The implementation of RBM in Chugai

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Innovation all for the patients

CHUGAI

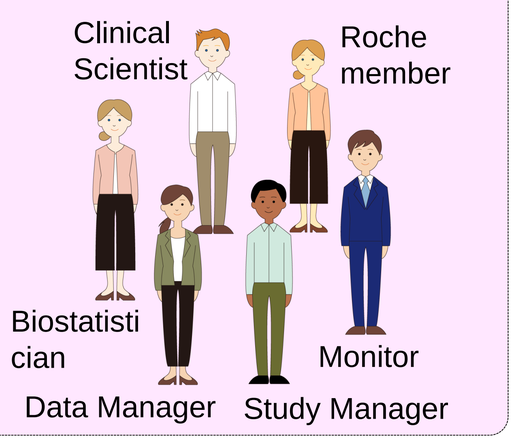
Roche A member of the Roche group

Summary

In Chugai, the RBM project team was launched in February 2015 and the RBM methodology has been deployed in all clinical studies since 2017. I would like to introduce activities carried out by the RBM project team and the Chugai RBM methodology: what kinds of policies each study team has to follow and what kinds of documents each study team has to prepare in study set-up phase and conduct phase e.g.) Study selection criteria, RACT, SDV frequency, functional plans and central monitoring.

RBM project team activity

RBM project team is consisted of several department members.



RBM project team was launched

The number of pilot studies;
- 2 studies for developing RACT
- 2 studies for performing central monitoring

All studies using RBM

The number of studies;
P1 study: 9
P2 study: 2
P3 study: 2

2015 | 2016 | 2017 | 2018

RBM process and templates of RACT and functional plans were developed, referring to Roche RBM methodology

Deployment activities;
- Poster session, hands-on session
- e-learnings
- Monthly Newsletter email
- Presentation in each department meeting

RBM maintenance team is supporting each study team

Chugai RBM Methodology

RBM implementation study criteria

*) At the beginning of each clinical study, study team decides 'Central monitoring' is necessary to be performed based on the following study criteria.

- < 3 investigational sites
- <12 months/ 1 trial duration
- < 3 months/ 1 subject trial duration
- <20 subjects

Study	RACT	Functional plan	Central monitoring	RACT reflected monitoring
P I , CP study	V	V	NA	V
P I/II, P II study	V	V	V *	V
P III study	V	V	V	V
P IV study	V	V	V	V
Compassionate Use for Japanese	V	V	V	V

Set up Phase

Develop RACT

Study team develops RACT in order to:
- Identify critical data and critical processes
- Assess risks (30 items/12 categories** in the template) in terms of 'Impact', 'Probability' and 'Detectability' by scoring
- Determine risk mitigation plans for each identified risk

**) '30 items/12 categories' are based on the Roche RACT template.

By scoring each risk item, the overall study risk level is automatically calculated.

Overall Study Risk Level		
High	Medium	Low

Develop each functional plan

Study team develops each functional plan based on RACT output (risks and mitigations).

TMP (Trial monitoring plan) — Monitor
Describes what activities should be done at off-site or at on-site

MDRP (Medical data review plan) — Clinical Scientist
Describes medical data review focusing on critical data

DQRP (Data quality review plan) — Data Manager
Describes review tasks mainly performed by DM and provides a list of critical data fields to be SDVd

Central monitoring

CMP (Central monitoring plan)

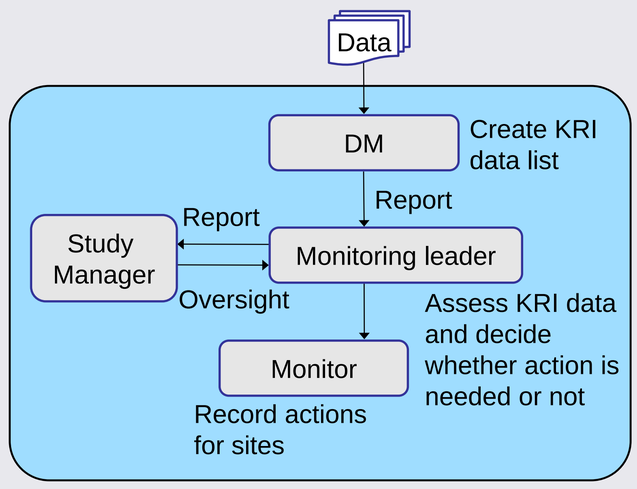
The definition of 'Central monitoring' in Chugai RBM is the process to assess site performance by using Key Risk Indicator (KRI) data.

Thresholds are assigned for each KRI in 3 ranges; an acceptable range (green), an awareness range (yellow) and a warning range (red).

In case, 'Central monitoring' is not performed based on the study criteria, DM provides other data list that can be checked the progress of visit/AE data entry and query response.

Chugai standard KRIs: (Rave data)
1. Proportion of visit data entry
2. Proportion of AE data entry
3. Query rate for system query
4. Query rate for manual query
5. Proportion of query response for system query
6. Proportion of query response for manual query
7. AE reporting rate
8. Proportion of discontinuation
9. Number of discontinuations
10. Number of deviations
11. Number of major deviations

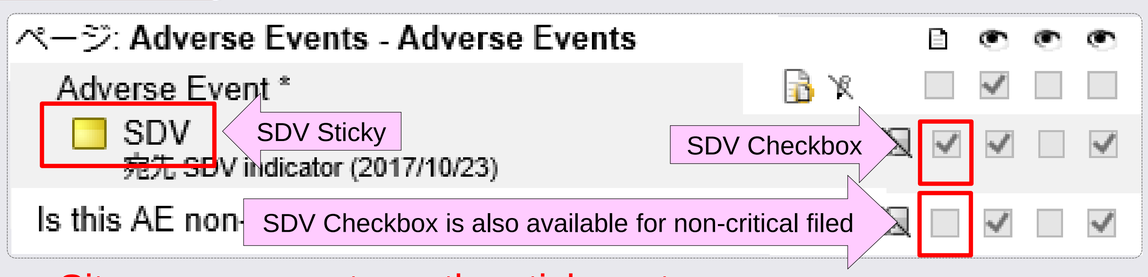
Central monitoring workflow



SDV/SDR

The RACT outcome determines the amount of SDV/SDR to be performed, per subject.

Critical data fields to be SDVd are set up in Rave with 'Sticky Notes' function by using Custom Function, and monitors can quickly identify them.



- Site users cannot see the sticky notes.
- If data is changed after the SDV checkbox has been checked, the SDV marker will be unticked and the sticky note will reappear.

Monitoring Activity	Overall Study Risk Level		
	High	Medium	Low
SDR of Critical Data and Processes for 1st Randomized Subject at each site	100%	100%	100%
SDR of Critical Data and Processes for Subsequent Randomized Subjects	33%:1 in 3 subjects	20%:1 in 5 subjects	10%:1 in 10 subjects
SDV of Critical Data Fields for 1st Randomized Subject at each site	100%	100%	100%
SDV of Critical Data Fields for Subsequent Randomized Subjects	25%	15%	5%

Conduct Phase