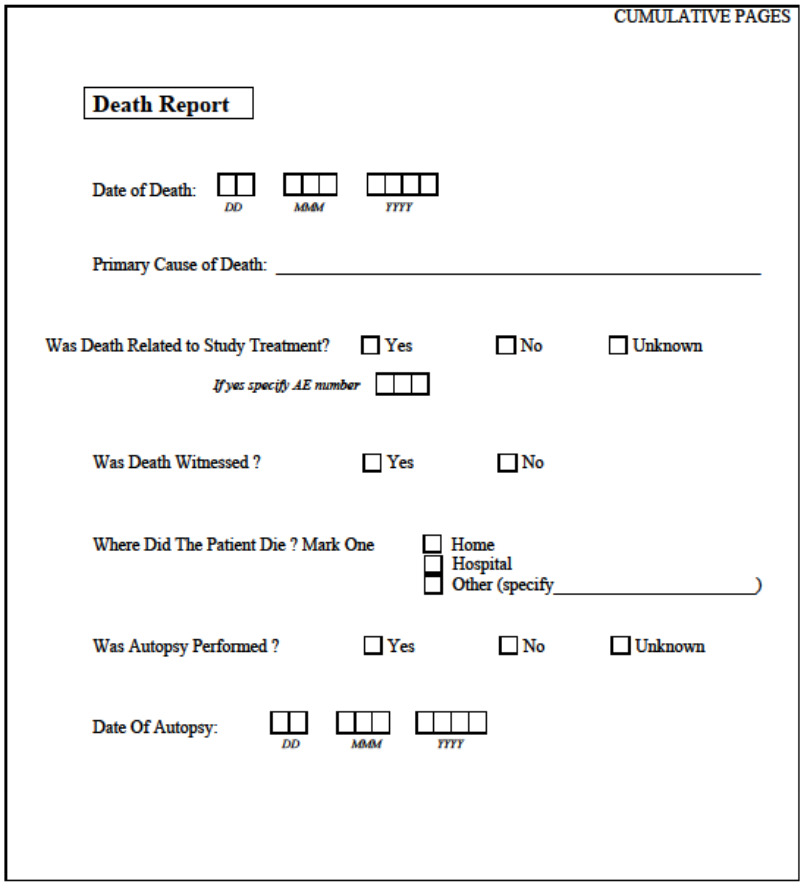
When it gets more complex



CUMULATIVE PAGES

Death Report

Date of Death: ☐☐ (DD) ☐☐☐ (MMM) ☐☐☐☐ (YYYY)

Primary Cause of Death: _____

Was Death Related to Study Treatment? ☐ Yes ☐ No ☐ Unknown

If yes specify AE number ☐☐☐

Was Death Witnessed ? ☐ Yes ☐ No

Where Did The Patient Die ? Mark One
☐ Home
☐ Hospital
☐ Other (specify_____)

Was Autopsy Performed ? ☐ Yes ☐ No ☐ Unknown

Date Of Autopsy: ☐☐ (DD) ☐☐☐ (MMM) ☐☐☐☐ (YYYY)

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When it gets more complex

[DS]
[SUPPDS]

CUMULATIVE PAGES

Death Report — DSCAT = "DISPOSITION EVENT

Date of Death: DD MMM YYYY — DSSTDTC

Primary Cause of Death: — DSDECOD = "DEATH"

DTHRELST in SUPPDS

Was Death Related to Study Treatment? Yes No Unknown

If yes specify AE number — Linked via RELREC

Was Death Witnessed ? Yes No

DTHWIT in SUPPDS

Where Did The Patient Die ? Mark One — Home / Hospital / Other (specify)

LOCDTH in SUPPDS

Was Autopsy Performed ? Yes No Unknown

AUTOPSY in SUPPDS

Date Of Autopsy: DD MMM YYYY

AUTOPDTC in SUPPDS

CRO A

[DS]
[FU]

CUMULATIVE PAGES

Death Report — DSCAT = "DISPOSITION EVENT

Date of Death: DD MMM YYYY — DSSTDTC

Primary Cause of Death: — DSDECOD = "DEATH"

Was Death Related to Study Treatment? Yes No Unknown

DTHRELST — If yes specify AE number — Linked via RELREC

Was Death Witnessed ? Yes No

DTHWIT

Where Did The Patient Die ? Mark One — Home / Hospital / Other (specify)

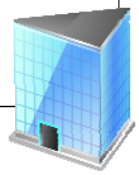
LOCDTH

Was Autopsy Performed ? Yes No Unknown

AUTOPSY

Date Of Autopsy: DD MMM YYYY — FUDTC

FUORRES where FUTESTCD =



CRO B

[DD]
[PR]

CUMULATIVE PAGES

Death Report

Date of Death: DD MMM YYYY — DDDTC

Primary Cause of Death: — "PRCDTH"

Was Death Related to Study Treatment? Yes No Unknown

If yes specify AE number — Linked via RELREC

Was Death Witnessed ? Yes No

"DTHWIT"

Where Did The Patient Die ? Mark One — Home / Hospital / Other (specify)

"LOCDTH"

Was Autopsy Performed ? Yes No Unknown

PRTRT = "AUTOPSY" — [Not Submitted]

Date Of Autopsy: DD MMM YYYY — PRSTDTC

DDORRES where DDTESTCD =

CRO C

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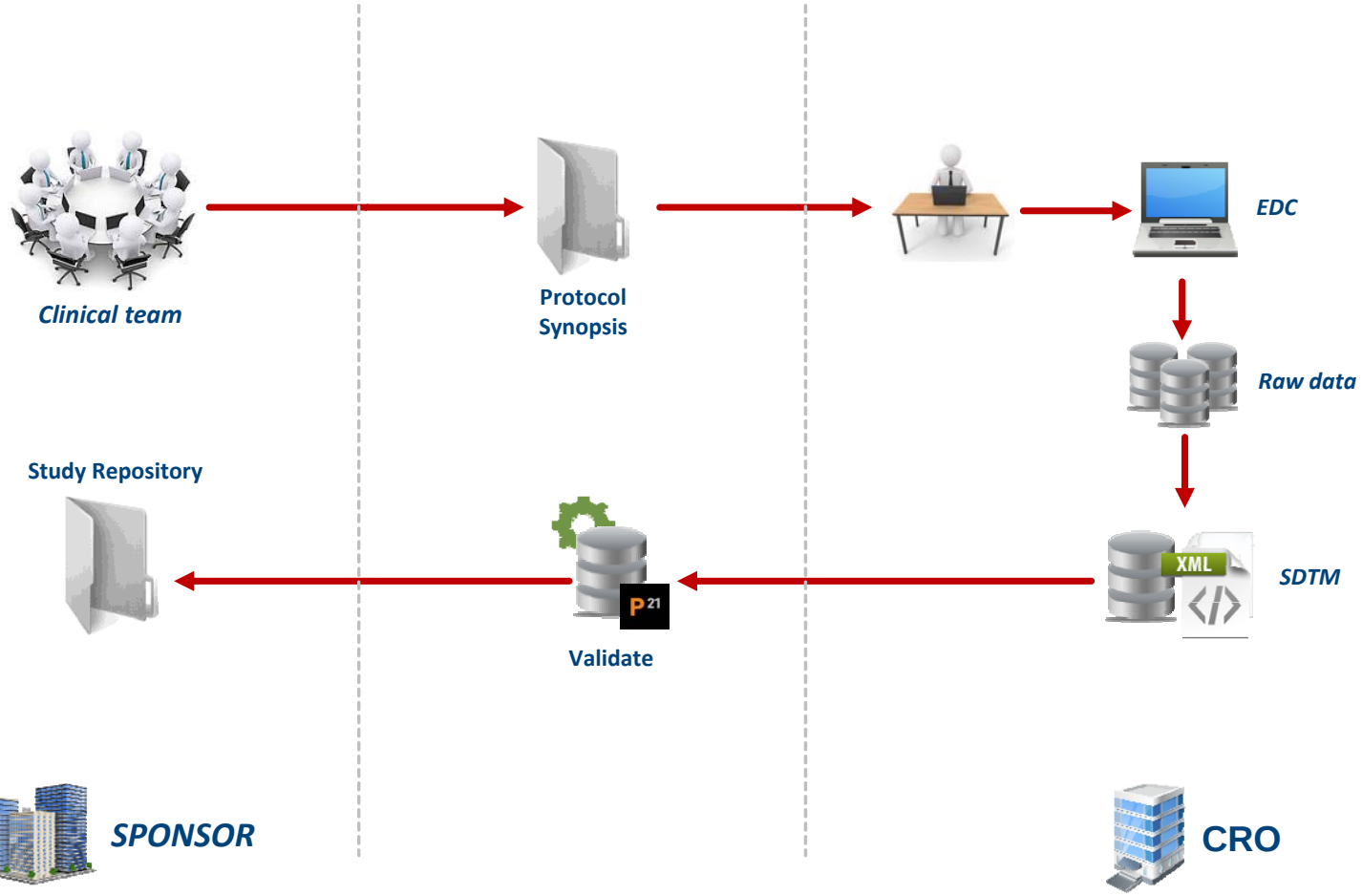
Oversight and Quality Control



Outsourcing Model I: **Let the CRO decide**

ADVANTAGES of this model

- Minimal investment from sponsor company
- Quick initiation of study set-up activities after final protocol

DISADVANTAGES of this model

- Minimal control by sponsor
- Quality Control is re-active
- Across trial variation unavoidable ➔ *Data will be difficult to pool or re-use*
- No consistency of submission package ➔ *Costly conversion required*

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When does this model work?

- ✓ Select 1 CRO and remain with this CRO throughout development program
- ✓ Define some conventions, such as formats of USUBJID, reference dates,…
- ✓ Sell your assets before planning a submission

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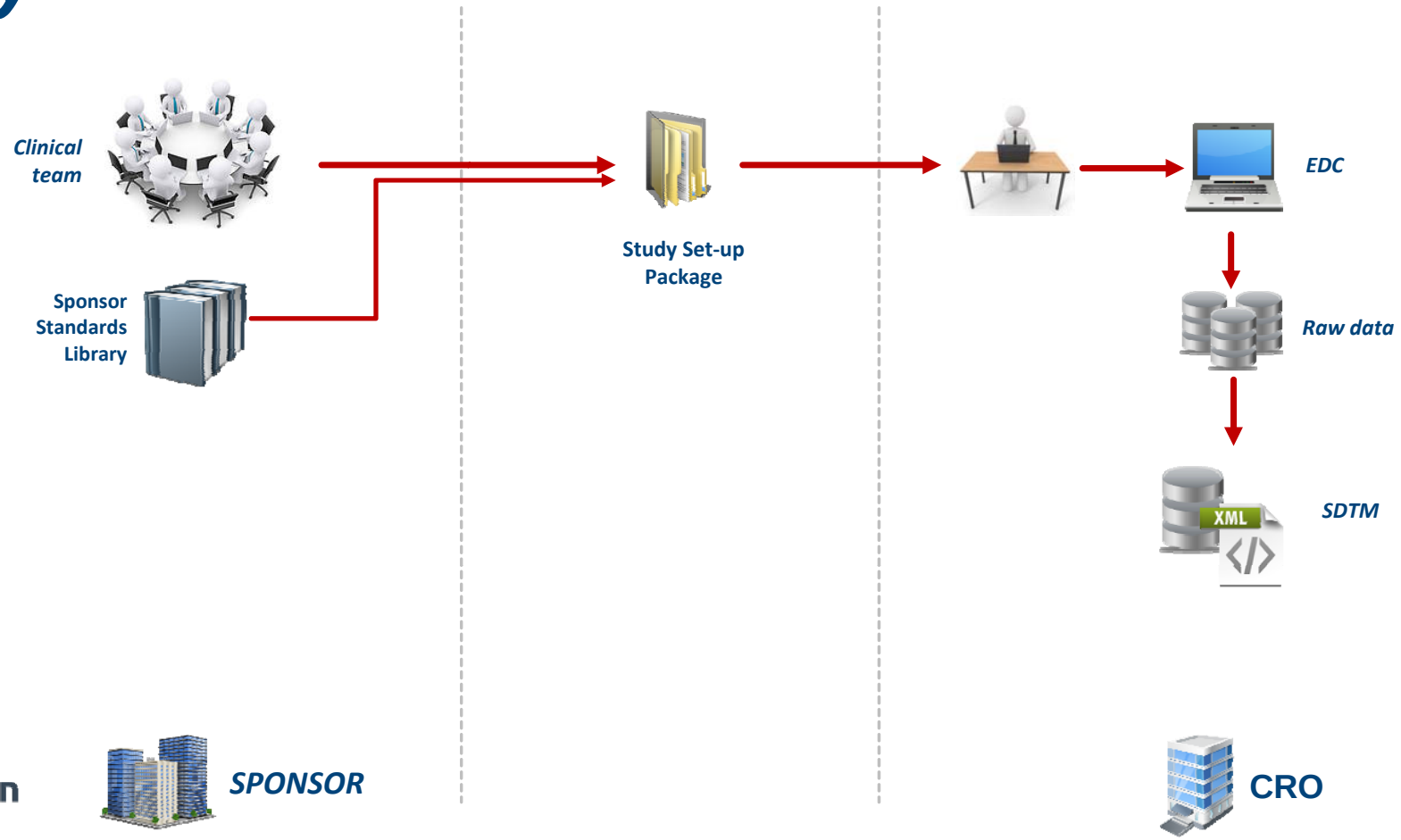
Outsourcing Model II: With Standards Library



Example Standards Library

AE		ADVERSE EVENTS	DCM ID: AE_GL_001	
STUDYID	STUDYID	Study	[Free text]	[Preprinted]
SITEID	SITEID	Site	[Free text]	[Preprinted]
SUBJID	SUBJID	Subject	[Free text]	[Preprinted]
Adverse Events				
[Not Submitted]	AEYN	Were any adverse events experienced?	[Radiobutton {Yes; No}]	NY
AESPID	AESPID	AE number	[Numeric field]	[Preprinted]
AETERM	AETERM	What is the adverse event term?	[Free text]	
AESTDTC	AESTDAT	Start Date	[Date {DD-MMM-YYYY}]	
	AESTTIM	Start Time	[24 hr clock]	
AEENDTC	AEENDAT	End Date	[Date {DD-MMM-YYYY}]	
	AEENTIM	End Time	[24 hr clock]	
If Yes, AEENRTPT = ONGOING	AEONGO	Is the adverse event still ongoing?	[Radiobutton {Yes; No}]	NY
AESEV	AESEV	Severity	[Radiobutton {Mild; Moderate; Severe}]	AESEV
AESER	AESER	Is the adverse event serious?	[Radiobutton {Yes; No}]	NY
		If Yes:		
AEREFID	AEREFID	SAE Number	[Free text]	
AESCONG	AESCONG	Congenital Anomaly	[Radiobutton {Yes; No}]	NY
AESDISAB	AESDISAB	Significant Disability	[Radiobutton {Yes; No}]	NY
AESDTH	AESDTH	Death	[Radiobutton {Yes; No}]	NY
AESHOSP	AESHOSP	Hospitalization	[Radiobutton {Yes; No}]	NY
AESLIFE	AESLIFE	Life Threatening	[Radiobutton {Yes; No}]	NY
AESMIE	AESMIE	Other Medically Important Event	[Radiobutton {Yes; No}]	NY
AEREL	AEREL	Relationship to Study Treatment	[Radiobutton {Not related; Unlikely Related; Possibly Related; Probably Related}]	REL
AEACN	AEACN	Action taken with Study Treatment	[Radiobutton {Dose Not Changed; Drug Withdrawn; Dose Reduced}]	ACN

SDTM CDASH CRF questions eDC build instructions Controlled terminology

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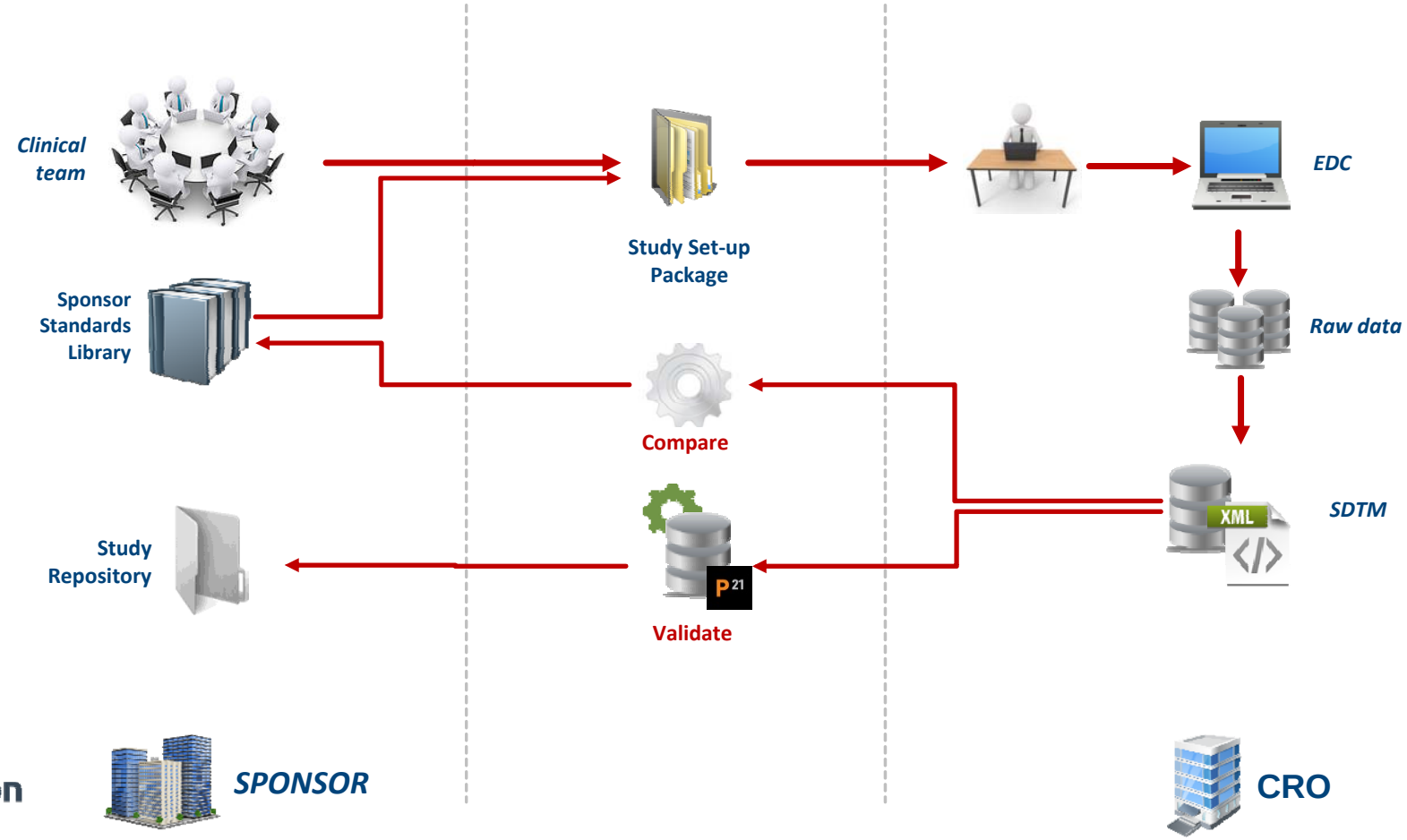
Provide Expectations

- *Set-up package*
  - Protocol
  - CRO guides for using Standards Library & standards governance
  - Sponsor Standards Library
    - Standard Data Collection Modules
    - CDISC SDTM Library
    - Data Standards Conventions

Oversight and Quality Control



Enables Additional Quality

- *Review of Annotated CRF*
  - Compare against sponsor Data Collection library
  - Enhances consistent data collection across CROs and Trials
  - Review SDTM mapping

- *Electronic Comparison of datasets and define.xml*
  - Check if data standards conventions were followed
  - Check consistency with Data Standards Library

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Outsourcing Model II: With Standards Library

ADVANTAGES of this model

- Moderate investment by sponsor company
- Can work with multiple CROs and get same results
- Consistent data collection and representation in CDISC SDTM

DISADVANTAGES of this model

- Quality Control is still re-active
- Review steps are needed to verify CRO's use of the library
- Increased communication with the CRO
- Need to maintain the library by an expert

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When does this model work?

- ✓ Working with One or Multiple CROs
- ✓ Small to midsize companies with a growing portfolio, but limited budget
- ✓ Access to standards SME

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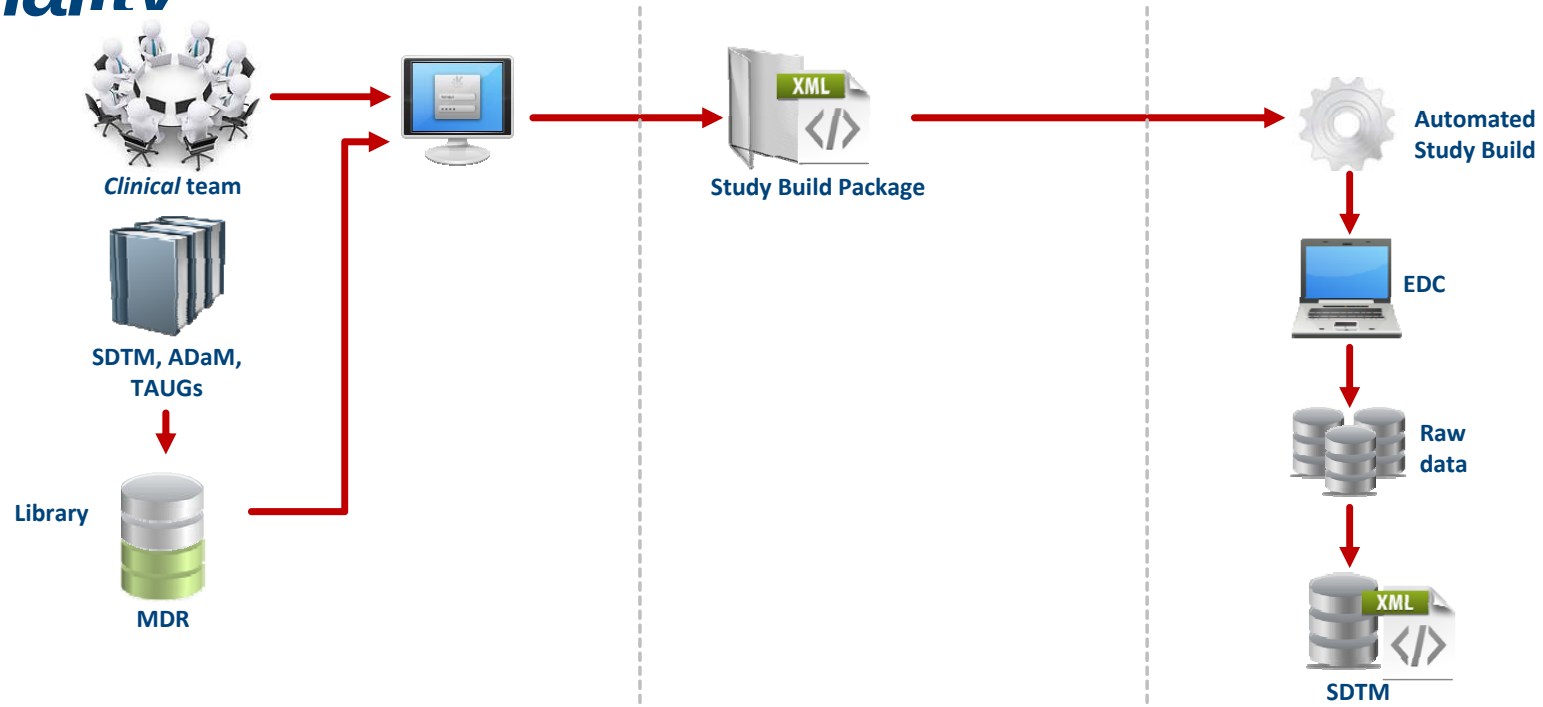
Outsourcing Model III: Extended Standards Functionality



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SPONSOR

CRO

Example Extended Standards Library

AE	ADVERSE EVENTS	DCM ID: AE_GL_001		
STUDYID	STUDYID	Study	[Free text]	[Preprinted]
SITEID	SITEID	Site	[Free text]	[Preprinted]
SUBJID	SUBJID	Subject	[Free text]	[Preprinted]

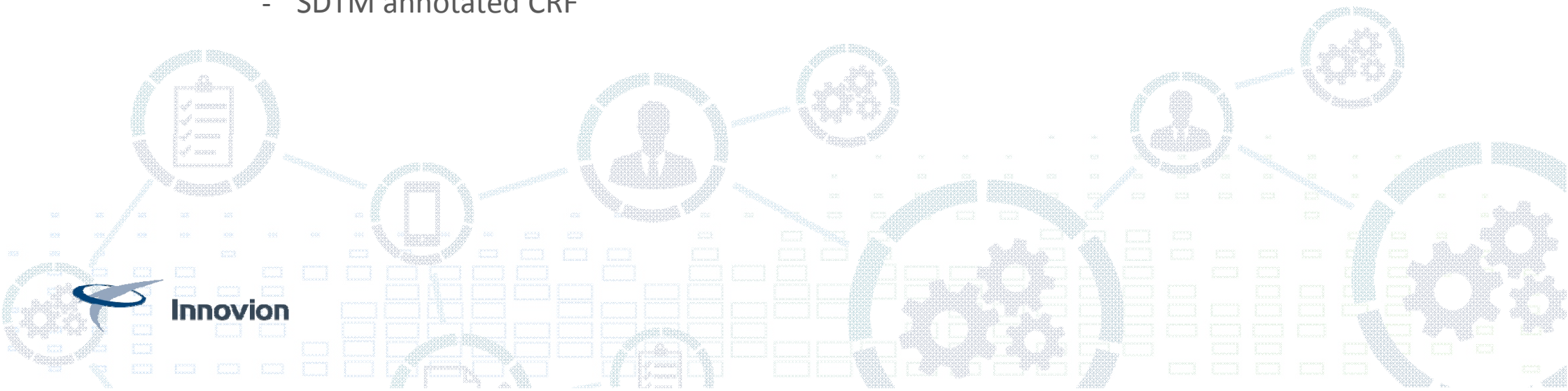
Adverse Events	Dataset	Description	Class	Structure	Purpose	Key Variables	Repeating	Reference Data
[Not Submitted]	AE	Adverse Events	EVENTS	One record per adverse event per subject	Tabulation	STUDYID,USUBJID,AECAT,AEDECOD,AESTDTC	Yes	No

Dataset	Variable	Label	Data Type	Length	Significant Digits	Format	Mandatory	Codelist	Origin	Pages	Method	Predecessor	Role	Comment	Core
AE	STUDYID	Study Identifier	text	12			Yes		Protocol				Identifier		Req
AE	DOMAIN	Domain Abbreviation	text	2			Yes	AE.DOMAIN	Assigned				Identifier		Req
AE	USUBJID	Unique Subject Identifier	text	18			Yes		Derived		USUBJID		Identifier		Req
AE	AESEQ	Sequence Number	integer	8			Yes		Derived		SEQ		Identifier		Req
AE	AEGRPID	Group ID	text	20			No		Derived		AEGRPID		Identifier		Perm
AE	AEREFID	Reference ID	text	20			No		CRF				Identifier		Perm
AE	AESPID	Sponsor-Defined Identifier	text	20			No		CRF				Identifier		Perm
AE	AETERM	Reported Term for the Adverse Event	text	200			Yes		CRF				Topic		Req
AE	AEMODIFY	Modified Reported Term	text	200			No		Assigned				Synonym Qualifier		Perm
AE	AELLT	Lowest Level Term	text	200			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AEDECOD	Dictionary-Derived Term	text	200			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AEPTCD	Preferred Term Code	integer	8			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AEHLT	High Level Term	text	200			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AEHLTCD	High Level Term Code	integer	8			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AEHLGT	High Level Group Term	text	200			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AEHLGTCD	High Level Group Term Code	integer	8			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AEBDSYCD	Body System or Organ Class Code	integer	8			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AESOC	Primary System Organ Class	text	200			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AESOCCD	Primary System Organ Class Code	integer	8			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AELOC	Location of Event	text	200			No	LOC	CRF				Record Qualifier		Perm
AE	AESEV	Severity/Intensity	text	20			No	AESEV	CRF				Record Qualifier		Perm
AE	AESER	Serious Event	text	1			No	NY_YN	CRF				Record Qualifier		Exp
AE	AEACN	Action Taken with Study Treatment	text	40			No	ACN	CRF				Record Qualifier		Exp
AE	AEACNOTH	Other Action Taken	text	200			No		CRF				Record Qualifier		Perm
AE	AEREL	Causality	text	20			No	REL	CRF				Record Qualifier		Exp
AE	AERELNST	Relationship to Non-Study Treatment	text	40			No		CRF				Record Qualifier		Perm

ID	Name	NCI Codelist Code	Data Type	Order	Term	NCI Term Code	Decoded Value	Extensible
ACN	Action Taken with Study Treatment	C66767	text		DOSE INCREASED	C49503	Dose Increased	N
ACN	Action Taken with Study Treatment	C66767	text		DOSE NOT CHANGED	C49504	Dose Not Changed	N
ACN	Action Taken with Study Treatment	C66767	text		DOSE REDUCED	C49505	Dose Reduced	N
ACN	Action Taken with Study Treatment	C66767	text		DRUG INTERRUPTED	C49501	Drug Interrupted	N
ACN	Action Taken with Study Treatment	C66767	text		DRUG WITHDRAWN	C49502	Drug Withdrawn	N
ACN	Action Taken with Study Treatment	C66767	text		NOT APPLICABLE	C48660	Not Applicable	N
ACN	Action Taken with Study Treatment	C66767	text		UNKNOWN	C17998	Unknown	N

Provide Specifications

- *Study Build Package*
  - Protocol
  - Electronic Study Specification
    - Define.xml
    - EDC Build File
    - SDTM annotated CRF



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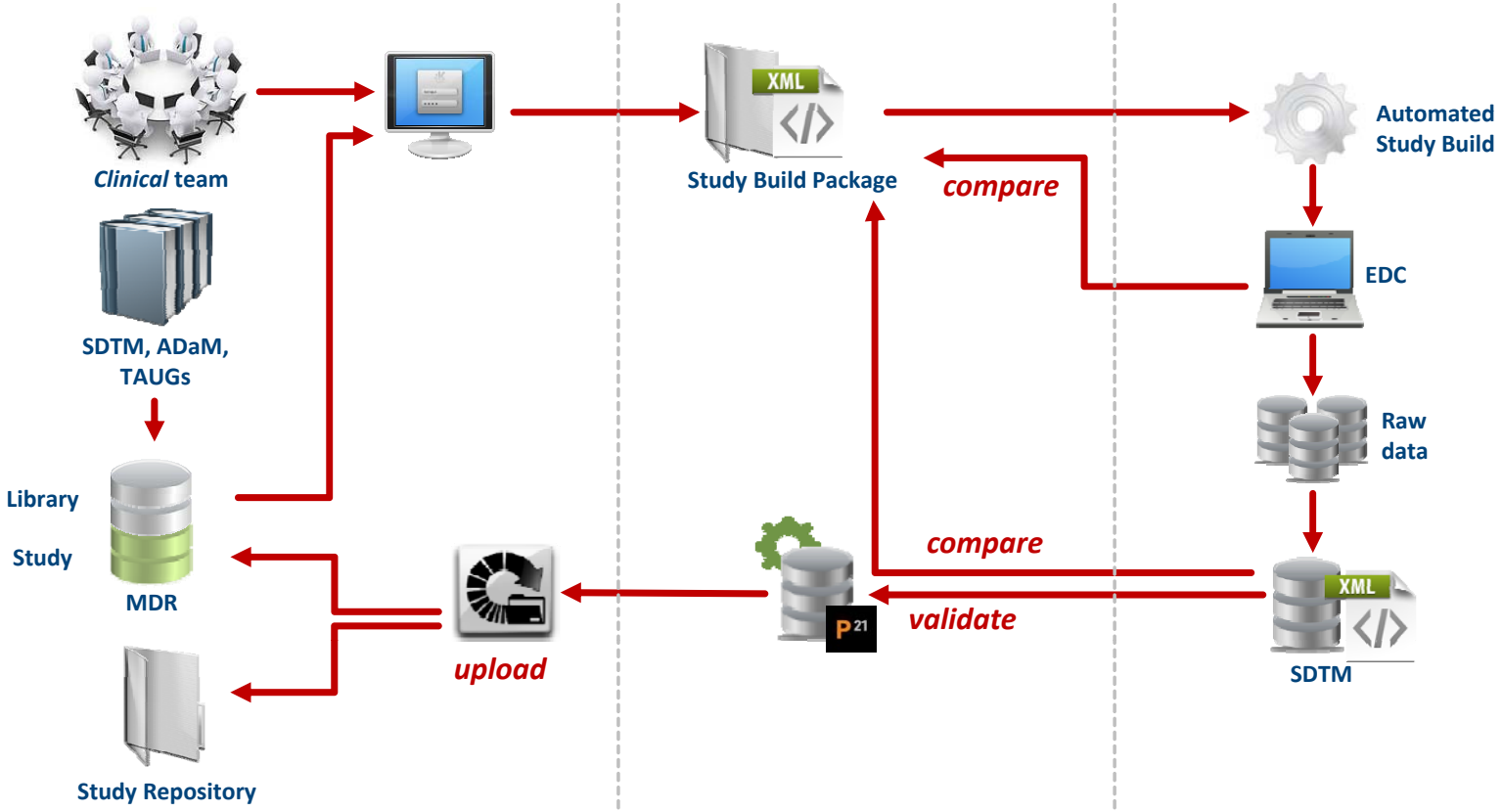
Oversight and Quality Control



Enables Highest Level Of Control & Quality

- *EDC system is automatically generated*
  - Ensures consistent data collection
- *Provides electronic SDTM specifications for the CRO*
  - Enables electronic check between specifications and CRO datasets
  - Ensures consistency with Data Standards Library
- *Ensures consistency*
  - Between Trials
  - Between CROs
  - Fit for use in analysis poolings and re-usability of trial data

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Standards Integration

Analysis Results

Table 1 Demographic Data - Per-Protocol

	Treatment 1	Treatment 2
Baseline body mass index (BMI) [kg/m**2]		
N	167	167
Mean	29.08	29.04
SD	4.84	4.80
Min	20.3	16.0
Median	28.69	28.47
Max	40.1	41.2
Baseline BMI (categorical) [N (%)]		
<25 kg/m**2	41 (24.6%)	71 (21.1%)
25-<30 kg/m**2	60 (35.9%)	130 (38.7%)
>=30 kg/m**2	66 (39.5%)	135 (40.2%)

CRF

VITAL SIGNS

PROTOCOL	ABC-DIA-0012
SUBJECT	20001
VISIT	WEEK 4

WERE VITAL SIGNS COLLECTED? ☐ YES ☐ NO

DATE __/___/____ (DD/MON/YYYY)

PLANNED TIMEPOINT	ACTUAL TIME	TEST	RESULT	UNIT	CLINICALLY SIGNIFICANT
1. PRE-DOSE	__:__	Height	___	cm	
		Weight	___	kg	
		Systolic Blood Pressure	___	mmHg	
		Diastolic Blood Pressure	___	mmHg	
		Pulse Rate	___	beats/min	
		Temperature	___	☐C ☐F	
		Respiratory Rate	___	breaths/min	
		Interpretation	☐NORMAL ☐ABNORMAL		☐YES ☐ NO
2. 30 MINUTES	__:__	Systolic Blood Pressure	___	mmHg	
		Diastolic Blood Pressure	___	mmHg	
		Pulse Rate	___	beats/min	
		Temperature	___	☐C ☐F	
		Respiratory Rate	___	breaths/min	
		Interpretation	☐NORMAL ☐ABNORMAL		☐YES ☐ NO

CDISC Data Models

ADaM Data

	STUDYID	USUBJID	SUBJID	BMI	BMIGR1	BMIGR1N	BMIGR2	BMIGR2N
2	9999-0001	9999-0001-000001	000001	27.777777778	<30 kg/m**2	1	25-<30 kg/m**2	2
3	9999-0001	9999-0001-000002	000002	25.509615702	<30 kg/m**2	1	25-<30 kg/m**2	2
4	9999-0001	9999-0001-000003	000003	26.175194521	<30 kg/m**2	1	25-<30 kg/m**2	2
5	9999-0001	9999-0001-000004	000004	35.15625	>=30 kg/m**2	2	>=30 kg/m**2	3
6	9999-0001	9999-0001-000005	000005	30.968858131	>=30 kg/m**2	2	>=30 kg/m**2	3
7	9999-0001	9999-0001-000006	000006	39.697163916	>=30 kg/m**2	2	>=30 kg/m**2	3
8	9999-0001	9999-0001-000007	000007	25.826446281	<30 kg/m**2	1	25-<30 kg/m**2	2
9	9999-0001	9999-0001-000008	000008	30.103806228	>=30 kg/m**2	2	>=30 kg/m**2	3
10	9999-0001	9999-0001-000009	000009	32.280962688	>=30 kg/m**2	2	>=30 kg/m**2	3
11	9999-0001	9999-0001-000010	000010	28.876133787	<30 kg/m**2	1	25-<30 kg/m**2	2
12	9999-0001	9999-0001-000011	000011	29.372397383	<30 kg/m**2	1	25-<30 kg/m**2	2
13	9999-0001	9999-0001-000012	000012	26.714052606	<30 kg/m**2	1	25-<30 kg/m**2	2
14	9999-0001	9999-0001-000013	000013	32.710619869	>=30 kg/m**2	2	>=30 kg/m**2	3
15	9999-0001	9999-0001-000014	000014	28.719723183	<30 kg/m**2	1	25-<30 kg/m**2	2
16	9999-0001	9999-0001-000015	000015	32.270420377	>=30 kg/m**2	2	>=30 kg/m**2	3

CDASH EDC Extract

	STUDYID	SUBJID	VISIT	VSPERF	VSDAT	VSTIM	VSSPID	VSTPT	HEIGHT	HEIGHTU	WEIGHT	WEIGHTU
1	9999-0001	000011	BASE LINE	YES	14/06/2017	8:55	1	PRE_DOSE	184	cm	100	kg
2	9999-0001	000011	BASE LINE	YES	14/06/2017	9:31	2	30 MINUTES				

	SYSBP	YSBP	DIAB	DIABU	PULSE	PULSEU	TEMP	TEMPU	RESP	RESPU	INT	VSCLSIG
1	130	mmHg	80	mmHg	62	BEATS/MIN	36	C	12	BREATHS/MIN	NORMAL	kg
2	150	mmHg	100	mmHg	95	BEATS/MIN	36	C	30	BREATHS/MIN	ABNORMAL	NO

SDTM Data

	STUDYID	DOMAIN	USUBJID	VSSEQ	VSSPID	VSTESTCD	VSTEST	VSORRES	VSORRESU	VSSTRESC	VSSTRESN	VSBLFL	VSDRVFL	VISITNUM	VISIT	VISITDY	VSDTC	VSDY
1	9999-0001	VS	9999-0001-000011	1	1	HEIGHT	HEIGHT	184	CM	184	184	Y		2	BASELINE	10	2017-06-14T08:55	PRE-DOSE
2	9999-0001	VS	9999-0001-000011	2	1	WEIGHT	WEIGHT	100	KG	100	100	Y		2	BASELINE	10	2017-06-14T08:55	PRE-DOSE
3	9999-0001	VS	9999-0001-000011	3		BMI	BODY MASS INDEX	29.54	KG/CM2			Y	Y	2	BASELINE	10	2017-06-14T08:55	PRE-DOSE
4	9999-0001	VS	9999-0001-000011	4	1	SYSBP	SYSTOLIC BLOOD PRESSURE	130	mmHG	130	130	Y		2	BASELINE	10	2017-06-14T08:55	PRE-DOSE
5	9999-0001	VS	9999-0001-000011	5	1	DIABP	DIASTOLIC BLOOD PRESSURE	80	mmHG	80	80	Y		2	BASELINE	10	2017-06-14T08:55	PRE-DOSE
6	9999-0001	VS	9999-0001-000011	6	1	PULSE	PULSE RATE	62	BEATS/MIN	62	62	Y		2	BASELINE	10	2017-06-14T08:55	PRE-DOSE
7	9999-0001	VS	9999-0001-000011	7	1	TEMP	TEMPERATURE	36	C	36	36	Y		2	BASELINE	10	2017-06-14T08:55	PRE-DOSE
8	9999-0001	VS	9999-0001-000011	8	1	RESP	RESPIRATORY RATE	12	BREATHS/MIN	12	12	Y		2	BASELINE	10	2017-06-14T08:55	PRE-DOSE
9	9999-0001	VS	9999-0001-000011	9	1	INTP	INTERPRETATION	NORMAL		NORMAL				2	BASELINE	10	2017-06-14T09:31	30 MINUTES
10	9999-0001	VS	9999-0001-000011	10	2	SYSBP	SYSTOLIC BLOOD PRESSURE	150	mmHG	150	150			2	BASELINE	10	2017-06-14T09:31	30 MINUTES
11	9999-0001	VS	9999-0001-000011	11	2	DIABP	DIASTOLIC BLOOD PRESSURE	100	mmHG	100	100			2	BASELINE	10	2017-06-14T09:31	30 MINUTES
12	9999-0001	VS	9999-0001-000011	12	2	PULSE	PULSE RATE	95	BEATS/MIN	95	95			2	BASELINE	10	2017-06-14T09:31	30 MINUTES
13	9999-0001	VS	9999-0001-000011	13	2	TEMP	TEMPERATURE	36	C	36	36			2	BASELINE	10	2017-06-14T09:31	30 MINUTES
14	9999-0001	VS	9999-0001-000011	14	2	RESP	RESPIRATORY RATE	30	BREATHS/MIN	30	30			2	BASELINE	10	2017-06-14T09:31	30 MINUTES
15	9999-0001	VS	9999-0001-000011	15	2	INTP	INTERPRETATION	ABNORMAL		ABNORMAL				2	BASELINE	10	2017-06-14T09:31	30 MINUTES

	STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL	QORIG	QEVAL
1	9999-0001	VS	9999-0001-000011	VSSEQ	15	VSCLSIG	CLINICALLY SIGNIFICANT	NO	CRF	

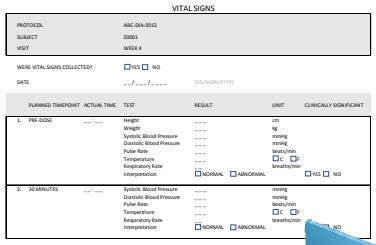
Built-in Traceability

Analysis Results

Table 1 Demographic Data - Per-Protocol

	Treatment 1	Treatment 2
Baseline body mass index (BMI) [kg/m**2]		
N	167	167
Mean	29.08	29.04
SD	4.84	4.80
Min	20.3	16.0
Median	28.69	28.47
Max	40.1	41.2
Baseline BMI (categorical) [N (%)]		
<25 kg/m**2	41 (24.6%)	71 (21.1%)
25-<30 kg/m**2	60 (35.9%)	130 (38.7%)
>=30 kg/m**2	66 (39.5%)	135 (40.2%)

CRF


VITAL SIGNS

PROTOCOL	ABC-DIA-0012
SUBJECT	20001
VISIT	WEEK 4

WERE VITAL SIGNS COLLECTED? ☐ YES ☐ NO

DATE __/___/____ (DD/MON/YYYY)

PLANNED TIMEPOINT	ACTUAL TIME	TEST	RESULT	UNIT	CLINICALLY SIGNIFICANT
1. PRE-DOSE	__:__	Height	___	cm	
		Weight	___	kg	
		Systolic Blood Pressure	___	mmHg	
		Diastolic Blood Pressure	___	mmHg	
		Pulse Rate	___	beats/min	
		Temperature	___	☐C ☐F	
		Respiratory Rate	___	breaths/min	
		Interpretation	☐ NORMAL ☐ ABNORMAL		☐ YES ☐ NO
2. 10 MINUTES	__:__	Systolic Blood Pressure	___	mmHg	
		Diastolic Blood Pressure	___	mmHg	
		Pulse Rate	___	beats/min	
		Temperature	___	☐C ☐F	
		Respiratory Rate	___	breaths/min	
		Interpretation	☐ NORMAL ☐ ABNORMAL		☐ YES ☐ NO

CDISC Metadata

ADaM data

	STUDYID	USUBJID	SUBJID	BMI	BMIGR1	BMIGR1N	BMIGR2	BMIGR2N
2	9999-0001	9999-0001-000001	000001	27.777777778	<30 kg/m**2	1	25-<30 kg/m**2	2
3	9999-0001	9999-0001-000002	000002	25.503615702	<30 kg/m**2	1	25-<30 kg/m**2	2
4	9999-0001	9999-0001-000003	000003	26.175194521	<30 kg/m**2	1	25-<30 kg/m**2	2
5	9999-0001	9999-0001-000004	000004	35.15625	>=30 kg/m**2	2	>=30 kg/m**2	3
6	9999-0001	9999-0001-000005	000005	30.960958131	>=30 kg/m**2	2	>=30 kg/m**2	3
7	9999-0001	9999-0001-000006	000006	29.637162916	>=30 kg/m**2	2	>=30 kg/m**2	3
8	9999-0001	9999-0001-000007	000007	25.826446281	<30 kg/m**2	1	25-<30 kg/m**2	2
9	9999-0001	9999-0001-000008	000008	30.103806228	>=30 kg/m**2	2	>=30 kg/m**2	3
10	9999-0001	9999-0001-000009	000009	32.280962583	>=30 kg/m**2	2	>=30 kg/m**2	3
11	9999-0001	9999-0001-000010	000010	28.676133787	<30 kg/m**2	1	25-<30 kg/m**2	2
12	9999-0001	9999-0001-000011	000011	29.372397363	<30 kg/m**2	1	25-<30 kg/m**2	2
13	9999-0001	9999-0001-000012	000012	26.714852608	<30 kg/m**2	1	25-<30 kg/m**2	2
14	9999-0001	9999-0001-000013	000013	32.719619869	>=30 kg/m**2	2	>=30 kg/m**2	3
15	9999-0001	9999-0001-000014	000014	28.715723183	<30 kg/m**2	1	25-<30 kg/m**2	2
16	9999-0001	9999-0001-000015	000015	32.270420377	>=30 kg/m**2	2	>=30 kg/m**2	3

Trial Arms (TA) [Location: ta.xpt]

Variable	Label	Key	Type	Length	Controlled Terms or Format	Origin	Derivation/Comment
STUDYID	Study Identifier	1	text	7		Protocol	
DOMAIN	Domain Abbreviation		text	2	["TA" = "Trial Arms"] <Domain Abbreviation (TA)>	Assigned	
ARMCD	Planned Arm Code	2	text	8	["PLACEBO" = "Placebo", "SCRNFAIL" = "Screen Failure", "WONDER10" = "Miracle Drug 10 mg", "WONDER20" = "Miracle Drug 20 mg"] <Planned Arm Code>	Assigned	
ARM	Description of Planned Arm		text	20	["Miracle Drug 10 mg", "Miracle Drug 20 mg", "Placebo", "Screen Failure"] <Description of Planned Arm>	Protocol	
TAETORD	Order of Element within Arm	3	integer	1		Assigned	
ETCD	Element Code		text	8		Assigned	
ELEMENT	Description of Element		text	40		Protocol	
TABRANCH	Branch		text	35		Protocol	
TATRANS	Transition Rule		text	1		Protocol	
EPOCH	Epoch		text	30		Protocol	

Analysis Datasets for Study CDISC-Sample (ADaM-IG 1.0)

Dataset	Description	Class	Structure	Purpose	Keys	Location	Documentation
ADSL	Subject-Level Analysis	SUBJECT LEVEL ANALYSIS DATASET	one record per subject	Analysis	STUDYID, USUBJID	adsl.xpt	Screen Failures are excluded since they are not needed for this study analysis. See Analysis Data Reviewer's Guide, page 6. Analysis Data Reviewer's Guide
ADQSADAS	ADAS-Cog Analysis	BASIC DATA STRUCTURE	One record per subject per parameter per analysis visit per analysis date	Analysis	STUDYID, USUBJID, PARAMCD, AVISIT, ADT	adqsadas.xpt	See referenced dataset creation program and Analysis Data Reviewer's Guide, Section 2.1 adqsadas.sas Analysis Data Reviewer's Guide
ADAE	Adverse Events Analysis Dataset	OCCURRENCE DATA STRUCTURE	one record per subject per adverse event	Analysis	STUDYID, USUBJID, AETERM, ASTDT, AESEQ	adae.xpt	See SAS program adae.sas

SDTM Metadata

ADaM Metadata

Outsourcing Model III: Extended Standards Functionality

ADVANTAGES of this model

- Full control
- Pro-active Quality Control
- High level of automation possible
- Many automatic quality checks
- Submission ready deliverables

DISADVANTAGES of this model

- Higher investment by sponsor company
- Continuous maintenance and governance of standards mandatory

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When does this model work?

- ✓ Midsize to large companies
- ✓ Training is provided
- ✓ Intuitive Interfaces for end-users

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AGENDA

- *Introduction*
- *Outsourcing and Oversight models*
- *Starter Pack*
- *Questions*

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Technology

- *Develop User Requirements*
- *Vendor and tool selection*
- *Implementation & Validation*
- *Infrastructure*

Collaboration

- *CRO Selection*
- *CRO Onboarding*
- *CRO Oversight*

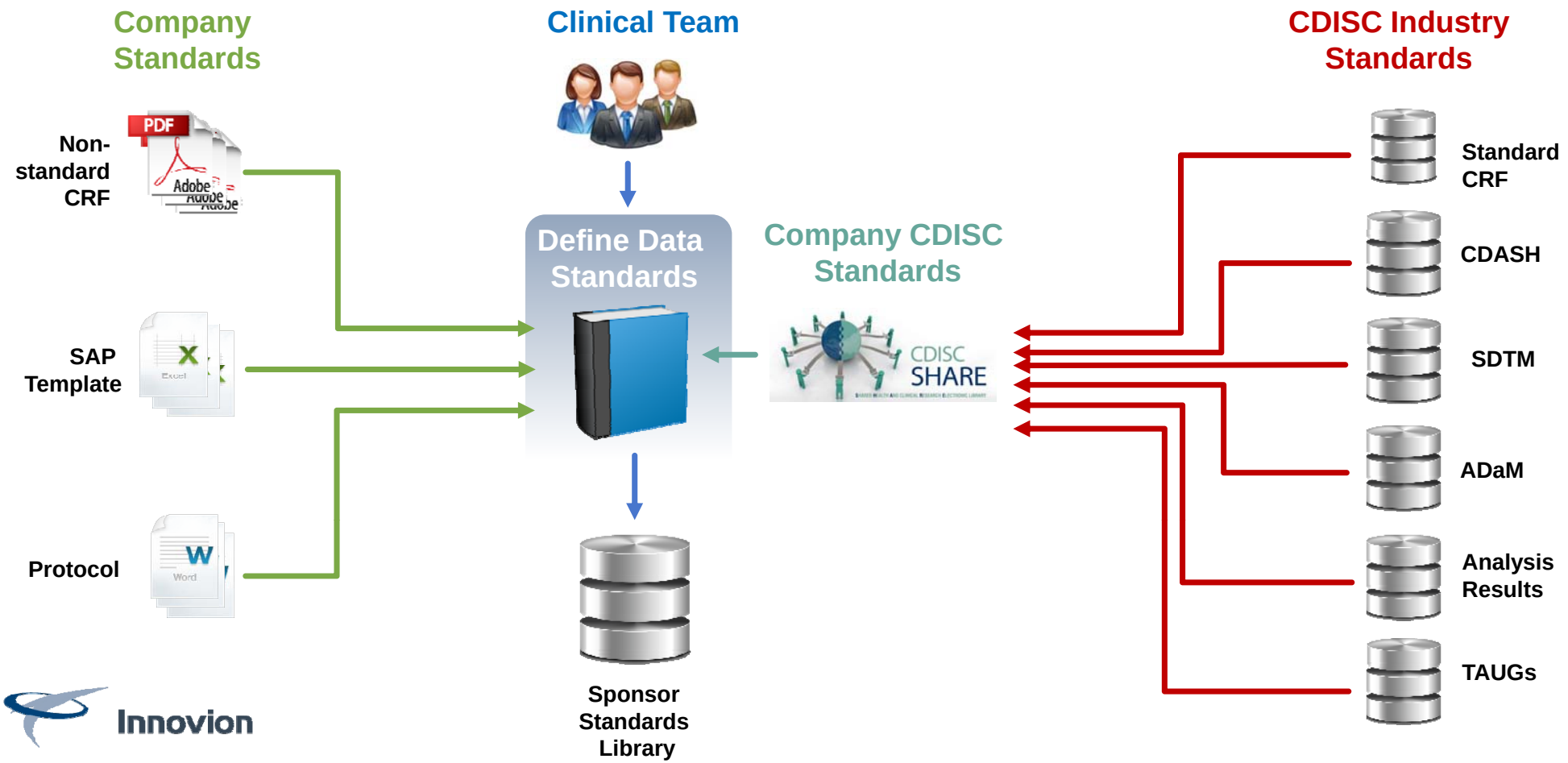
Data

- *Study specification*
- *Verify deliverables*
- *Submission readiness*

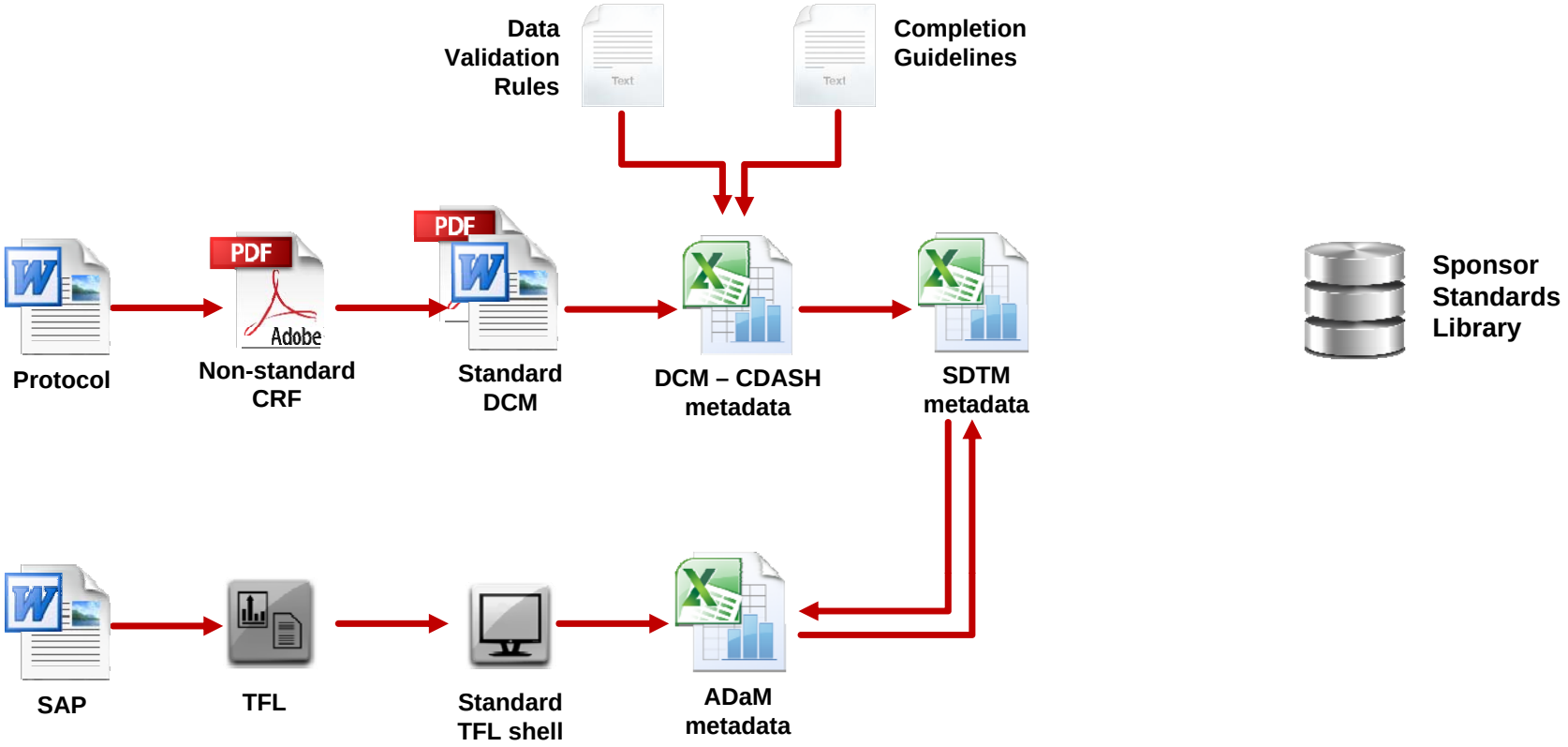
Data Standards

- *Data Collection Library (EDC)*
- *CDISC Library*
  - *CDASH*
  - *SDTM*
  - *ADaM*
  - *Controlled terminology*
- *Consistency*

Standards Library Sources



Standard Elements Definition Flow



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Standardize Data Collection Modules

AE		ADVERSE EVENTS	DCM ID: AE_GL_001	
STUDYID	STUDYID	Study	[Free text]	[Preprinted]
SITEID	SITEID	Site	[Free text]	[Preprinted]
SUBJID	SUBJID	Subject	[Free text]	[Preprinted]
Adverse Events				
[Not Submitted]	AEYN	Were any adverse events experienced?	[Radiobutton {Yes; No}]	NY
AESPID	AESPID	AE number	[Numeric field]	[Preprinted]
AETERM	AETERM	What is the adverse event term?	[Free text]	
AESTDTC	AESTDAT	Start Date	[Date {DD-MMM-YYYY}]	
	AESTTIM	Start Time	[24 hr clock]	
AEENDTC	AEENDAT	End Date	[Date {DD-MMM-YYYY}]	
	AEENTIM	End Time	[24 hr clock]	
If Yes, AEENRTPT = ONGOING	AEONGO	Is the adverse event still ongoing?	[Radiobutton {Yes; No}]	NY
AESEV	AESEV	Severity	[Radiobutton {Mild; Moderate; Severe}]	AESEV
AESER	AESER	Is the adverse event serious?	[Radiobutton {Yes; No}]	NY
		If Yes:		
AEREFID	AEREFID	SAE Number	[Free text]	
AESCONG	AESCONG	Congenital Anomaly	[Radiobutton {Yes; No}]	NY
AESDISAB	AESDISAB	Significant Disability	[Radiobutton {Yes; No}]	NY
AESDTH	AESDTH	Death	[Radiobutton {Yes; No}]	NY
AESHOSP	AESHOSP	Hospitalization	[Radiobutton {Yes; No}]	NY
AESLIFE	AESLIFE	Life Threatening	[Radiobutton {Yes; No}]	NY
AESMIE	AESMIE	Other Medically Important Event	[Radiobutton {Yes; No}]	NY
AEREL	AEREL	Relationship to Study Treatment	[Radiobutton {Not related; Unlikely Related; Possibly Related; Probably Related}]	REL
AEACN	AEACN	Action taken with Study Treatment	[Radiobutton {Dose Not Changed; Drug Withdrawn; Dose Reduced}]	ACN

SDTM CDASH CRF questions eDC build instructions Controlled terminology

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Create Library Metadata

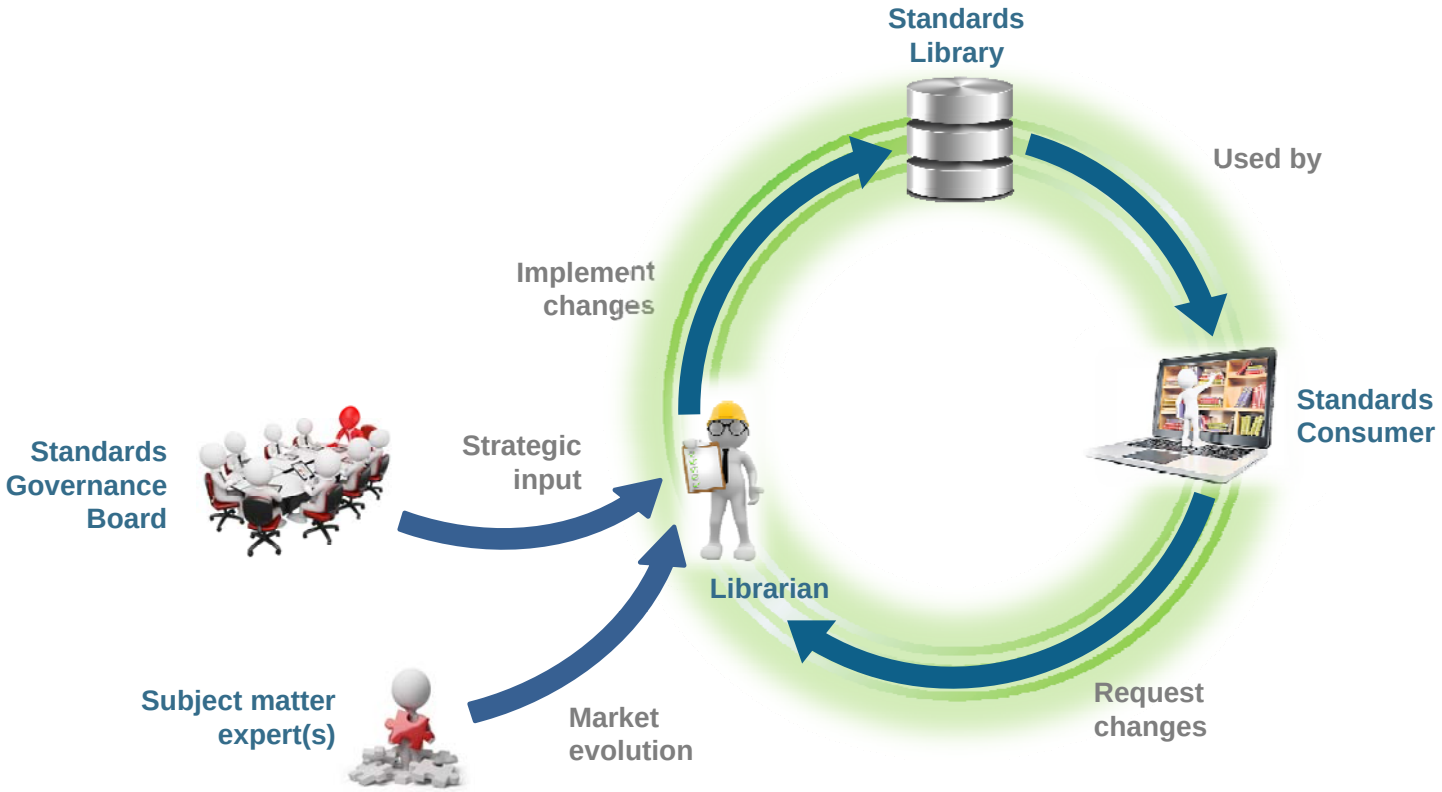
AE	ADVERSE EVENTS		DCM ID: AE_GL_001	
STUDYID	STUDYID	Study	[Free text]	[Preprinted]
SITEID	SITEID	Site	[Free text]	[Preprinted]
SUBJID	SUBJID	Subject	[Free text]	[Preprinted]

Dataset	Description	Class	Structure	Purpose	Key Variables	Repeating	Reference Data
AE	Adverse Events	EVENTS	One record per adverse event per subject	Tabulation	STUDYID,USUBJID,AECAT,AEDECOD,AESTDTC	Yes	No

Dataset	Variable	Label	Data Type	Length	Significant Digits	Format	Mandatory	Codelist	Origin	Pages	Method	Predecessor	Role	Comment	Core
AE	STUDYID	Study Identifier	text	12			Yes		Protocol				Identifier		Req
AE	DOMAIN	Domain Abbreviation	text	2			Yes	AE.DOMAIN	Assigned				Identifier		Req
AE	USUBJID	Unique Subject Identifier	text	18			Yes		Derived		USUBJID		Identifier		Req
AE	AESEQ	Sequence Number	integer	8			Yes		Derived		SEQ		Identifier		Req
AE	AEGRPID	Group ID	text	20			No		Derived		AEGRPID		Identifier		Perm
AE	AEREFID	Reference ID	text	20			No		CRF				Identifier		Perm
AE	AESPID	Sponsor-Defined Identifier	text	20			No		CRF				Identifier		Perm
AE	AETERM	Reported Term for the Adverse Event	text	200			Yes		CRF				Topic		Req
AE	AEMODIFY	Modified Reported Term	text	200			No		Assigned				Synonym Qualifier		Perm
AE	AELLT	Lowest Level Term	text	200			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AEDECOD	Dictionary-Derived Term	text	200			Yes	MedDRA	Assigned				Synonym Qualifier		Exp
AE	AEPTCD	Preferred Term Code	integer	8			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AEHLT	High Level Term	text	200			No	MedDRA	Assigned				Variable Qualifier		Req
AE	AEHLTCD	High Level Term Code	integer	8			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AEHLGT	High Level Group Term	text	200			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AEHLGTCD	High Level Group Term Code	integer	8			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AEBODSYS	Body System or Organ Class	text	200			No	MedDRA	Assigned				Record Qualifier		Exp
AE	AEBDSYCD	Body System or Organ Class Code	integer	8			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AESOC	Primary System Organ Class	text	200			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AESOCCD	Primary System Organ Class Code	integer	8			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AELOC	Location of Event	text	200			No	LOC	CRF				Record Qualifier		Perm
AE	AESEV	Severity/Intensity	text	20			No	AESEV	CRF				Record Qualifier		Perm
AE	AESER	Serious Event	text	1			No	NY_YN	CRF				Record Qualifier		Exp
AE	AEACN	Action Taken with Study Treatment	text	40			No	ACN	CRF				Record Qualifier		Exp
AE	AEACNOTH	Other Action Taken	text	200			No		CRF				Record Qualifier		Perm
AE	AEREL	Causality	text	20			No	REL	CRF				Record Qualifier		Exp
AE	AERELNST	Relationship to Non-Study Treatment	text	40			No		CRF				Record Qualifier		Perm

ID	Name	NCI Codelist Code	Data Type	Order	Term	NCI Term Code	Decoded Value	Extensible
ACN	Action Taken with Study Treatment	C66767	text		DOSE INCREASED	C49503	Dose Increased	N
ACN	Action Taken with Study Treatment	C66767	text		DOSE NOT CHANGED	C49504	Dose Not Changed	N
ACN	Action Taken with Study Treatment	C66767	text		DOSE REDUCED	C49505	Dose Reduced	N
ACN	Action Taken with Study Treatment	C66767	text		DRUG INTERRUPTED	C49501	Drug Interrupted	N
ACN	Action Taken with Study Treatment	C66767	text		DRUG WITHDRAWN	C49502	Drug Withdrawn	N
ACN	Action Taken with Study Treatment	C66767	text		NOT APPLICABLE	C48660	Not Applicable	N
ACN	Action Taken with Study Treatment	C66767	text		UNKNOWN	C17998	Unknown	N

Data Standards Governance Process



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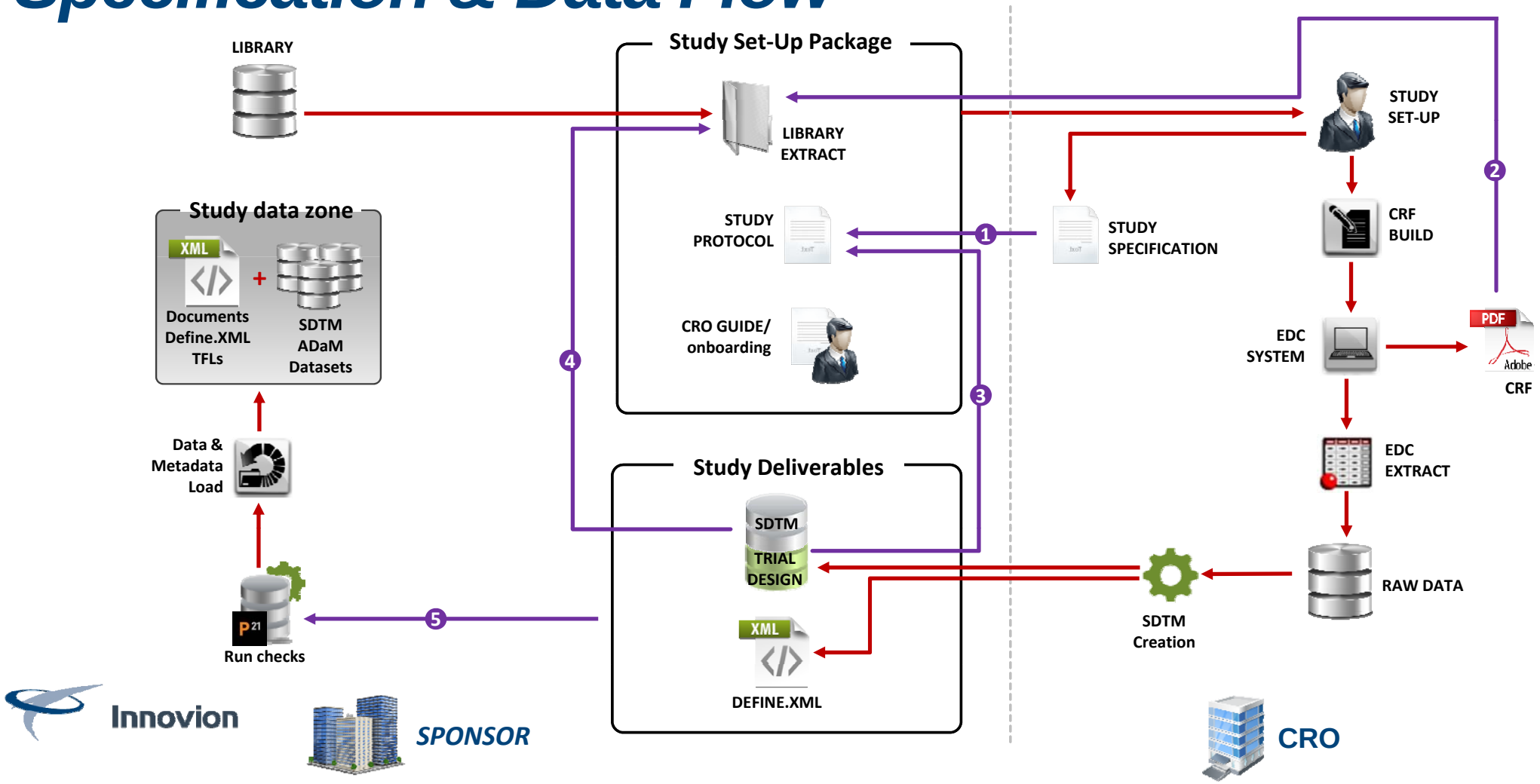
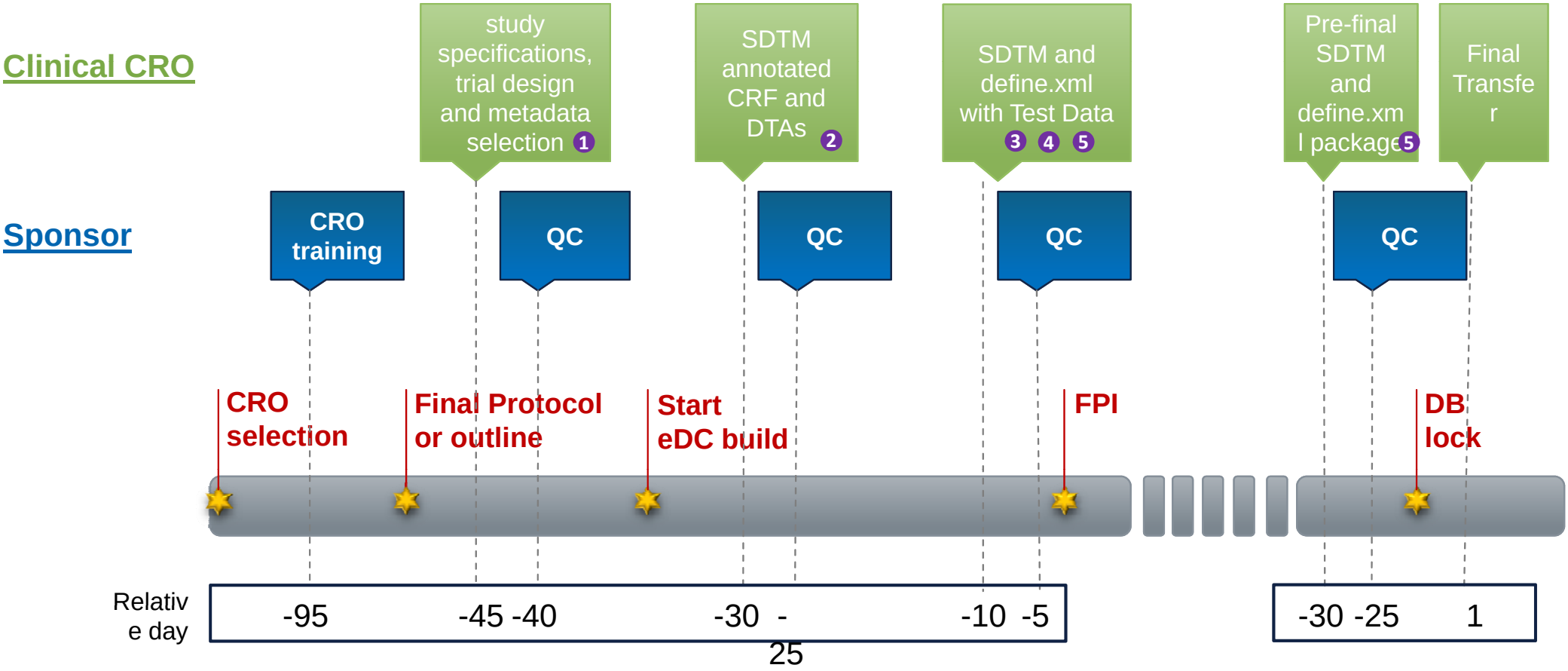
Specification & Data Flow

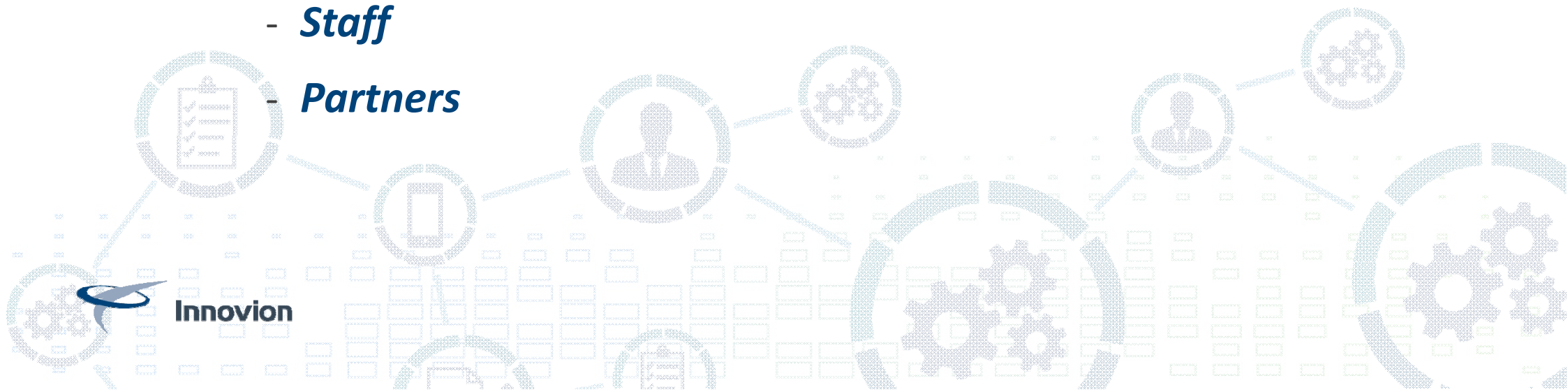


Quality Control Activities and Timelines



Conclusion

- *Higher level of standardization will lead to better quality*
  - Choose the approach that fits your company
    - ***Expectations***
    - ***Budget***
    - ***Staff***
    - ***Partners***



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Questions….

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Thank you for your attention