CDISC Italian User Network 2019

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e-Diary & CDISC: a real case in Vaccines

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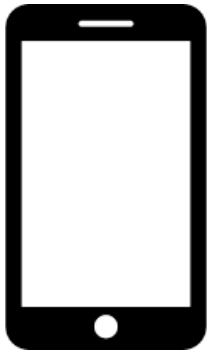
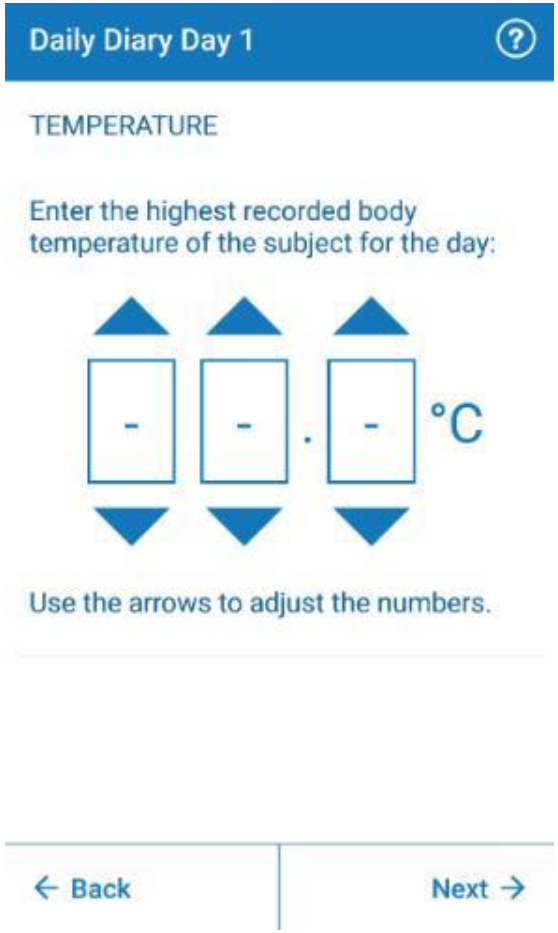
What e-diary is?



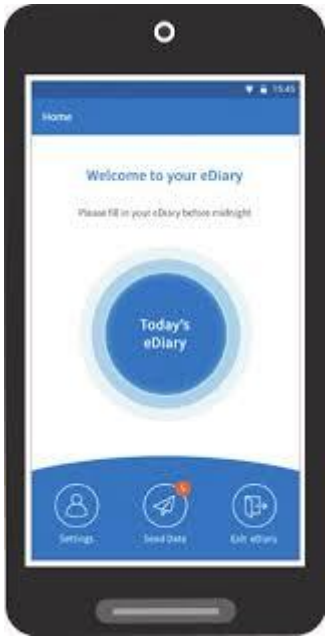
Electronic device to capture occurrence and severity of symptoms in Pharmaceutical clinical trials.

E-Diary provides the possibility to monitor safety and compliance, in accordance to ICH GCP E6 (R2 addendum, section 5.18) guidance, dated November 2016.



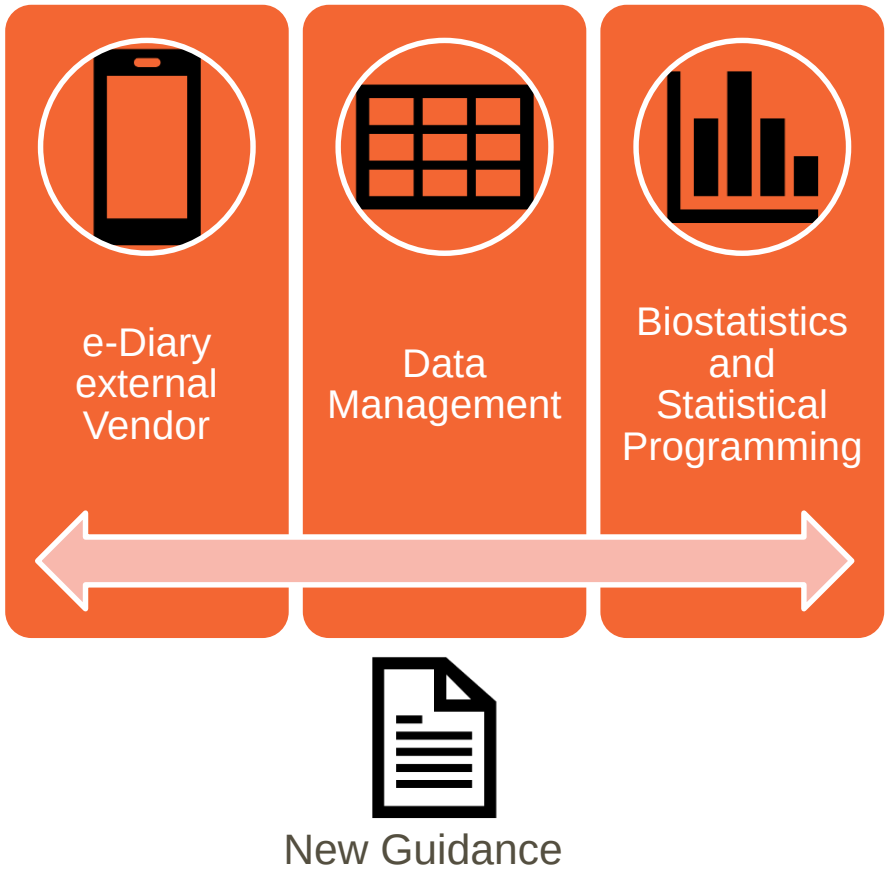
History of e-diary

from Paper Diary



to Electronic Diary

Pilot study in GSK



CDISC Implementation

CDASH
Starting point

How to handle data from an external vendor into CDASH?

1. Transferring all collected data without any modification
2. Move into CDASH with a recode (or a very simple mapping) of source data

Specific CDASH datasets are created for e-diary source (QS, XD)

The remap will be done in SDTM domains

CDASH
Data transfer and queries

	Electronic CRF	Electronic Diary Card
Extraction Tool	Daily basis	N.A.
Data Transfer	N.A.	Monthly basis
Queries	Reconciliation (*live*)	N.A.
Data Corrections Forms	N.A.	Send the form and wait for new transfer (*lag in time*)

SDTM
CE example #1

CE
(approximately 30000 rows)

– eCRF data (1.5%)
– eDiary data (98.5%)

NOTE: 2 different sources, 2 different SDTM mappings

DOMAIN	CETERM	CEOCCUR	VISITNUM	CEDTC	CEDY	CETPT	CEELTM	CETPTREF	CEEVINTX
CE	ERYTHEMA	N	10	2018-02-08T18:28	1				TODAY
CE	ERYTHEMA	N	.		.	DAY 1, 60 MINUTES	PT60M	VACCINATION - VISITNUM 10	VACCINATION TO DAY 1, 60 MINUTES
CE	PAIN	Y	10	2018-02-08T18:28	1				TODAY
CE	PAIN	Y	.		.	DAY 1, 60 MINUTES	PT60M	VACCINATION - VISITNUM 10	VACCINATION TO DAY 1, 60 MINUTES
CE	SWELLING	Y	10	2018-02-08T18:28	1				TODAY
CE	SWELLING	Y	.		.	DAY 1, 60 MINUTES	PT60M	VACCINATION - VISITNUM 10	VACCINATION TO DAY 1, 60 MINUTES

SDTM
CE example #2

If no daily answer, then the diary is set up to consider the worst case scenario so at the moment **blank is an unknown status and the device keep on soliciting the event**.

If a subject misses day 7, the system wait until the diary is entered again.

DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7	DAY 8	DAY 9	DAY 10	DAY 11
N	N	N	N	N	N	.	.	.	Y	N

How to interpretate results? Imputation of missing values?

SDTM
Handle inconsistencies and issues within SDTM

A subject forgot to answer the first day to the diary, but then called the site to report the event occurred.

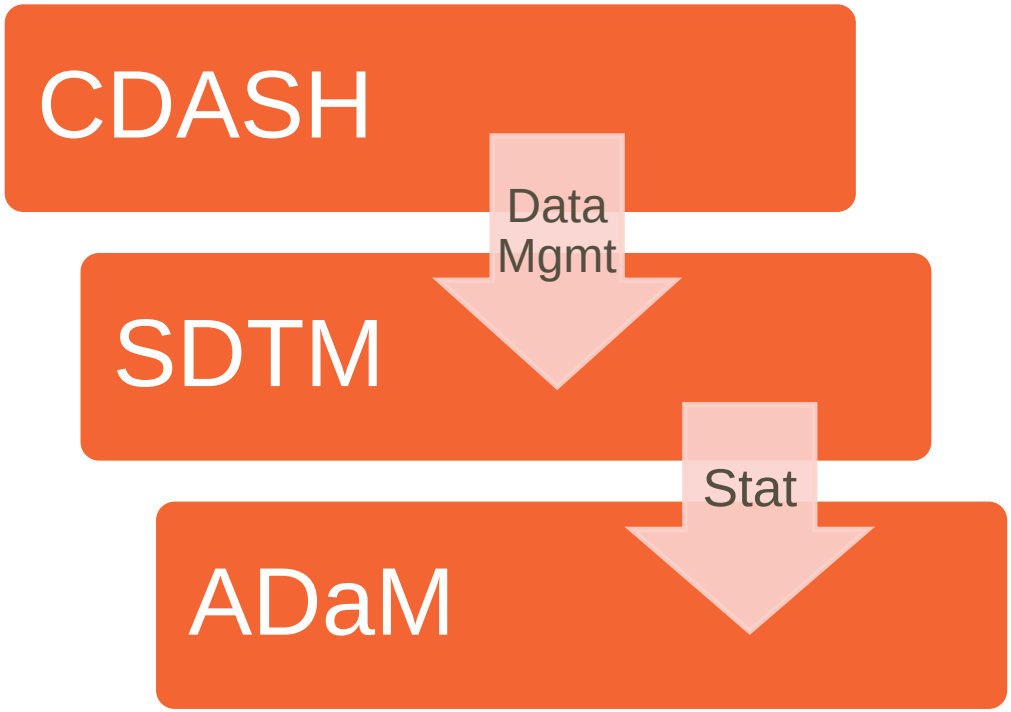
Missing day 1

DOMAIN	CETERM	CEOCCUR	CESTAT	VISITNUM	CEDTC	CEDY
CE	HEADACHE	N		10	2018-04-04T19:06	2
CE	HEADACHE	N		10	2018-04-05T19:44	3
CE	HEADACHE	N		10	2018-04-06T18:55	4
CE	HEADACHE	N		10	2018-04-07T18:59	5
CE	HEADACHE	N		10	2018-04-08T18:52	6
CE	HEADACHE	N		10	2018-04-09T18:58	7

DOMAIN	AETERM	AEDECOD	AEBODSYS	AESOC	AESEV	AESTDTC	AEENDTC	AESTDY	AEENDY
AE	HEADACHE	Headache	Nervous system disorders	Nervous system disorders	MILD	2018-04-03	2018-04-03	1	1

How to analyze above data?

ADaM



ADaM is more flexible than SDTM

Always focus on traceability

ADaM
ADCE example #1

Selection of correct records from SDTM.CE

Delete records where CEOCCUR = ' ' and CESTAT = 'NOT DONE' and CEREASND = 'NOT APPLICABLE'

Select Subjects present in ADSL.

In case of missing time points in sdtm.ce per reaction for Day 1,60 MINUTES to Day 8 impute all missing time points with AVAL= -8 and AVALC='NO RESULT'.

No imputation of time points for reactions after Day 8.

See ADRG section 3.6 for imputation rule of observations.

ADaM
ADCE example #2

Creation of ATPT

Observations from CE originating from eDIARY:

1) If CE.CETPT is blank and CE.CETERM is not 'LOCAL REACTIONS' and CE.CETERM is not 'SYSTEMIC REACTIONS' and CE.CEDTC is filled then derive as follows:

Concatenate 'DAY ' with CEDTC - PyySxSDT +1 (where Aperiod = yy. ASPER =x)

Observations from CE originating from eCRF:

2) If CE.CETPT is not blank then ATPT equals to CE.CETPT.

3) If CE.CETPT is blank and (CE.CETERM = 'LOCAL REACTIONS' or CE.CETERM = 'SYSTEMIC REACTIONS') and (CE.CEOCCUR = 'N') then output the observation once for the ATPT value: "DAY 1, 60 MINUTES" for each local or systemic reaction as defined in the controlled terminology.

4) If CE.CETPT is blank and (CE.CETERM = 'LOCAL REACTIONS' or CE.CETERM = 'SYSTEMIC REACTIONS') and CE.CESTAT = 'NOT DONE' then delete the record and do not output any records for ADCE.ATPT values.

Why e-Diary?

Pros of using E-Diary

- Electronic system have alarms to remind subjects to fill the e-diary
- Subjects feel more comfortable to complete an electronic diary instead of using papers
- Electronic system alerts can be put in place to inform Company about issues if some criteria are met

Patient first and more knowledge of subjects health status live

- Daily monitoring can be done on subjects diaries from a compliance point of view
- Safety monitoring can be done during the solicitation period
- Subjects are not allowed to enter retrospective or prospective informations
- Data entries are standardized

Corrective actions can be put in place for above points with more effect on the study conduct (less protocol deviations, more reliable results, etc…)

Conclusions

Paper Diary

- Reviewed at the subsequent clinical visit, if returned
- Possibility to skip entries
- It can be filled retrospectively (incomplete/inaccurate data)

e-Diary

- Real time in-stream data
- Subjects have to fill e-Diary every day: not possible to fill previous or subsequent days and partial fields
- The integrity of data is more reliable

Thank you

Conflict of Interests: Stefano Lombardi and Gabriele Filippo Di Domenico are employees of GSK group of Companies.