Case Study on Central Monitoring in RBM

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BACKGROUND

Because of ICH-E6(R2), the number of trials by RBM has been increasing.

The method of Central Monitoring in RBM has not been established. Several reports have been published US and EU. But, in Japan, sample size of clinical trial is smaller than US and EU. Their methods don't necessarily conform to Japan.

In A2 Healthcare, we have already any experience of RBM trials. We introduce the method of data monitoring by central monitoring for RBM and the case of some results by central monitoring.

DEFINITION OF RBM

3 Monitoring activities

On-site Monitoring

Activities for subjects and sites processes conducted within the sites

Off-site Monitoring

Activities for subjects and sites processes conducted outside the sites

Central Monitoring

Activities for data check across sites conducted outside the sites

THE ROLE OF CENTRAL MONITORING

To realize “Protection of subjects” and “Reliability of trial results” which is the purpose of RBM by the following.

- **For all data and information to be collected in the trial**
- **Monitoring them from a trial perspective in a bird’s-eye view**
- **Confirm the effect of BiQ over data**
- **Early detection of risk**
- **Action instructions for on-site / off-site monitoring**

***BiQ : Built in Quality**

THE ROLE OF CENTRAL MONITORING

Important points

- Which data and what risk can be extracted
- Data extraction method and visualization method are appropriate
- Easy to understand data analysis method and result
- Easy to drill down and be able to visualize
- Don’t be too direct instructions for on-site / off-site
- Confirm the process where the judgment source data occurred

THE ROLE OF CENTRAL MONITORING

About “Which data and what risk can be extracted”

- Monitoring “risk mitigate activities are working”
- Monitoring of trend bias among sites
- Monitoring of outliers of individual subjects
- Monitoring of safety

- Monitoring of fraud

CASE STUDY ON CENTRAL MONITORING

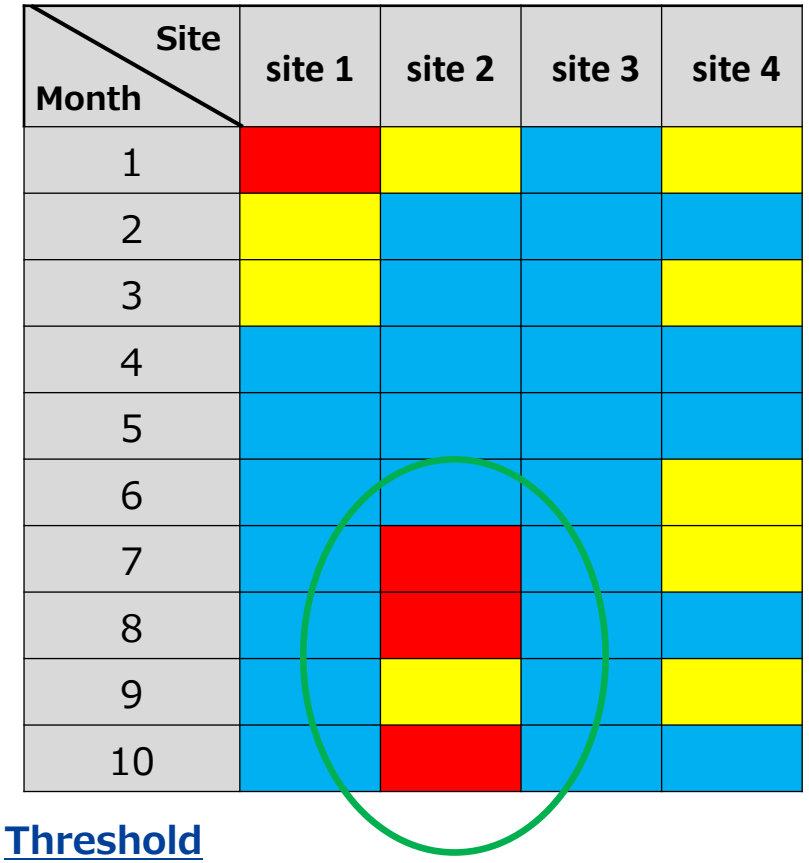
In Japan, there are many small size clinical trials.

We need to find the risk from data of a few subjects.

Following, we introduce cases where risks are found with a few subjects.

CASE STUDY ON CENTRAL MONITORING

Case1. Data entry speed



Month \ Site	site 1	site 2	site 3	site 4
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				

Threshold

Rate that data entry is delayed by 5days

0% 0%< <=25% 25%<

Site2

From 7th month, the delay rate is increasing.

Instruction to implement On-site monitoring from CM.

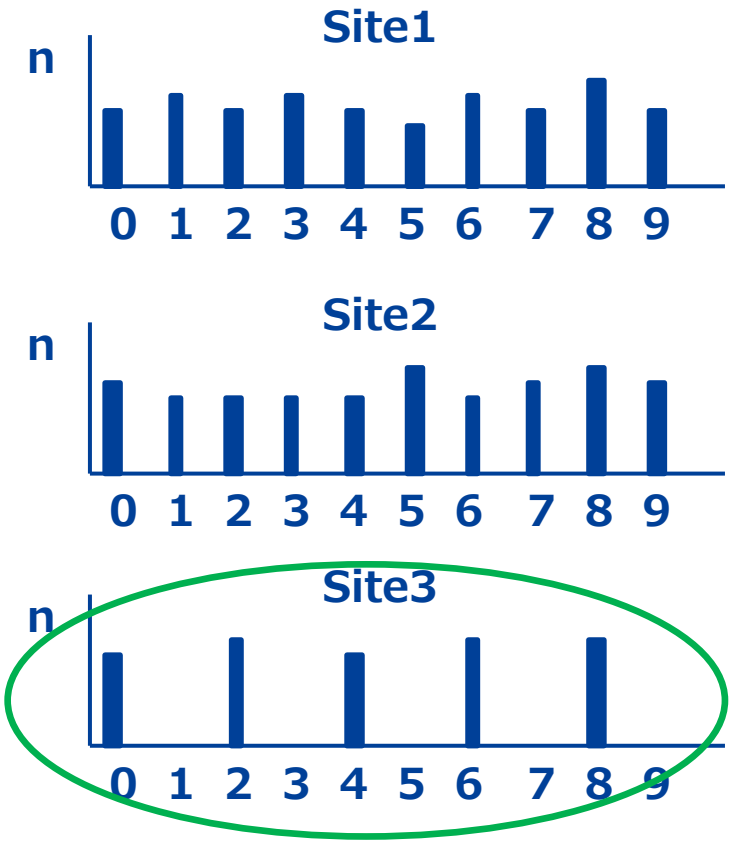
CRC was replaced.

The handover was not enough.

Conducted training additionally.

CASE STUDY ON CENTRAL MONITORING

Case2. Last digit frequency



Last digit (Blood pressure)

Site3

Only even numbers!

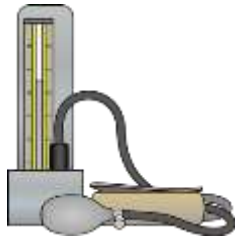
Fraud data?!

Instruction to implement On-site monitoring from CM.

Manually Sphygmomanometer.

Scale is by 2mmHg.

Correct Data!!



CASE STUDY ON CENTRAL MONITORING

Case3. Correlation

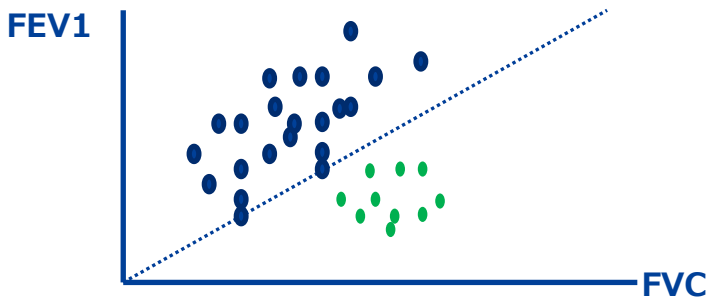
respiratory function test

subject	FEV1	FVC	FEV1/ FVC(%)
001	2.81	3.55	79.15
002	1.98	2.84	69.72
003	4.22	5.20	81.15
004	3.56	3.64	97.80
005	2.36	2.05	86.86
006	3.36	2.30	68.45
007	2.22	3.03	86.20

115.12 ?

146.09 ?

73.27 ?



Site A

FEV1	FVC	FEV1/FVC
XXX	XXX	XXX
XXX	XXX	XXX
XXX	XXX	XXX

Site B

FVC	FEV1	FEV1/FVC
XXX	XXX	XXX
XXX	XXX	XXX
XXX	XXX	XXX

The order of description of the test was different by sites.

Incorrect posting to e-CRF.

We can find the mistakes by checking the correlation of items.

CONCLUSIONS

In clinical trials with a large number of subjects and data, various analyzes can be performed using statistical methods in Central Monitoring.

However, in small size clinical trials, risk and signal can be detected by devising analytical methods considering the characteristics of data. Detection of risks and signals in RBM doesn't require statistical test results to determine something. It only need to know the trend.

It's possible to analyze them by watching the correlation of multiple items rather than analyzing with one item.

REFERENCE

1) Richard C. Z. (2014). Risk-Based Monitoring and Fraud Detection in Clinical Trials Using JMP® and SAS®
2) TransCelerate BioPharma Inc. (2013). Position paper: Risk-based monitoring methodology.
3) Tomoaki Kamiyoshihara. (2017). “臨床PLとしてRBM実装経験から今後システムにきたいすること”. SAS Life Science Forum Japan 2017.