



Let's include every data point:

*Overview of Analytical Risk-based Monitoring
with Spotfire Visualizations*

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Agenda

1. Introduction to ARBM
2. Advantages
3. Process
4. Requirement Layout
5. Examples of Quality checks
6. Visualisations illustrations
7. Self Validation Technic

1. Introduction to ARBM

1 Analytical Risk

Analytical Risk Based Monitoring is a clinical trial-monitoring method that fulfills regulatory requirements and helps to identify potential risks. Risks with trial conduct, subject's safety, data integrity, protocol compliance and other factors affecting quality or safety.

2 Quality of Data

The quality of the data can be improved by identifying critical data, performing risk assessment, and developing monitoring plans. With this, reoccurrence of issues can be avoided, frequency of monitoring is reduced, and improves Sponsor oversight of clinical investigations.

3 Mitigating Risk

Mitigate risks by taking measurements to decrease the chances, impact, and/or increase the detectability of issues should they occur.

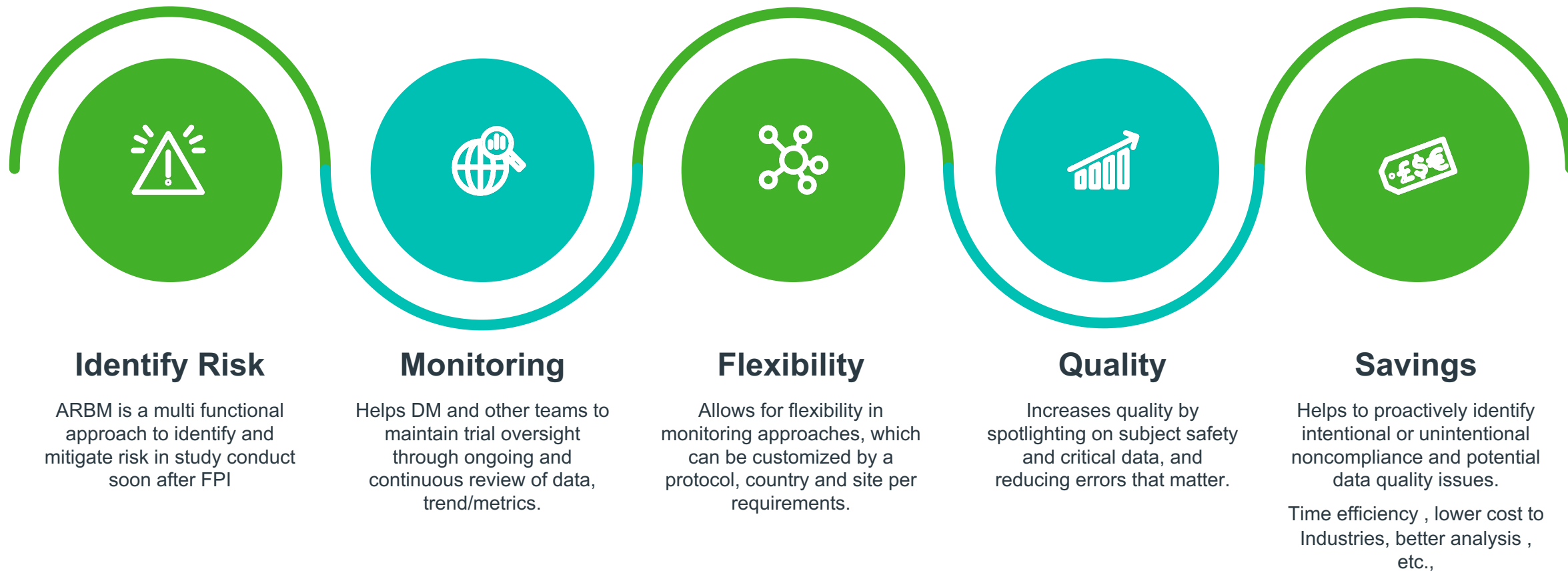
4 Quality Factors

Determine Quality factors by examining the objectives of the trial and defining factors critical to meet End point objectives, while maintaining the safety of subjects.

5 Data Visualization

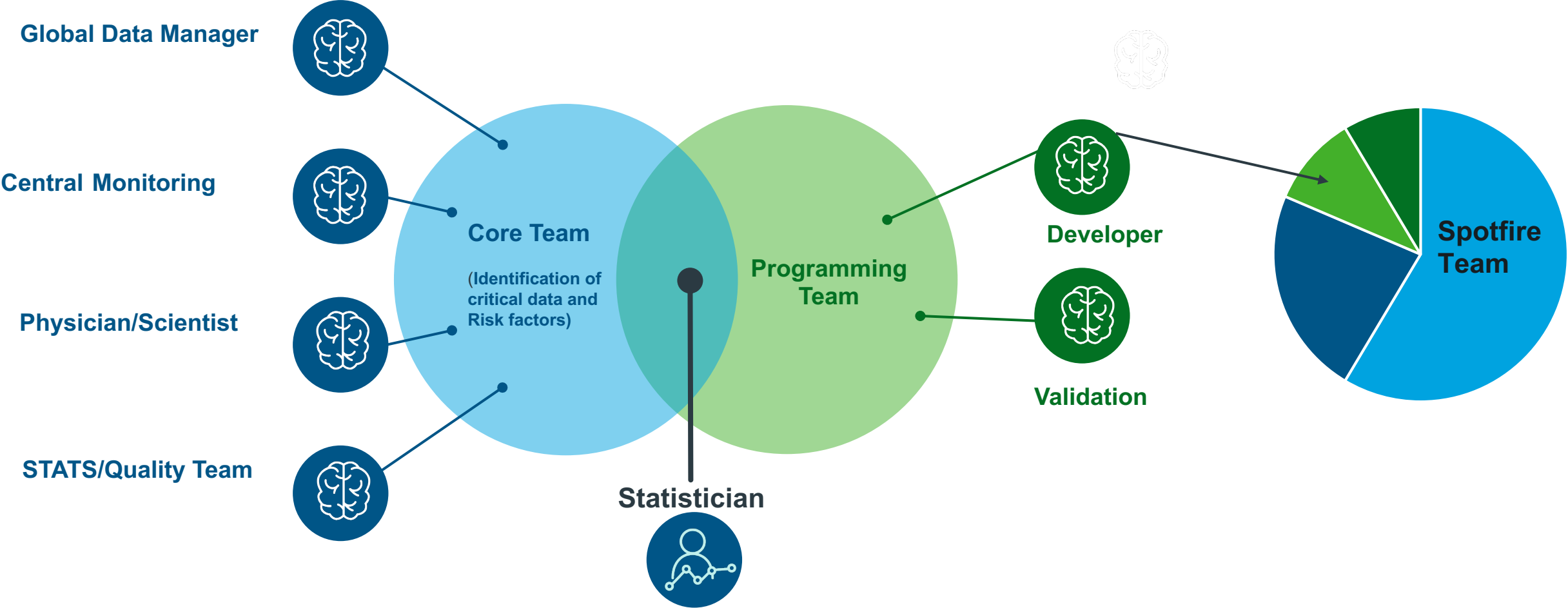
Spotfire helps to visualize the data and easy accessible to each risk factor by Project, Country and Site.

2. Advantages

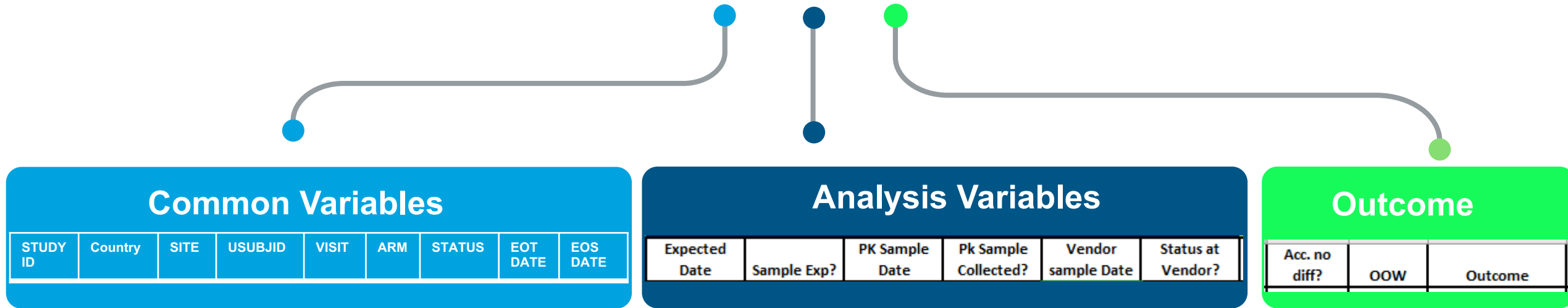


3.Process

As Spotfire team is independent, Programmer have to send final dataset along with visualisation instructions



4.Requirements layout



- Each component plays a different role.
- Data comes from different vendors.
- Input files- Sas7bdat, Excel, csv, txt etc.,
- Important to understand the purpose of Quality check
- Final Datasets: Excel and Sas7bdat

Sample Data: Check whether PK samples were collected at scheduled visits

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R
1	Common variables									Analysis Variables						Outcome Variables		
2	STUDYID	CNTRY	SITE	USUBJID	VISIT	ARM	Status	EOT Date	EOS Date	Expected Date	Sample Exp?	PK Sample Date	Pk Sample Collected?	Vendor sample Date	Status at Vendor?	Acc. no diff?	OOW	Outcome
3	ABC1234	GE	GE1234	81120	C1D1	X	RND			RND+28	Y	2-Aug	Y	2-Aug	Done	No	No	No Issue
4	ABC1234	GE	GE1234	81120	C2D1	X	RND			C1D1+28	Y	1-Sep	Y		Missing	-	No	Missing at Vendor
5	ABC1234	GE	GE1234	81120	C2D14	X	RND			C2D1+14	N	15-Sep	Y	15-Sep	Done	No	Yes	Excessive Sample
6	ABC1234	GE	GE1234	81120	C3D1	X	RND			C2D1+28	Y	29-Sep		29-Sep	Done	-	Yes	Missing at Rave
7	ABC1234	GE	GE1234	81120	C3D8	X	RND			C3D1+8	N	31-Oct	Y	31-Oct	Done	Yes	No	Acc mismatch
8	ABC1234	GE	GE1234	81120	C3D9	X	RND			C3D8+1	Y	Ex:(1st Nov)						Both PK and Vendor are missing
9	ABC1234	GE	GE1234	81120	C3D10	X	RND			C3D9+1	Y	Ex:(2nd nov)						Missing Visit
10	ABC1234	GE	GE1234	81120	C3D20	X	RND			C3D10+10	Y	Ex:(12th nov)						Expected Visit
11	ABC1234	GE	GE1234	81120	C4D1	X	RND	20-Nov		C3D1+28	N	-	-	-	-	-	-	No Issue
12	ABC1234	GE	GE1234	81120	C5D1						Y							NR
13	ABC1234	GE	GE1234	81120	EOT	X	RND			30+Last dose	-					NA	NA	NR
14	ABC1234	GE	GE1234	81120	FUP xx	X	RND			Evry 8 wks	-					NA	NA	NA
15	ABC1234	GE	GE1234	81120	EOS	X	RND			No Derv	-					NA	NA	NR

- Outcome flags should be derived based on criticality of error and it should be meaningful.
- Keep columns related to Quality check
- Label names should be crystal clear(Write as Accession instead of Acc.)
- Flag as NA if visits are not related to Quality Check.

Some common oversight: PK Evaluations

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R
1	Common variables									Analysis Variables						Outcome Variables		
2	STUDYID	CNTRY	SITE	USUBJID	VISIT	ARM	Status	EOT Date	EOS Date	Expected Date	Sample Exp?	PK Sample Date	Pk Sample Collected?	Vendor sample Date	Status at Vendor?	Acc. no diff?	OOW	Outcome
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14	ABC1234	GE	GE1234	81120	FUP xx	X	RND			Evry 8 wks	-					NA	NA	NA
15	ABC1234	GE	GE1234	81120	EOS	X	RND			No Derv	-					NA	NA	NR

1 and 4-Show labels and should be meaningful

2- Add derived expected dates

3- Dates are truncated, check with CM if we need to create risk flag

5- Show source visits too

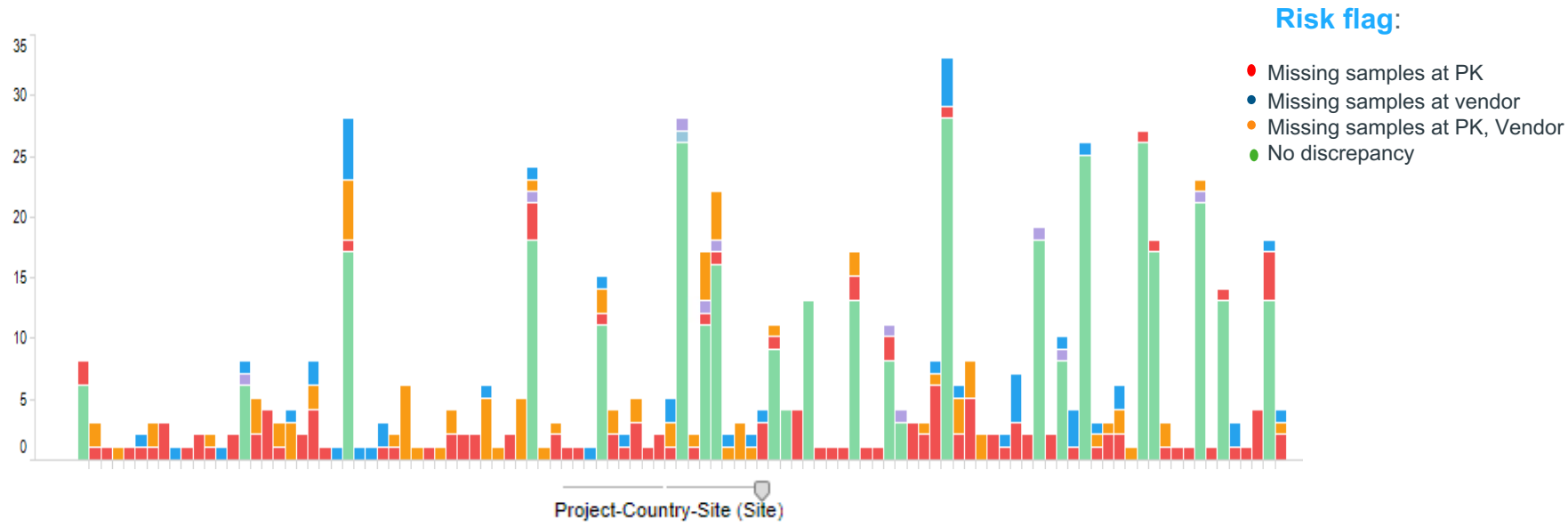
6- Check with CM before including records after EOT.

7 and 8- Expected/Missing visits should not be imputed beyond EOT/EOS

9 and 10- Flag records as N/A or NR if they are not required to analysis

11- Flag in Column M is missing so we need to adjust flag accordingly "Pk flag is missing and Missing at Rave".

Visualisations: PK evaluations



Risk flag:

- Missing samples at PK
- Missing samples at vendor
- Missing samples at PK, Vendor
- No discrepancy

Subject
Type to search in list
(All) 8 values
42479418930000
42479419660000
42479419740000
42479421000000
42479421010000
42479421130000

Geographic hierarchy
Type to search in list
☒ Africa
☒ Asia
☒ China
☒ India
☒ Japan
☒ Europe

Treatment Date Discontinuation
3/4/2016 7/15/2017

PK Evaluations Data

STUDYID	CNTRY	SITE	USUBJID	VISIT	ARM	Status	EOT Date	EOS Date	Expected Date	Sample Exp?	PK Sample Date	Pk Sample Collected?	Vendor sample Date	Status at Vendor?	Acc. no diff?	OOW	Outcome
ABC1234	GE	GE1234	81120	C1D1	X	RND			RND+28	Y	2-Aug	Y	2-Aug	Done	No	No	No Issue
ABC1234	GE	GE1234	81120	C2D1	X	RND			C1D1+28	Y	1-Sep	Y		Missing	-	No	Missing at Vendor
ABC1234	GE	GE1234	81120	C2D14	X	RND			C2D1+14	N	15-Sep	Y	15-Sep	Done	No	Yes	Excessive Sample
ABC1234	GE	GE1234	81120	C3D1	X	RND			C2D1+28	Y	29-Sep		29-Sep	Done	-	Yes	Missing at Rave
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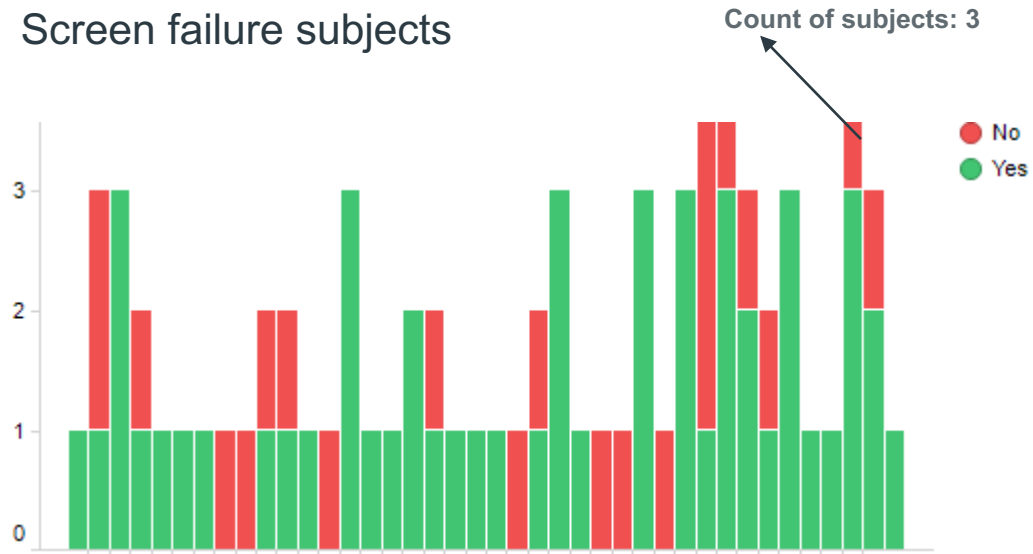
5. Examples of Quality Checks

- Eligibility inclusion/exclusion criteria check
- Subject Disposition
- PK evaluations
- Disease Evaluations must be conducted every 28 days (+/- 4 d)
- Visit compliance
- Subjects should keep to the planned dosing schedule per protocol.
- Hematology and Chemistry sample collection must be done within 48 hours of Day 1 of all Visits
- Vital Signs to be measured in Screening Phase, EOT and during each Treatment Cycle
- Summary of all Quality checks: Trending on overall site quality

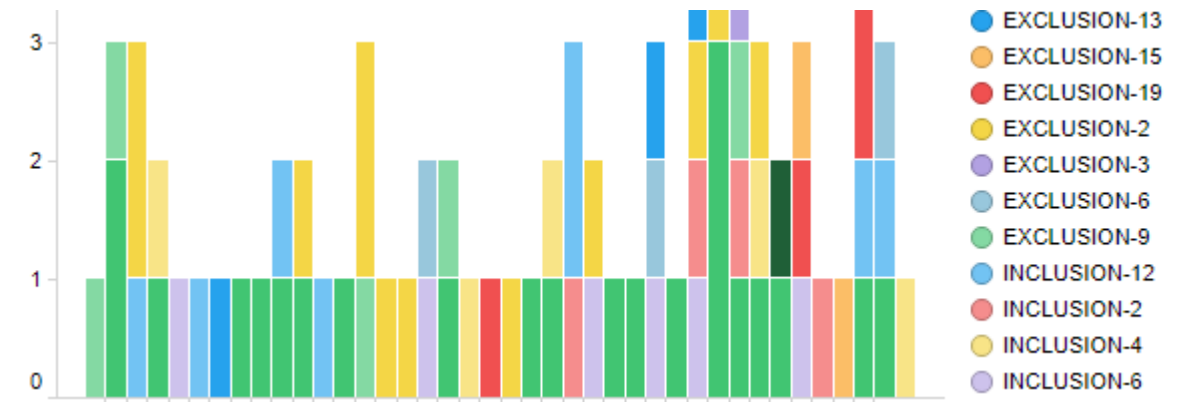
6. Visualisations illustrations

Example1: Eligibility inclusion/exclusion criteria check

Screen failure subjects



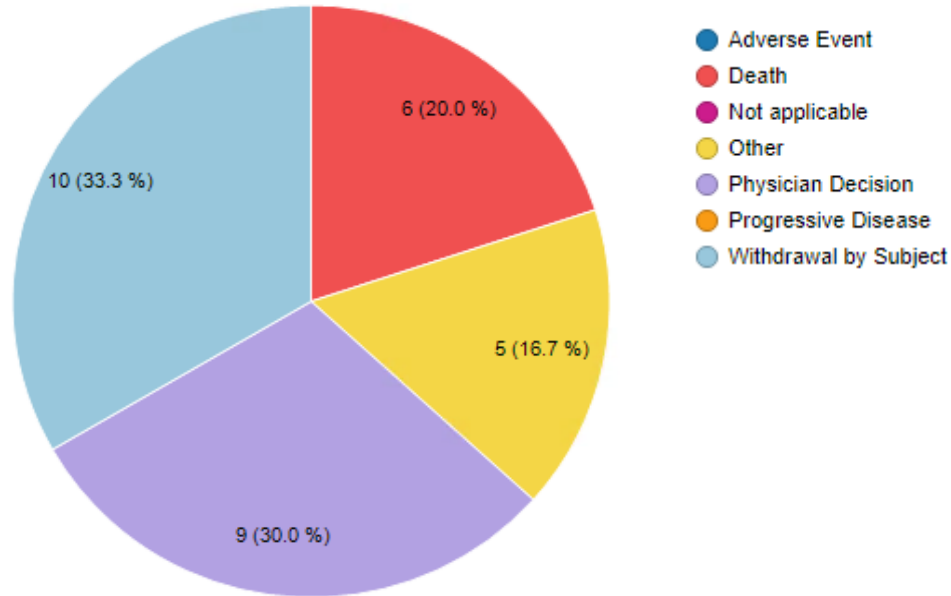
Screen failures - Reasons



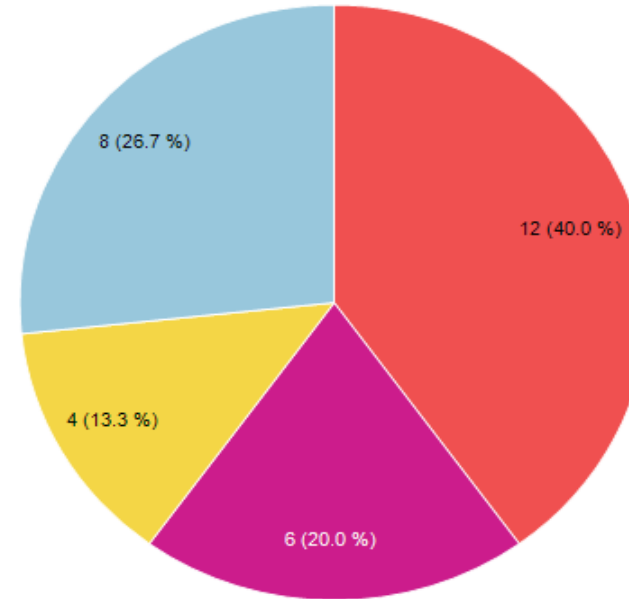
- Counts and Percentages will be popped up if we place cursor on any Project, Country or Site.
- High risk sites on the graph can be easily identified by looking at bars.

Example2: Subject Disposition

Reasons for Treatment Discontinuation

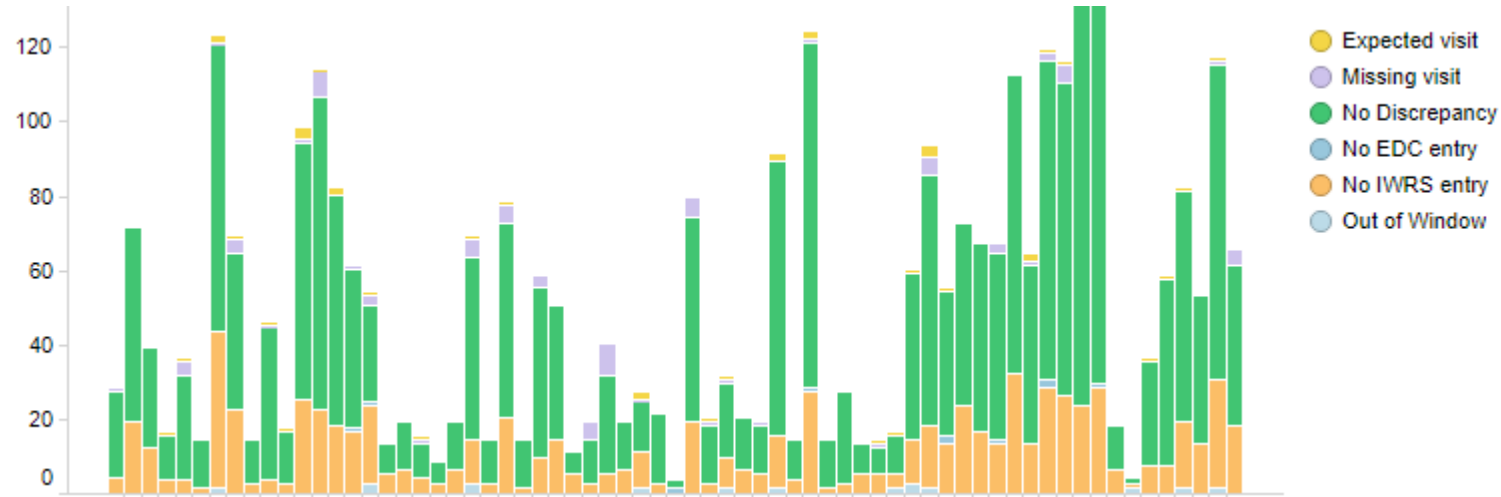


Reasons for Trail Discontinuation

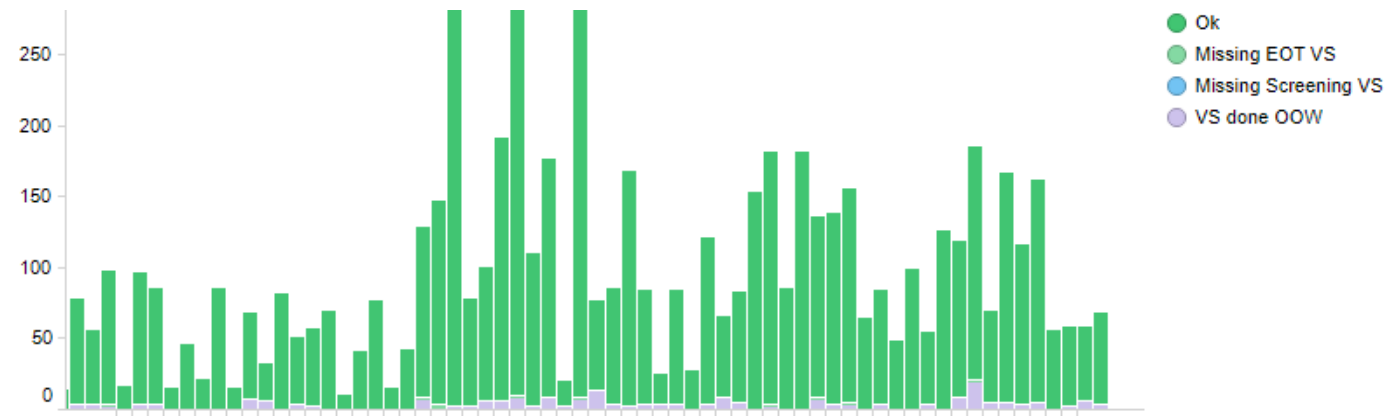


- Easy to know whether the Issue is from latest data transfer or already occurred in past.
- Final dataset can also be displayed just below the graphs or in separate page.
- Each flag color should be unique.
- Separate filters cannot be applied for each graph when we have multiple graphs on single page.
- Graphs and Data will change by default when filters applied.

Example3: Visit compliance

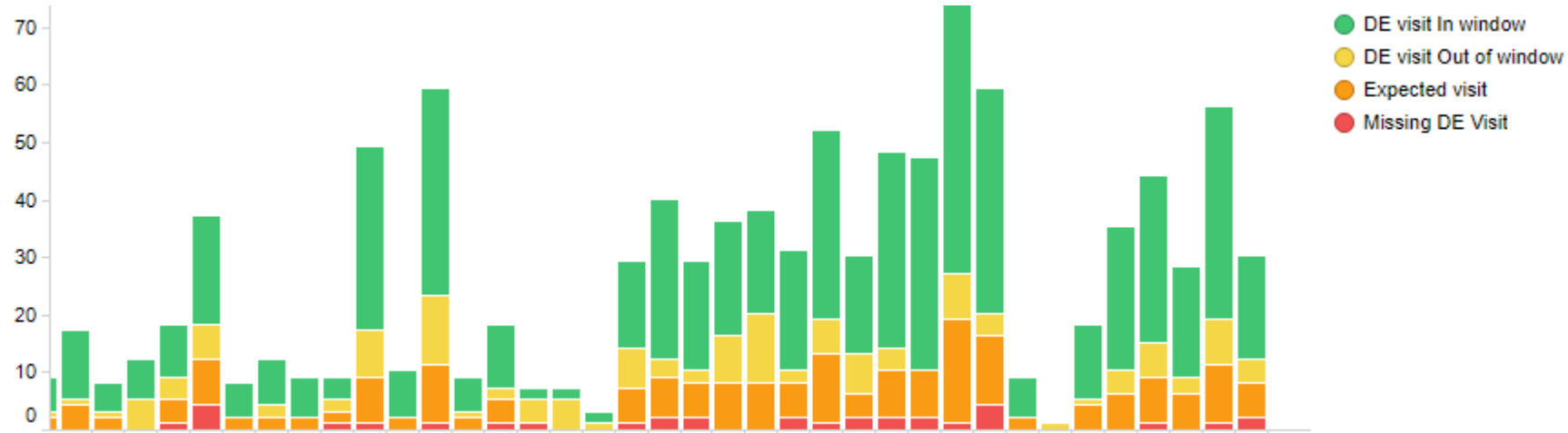


Example4: Vital Signs to be measured in Screening Phase, EOT and during each Treatment Cycle



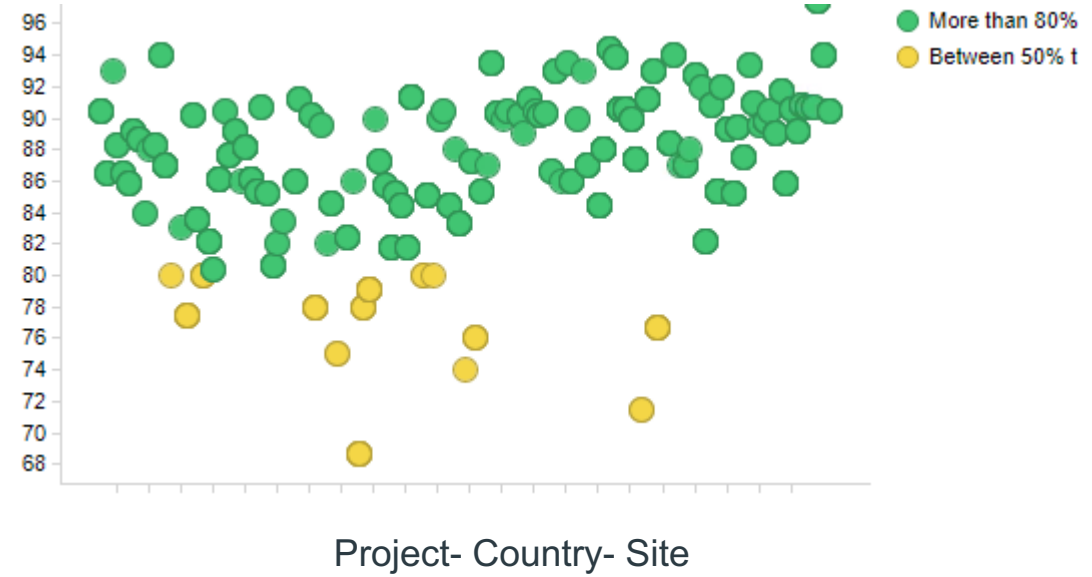
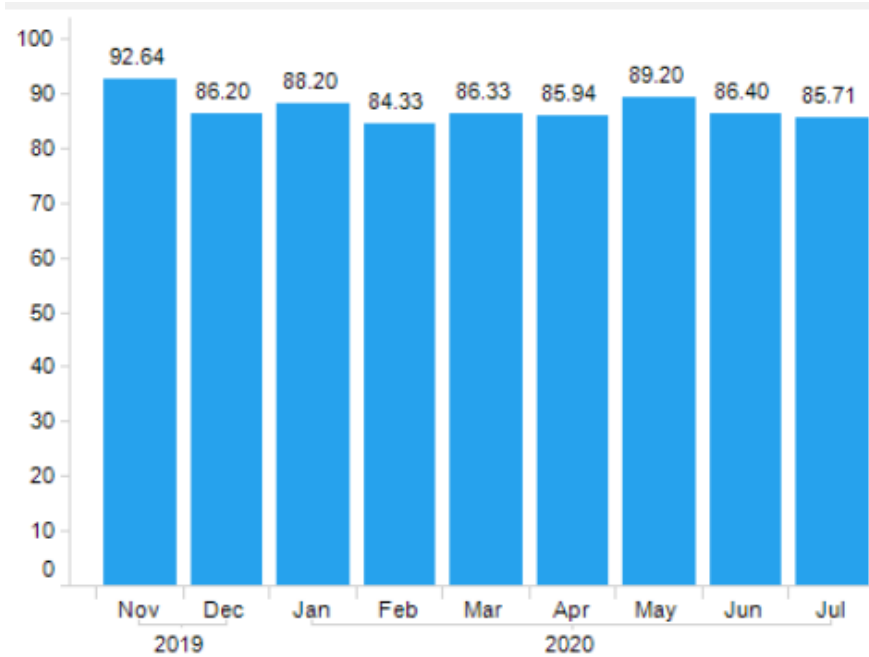
- Y-axis : Number of subjects
- X-axis : Project, Country and Site

Example5: Disease Evaluations must be conducted every 28 days (+/- 8 d)



- Time and events information will be available in requirements or in protocol
- Please also include Excessive samples in the analysis

Example6 : Summary of all Quality checks: Trending on overall site quality



- Left hand side: Weighted average counts and percentages compliance by Month
- Right hand side: Compliance by Project, Country and Site



7. Self Validation Technic

- Check summary statistics on Outcome flags by Project, Country and Site
- Select each outcome and check whether observations meets conditions(the other way around).
- Source information are the key columns for Site review.
- Outcome flags should not be missing.
- Include all data from source data unless specified.
- Duplicate records should also be included and flag them as Duplicate.
- Expected/Missing visits should not be imputed beyond EOT/EOS.
- Order & list of columns, labels and their formats should always match with requirements when preparing data for Visualisations to avoid rework.
- Performance of Visualisations.

Thank you!!!
Any Questions?