



Risk Based Monitoring

REX
&
New challenges

Agenda

❖ RBM implementation

- Milestones
- Our vision and strategy
- Change management
- Metrics

❖ Process Continuous improvement

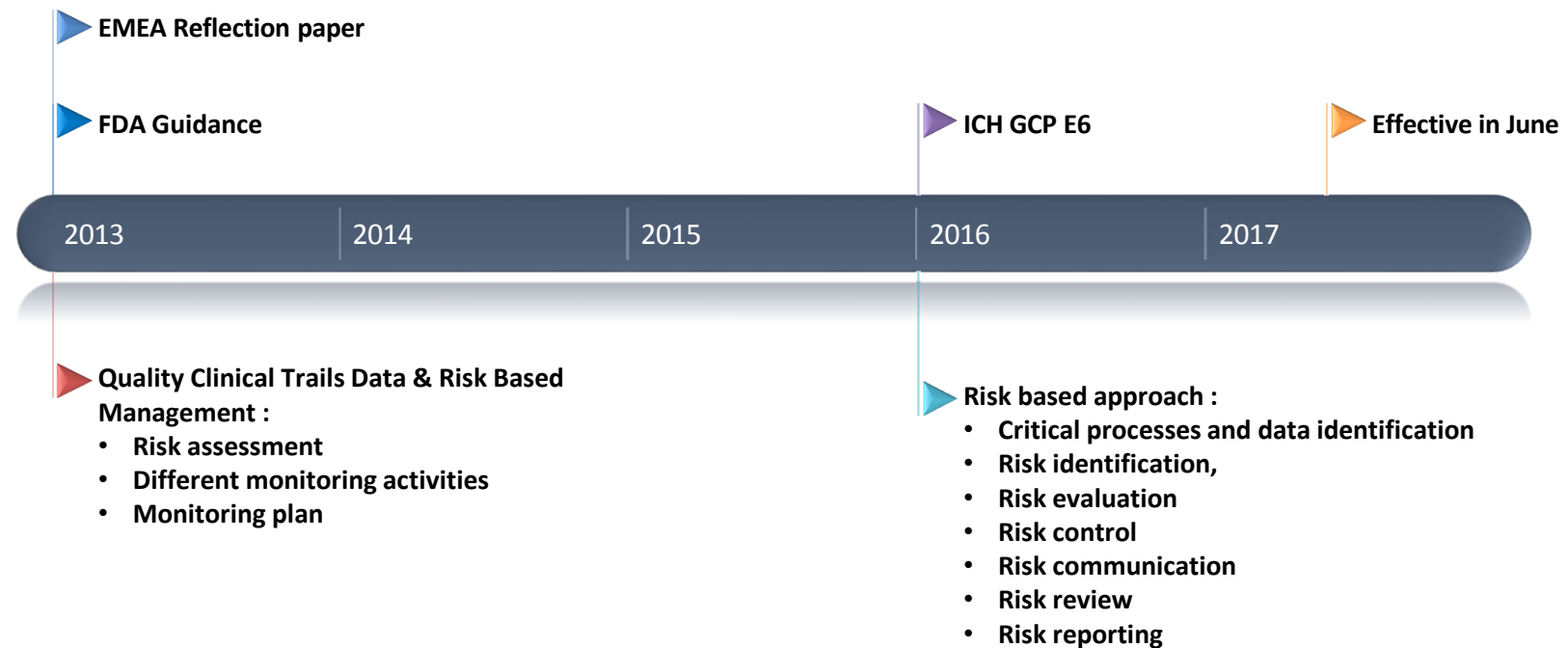
- PIL, Small trials
- Next challenges

RBM Implementation

Milestones



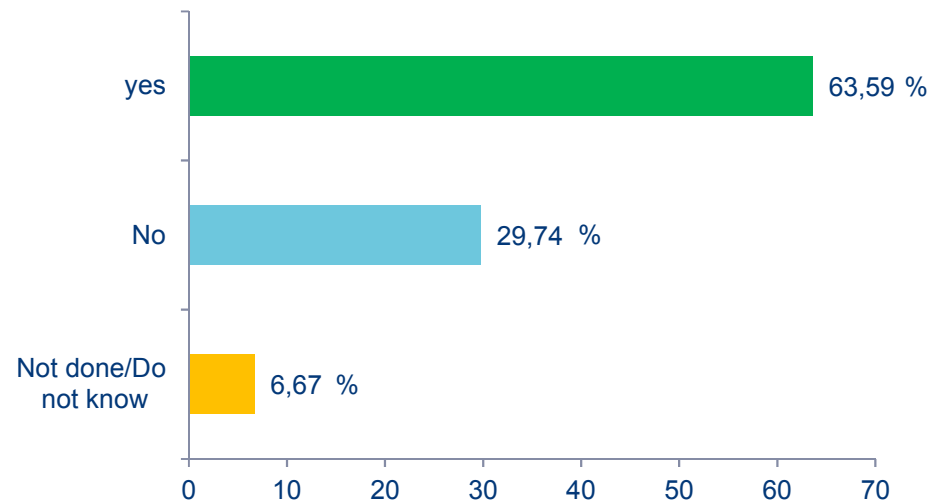
Milestones - Guidelines



Milestones - Guidelines

OmniComm : RBM&ICH-E2 (R2) adoption industry Survey* - July 2018

Are you currently using RBM?



***195 answers :**



Our milestones

13/11/2018

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Implementation
to all new studies

2013

2014

2015

2016

2017

2018

2019

2019

Strategy set-up

2 pilot studies

REX

Continuous improvement phase

Process review

Next challenges

Methodology

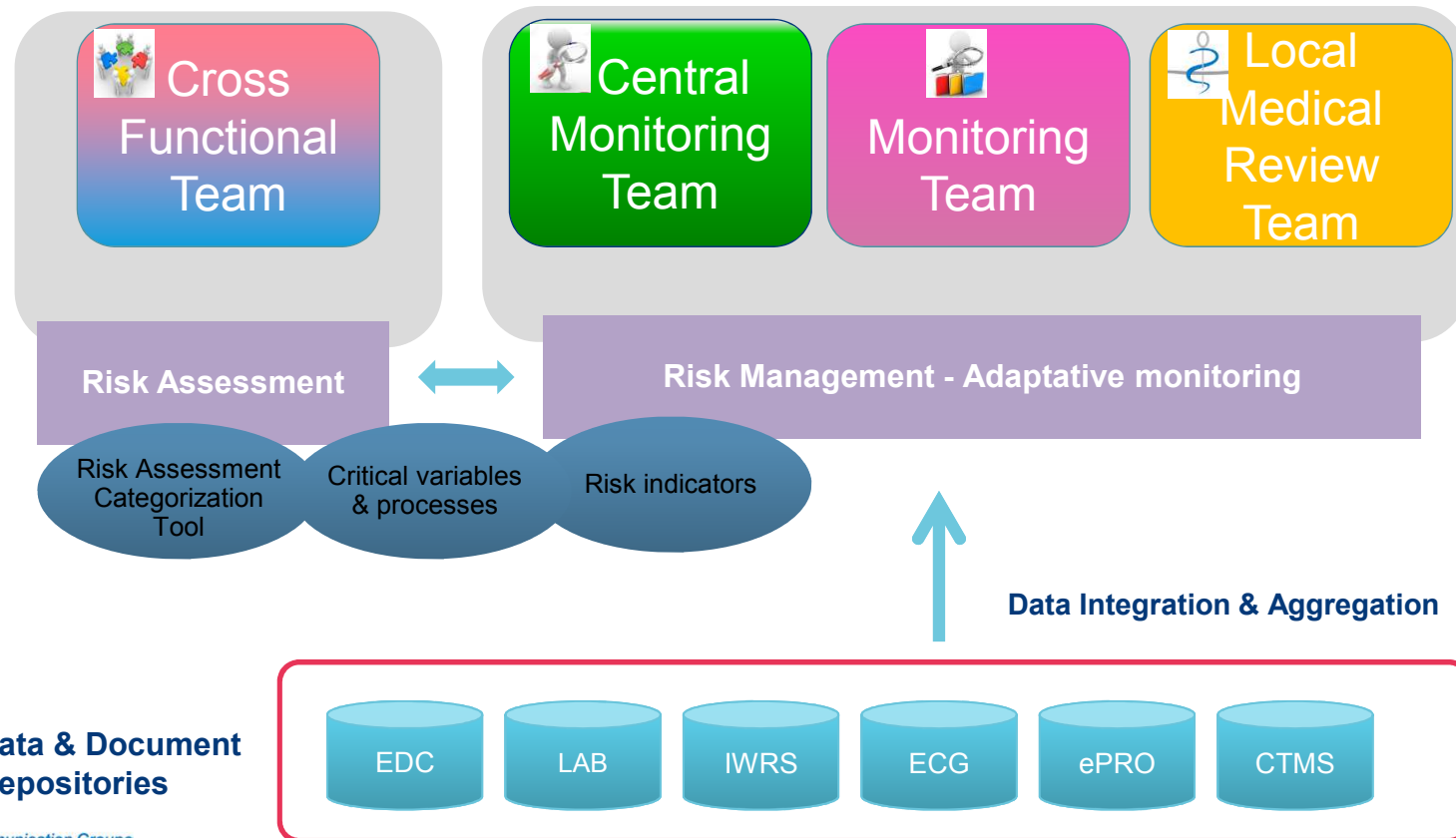
- Complete Risk Assessment Categorization Tool (RACT)
- Identification of Critical Data and Processes
- Define risk indicators / Thresholds
- Central, on-site/off site monitoring

RBM Implementation

Our vision and strategy



Our vision of RBM : Cross functional cooperation



Data & Document Repositories

Our vision of RBM : Central monitoring team

A remote evaluation carried out at regular intervals to assess study quality and identify potential risks



Data Review & Surveillance

1. Data Review & Surveillance (DRS) meetings
2. Targeted validation (validation plan)
3. Reviews of data

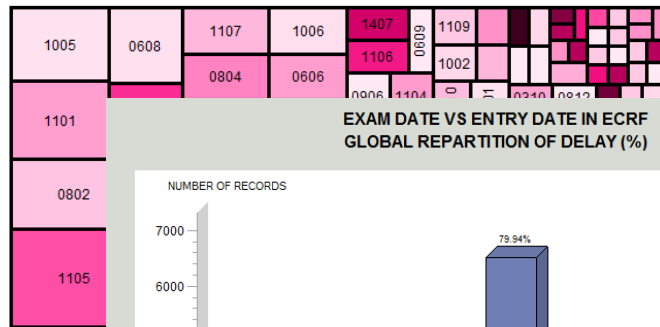
Data Review & Surveillance meetings

- From analysis of risk indicators, identify country/ sites with potential unusual behaviour
 - ❖ from other countries/sites
 - ❖ from thresholds
- Frequency : every 2 months (but adapted to study recruitment)

Data Review & Surveillance meetings

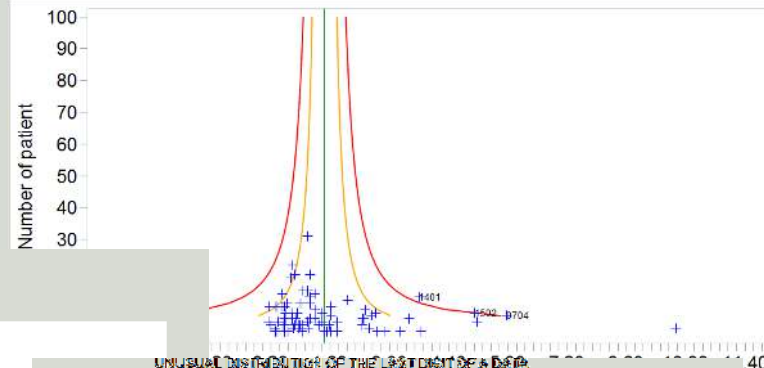
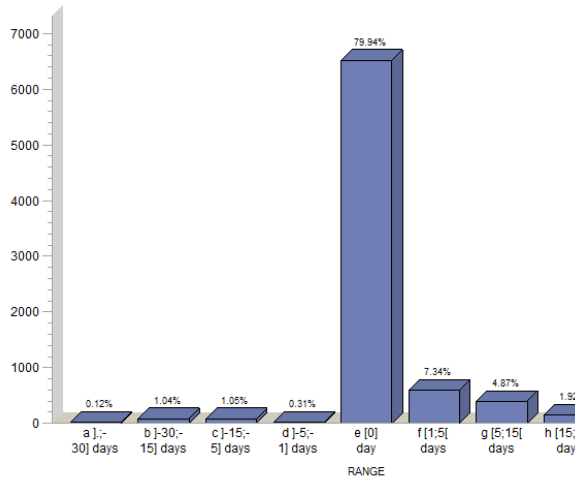
**GEOGRAPHICAL PATIENTS DISTRIBUTION BY CENTRE
NUMBER OF DEVIATIONS IMPORTANT BY VISIT**

CENT_ID

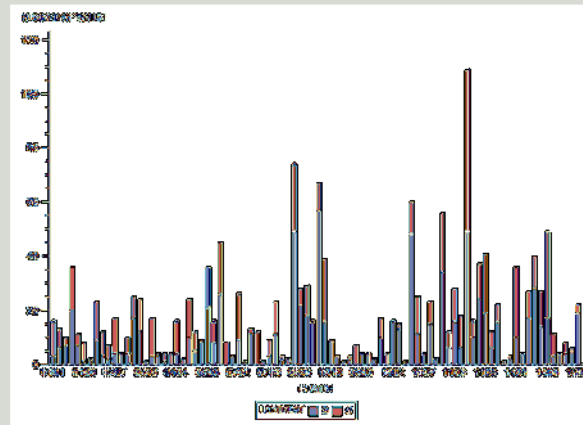


**EXAM DATE VS ENTRY DATE IN ECRF
GLOBAL REPARTITION OF DELAY (%)**

NUMBER OF RECORDS



UNUSUAL DISTRIBUTION OF THE LAST DATE OF DATA
Panel: BARTHEL - Item: IT5061 - Label: BARTHEL IT5061

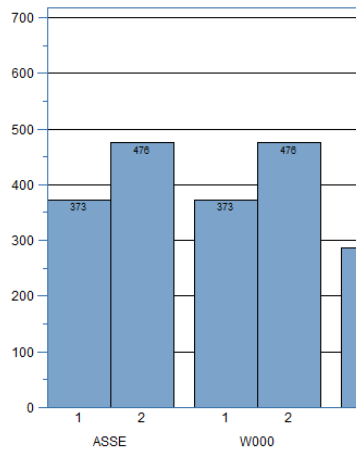


Data Reviews

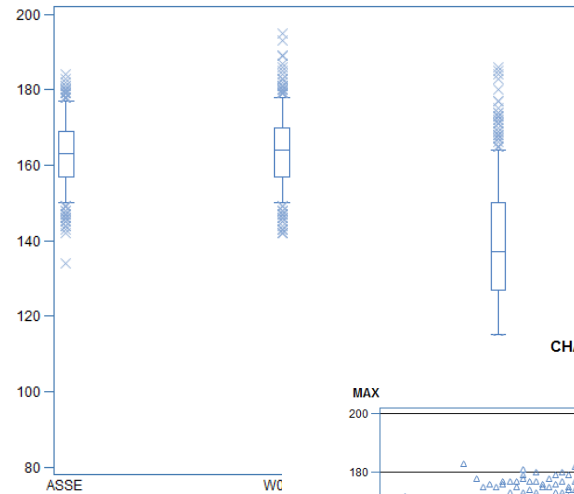
- Global review of data during preparatory/final blind reviews
- Strategy: defined at the beginning of the study (frequency, specific population, cut-off date)
- Review done on clean data

Data Reviews

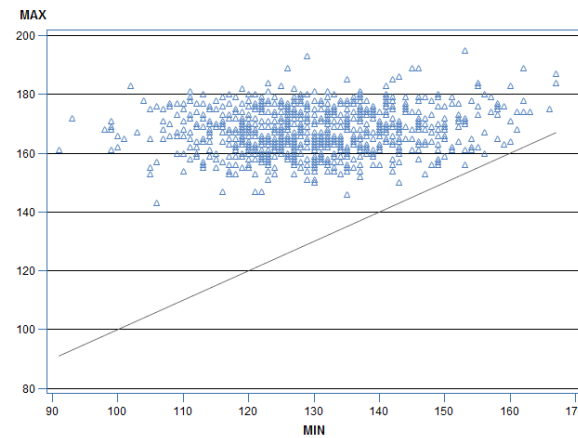
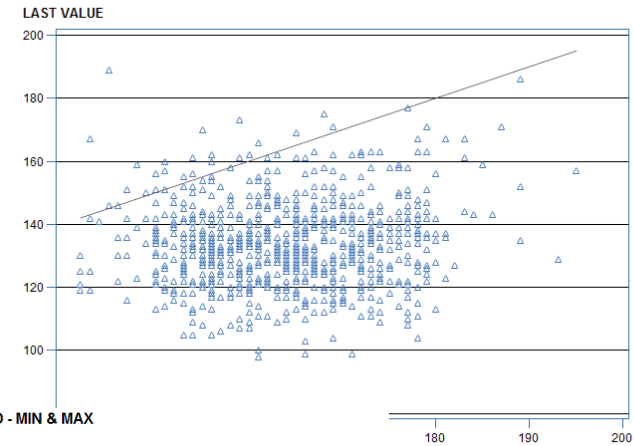
NUMBER OF PATIENTS



Legend - Number of PATIENTS ■ WITH NUMERIC VALUES



CHANGED - BASELINE (W000) & LAST VALUE (W012)



RBM Implementation

Change management



Global change of mindset

RBM means

increase quality by :

- Risk assessment at project/Study/ Site level
- Focusing on critical data& processes
- Adaptability to reassess project/study risk throughout data analysis
- Adaptability to reassess site oversight throughout performance analysis

RBM does not mean

- Take risks
- Less oversight
- Less contacts with sites



REX after 1st pilot study – feedback questionnaires

- Feedback from Investigational sites and Servier monitors



Investigators understand the role of RBM improving quality and efficiency

58
%

More responsible for the quality control and entry of data

39
%

Focus on data and processes for the patients safety and data reliability

=

Impact on the workload



86% monitors have impression of being focused on what really matter

New roles/responsibilities

NEW RESPONSABILITIES



NEW ROLES

- Data-manager: detects risks and trends through risk indicators analysis and data reviews
- RBM referents : help teams in RBM implementation on their study and answer questions about RBM process.
- RBM process referent for global evaluation of the process

RBM Process efficiency

Metrics

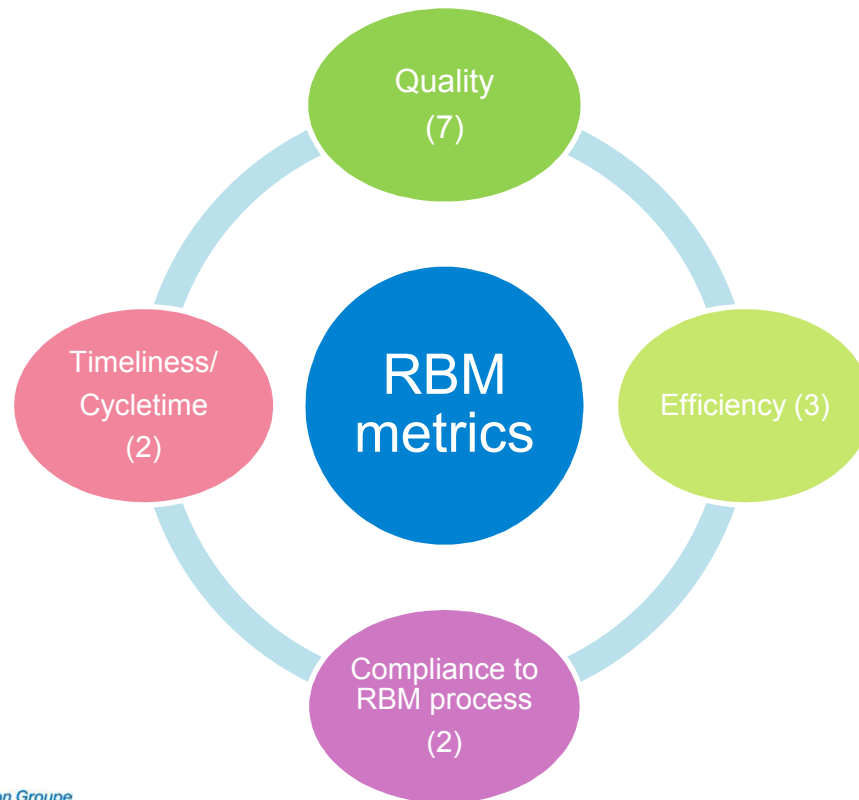


Metrics

To measure:

- the impact and effectiveness of the RBM methodology on managing quality and risks associated with the conduct of clinical studies
- if the RBM methodology works from the standpoint of operational impact on an organization, clinical sites and investigators.
- if the conduct of clinical study is compliant with RBM process

Metrics



- To compare:

With previous studies using traditional monitoring strategy

Within the study: not monitored patients (not SDV/SDR) with monitored patients (SDV/SDR)

Metrics - Dashboard

Dimension	Metric
Quality	Number and classification of major/critical audit/inspections findings per audited site
	Mean number of important protocol deviations per patient
	Mean number of important protocol deviations per not SDV/SDR patients
	Mean number of days between SAE/ERIN onset and reporting
	Mean number of days between SAE/ERIN onset and reporting for not SDV/SDR patients
	AE monthly rate
	AE monthly rate on not SDV/SDR patients

Timeliness/ Cycle time	Median number of days from visit to CRF data entry
	Median number of days from query open to close

Efficiency	Time spent by CRAs for study activities
	Mean number of visits performed between 2 monitoring visits
	Mean interval between On-site Monitoring visits per site

Compliance to RBM process	% of SDR performed vs % of SDR planned in MP
	% of SDV performed vs % of SDV planned in MP

Metrics - Dashboard

- Measured at each DRS time point
- Retrieved for all studies to obtain a global dashboard



REX after 1st pilot study – Metrics vs benchmark

Based on Risk-Based Monitoring update – Volume V (2016):

TransCelerate utilizes a core group of 8 metrics focused on quality, efficiency and cycle time. A blind third party has collected metrics from member companies where RBM has been implemented.

Metrics	Trancelerate expected outcome	Our outcome (vs internal benchmark)
Mean number of days from patients visit to eCRF data entry	no change or time reduction Vs baseline	Significant reduction
Mean number of days from query open to close	result not changed Vs baseline	Significant reduction
Significant protocol deviations rate per treated subject	protocol deviations decreased Vs baseline	Significant reduction
Average interval between on-site monitoring visits per site	an increase of the interval between on-site visits vs baseline	Decrease of interval at beginning – Significant reduction after 14 month

RBM Process Continuous Improvement



Small Trials

PIL

Small trials : PKH/CL1

- Fast study, need more reactivity
- Statistical methods with few data can generate false positive
- Few risk indicators to be followed
- No DRS meeting but frequent review of these risk indicators

RBM should not be « a one fit it all » strategy
=> adaptative strategy

PIL (Patient identification List) = Patients to be SDV/SDR

- Automatic randomized program:
 - Too frequent run => rounded calculation led to a higher percentage of SDV/SDR
 - Too unfrequent run => monitors does not know which patients to SDV/SDR when they go on-site
- PIL identified at the start of the study (1st, 3rd, 7th... subsequent included patients)

Tools should be a help, not a constraint

Next Challenges

Next Challenges

RBM => RBQM
Risk Based Quality Management

RBQM

Next Challenges

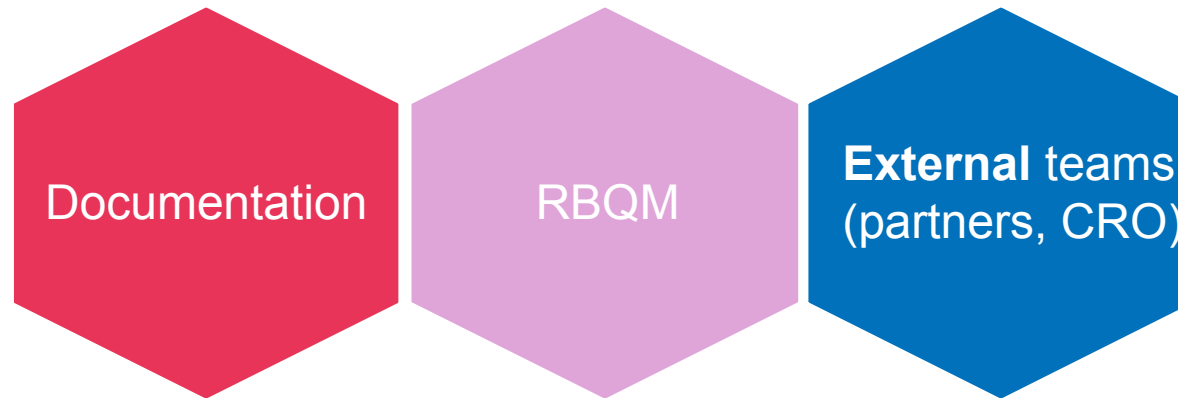
How to document all the actions taken,
the follow-up of these actions

Documentation

RBQM

Next Challenges

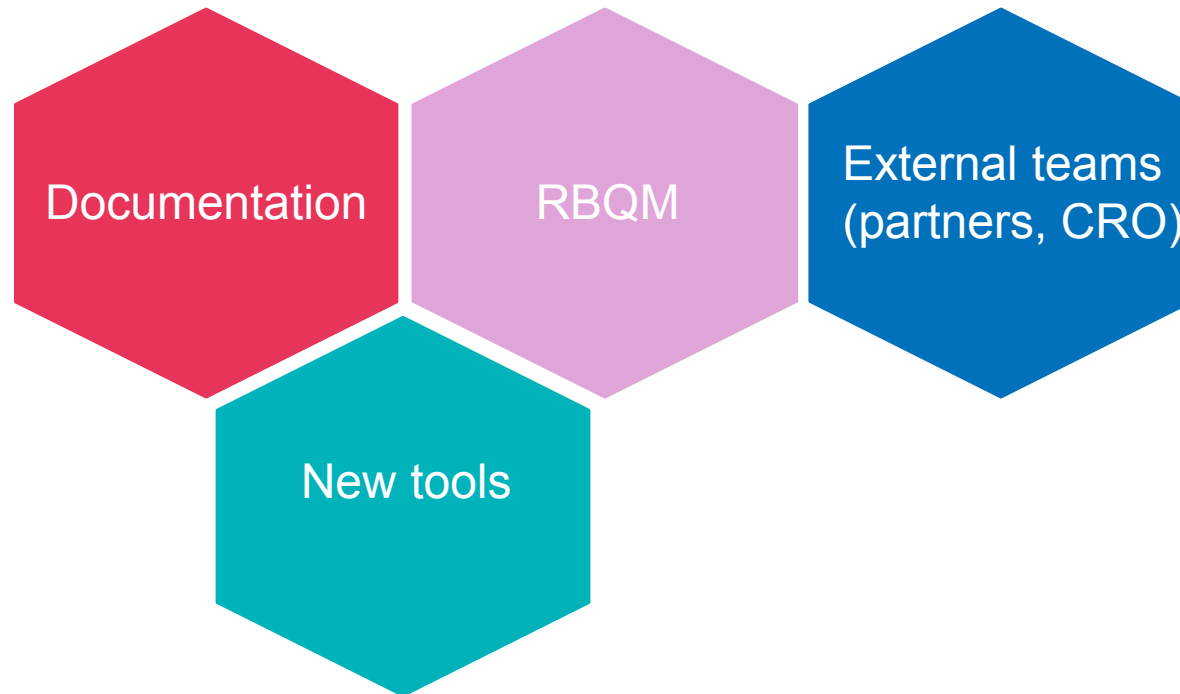
adapt our tools/processes



Next Challenges

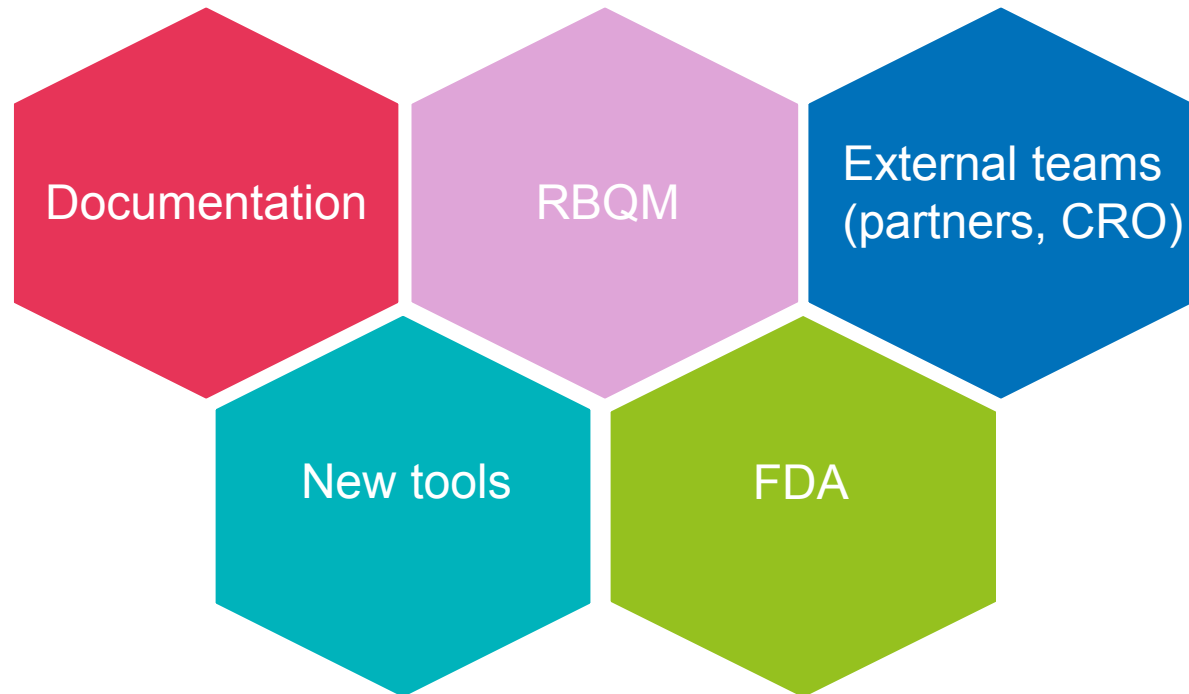
Identify benefice/costs

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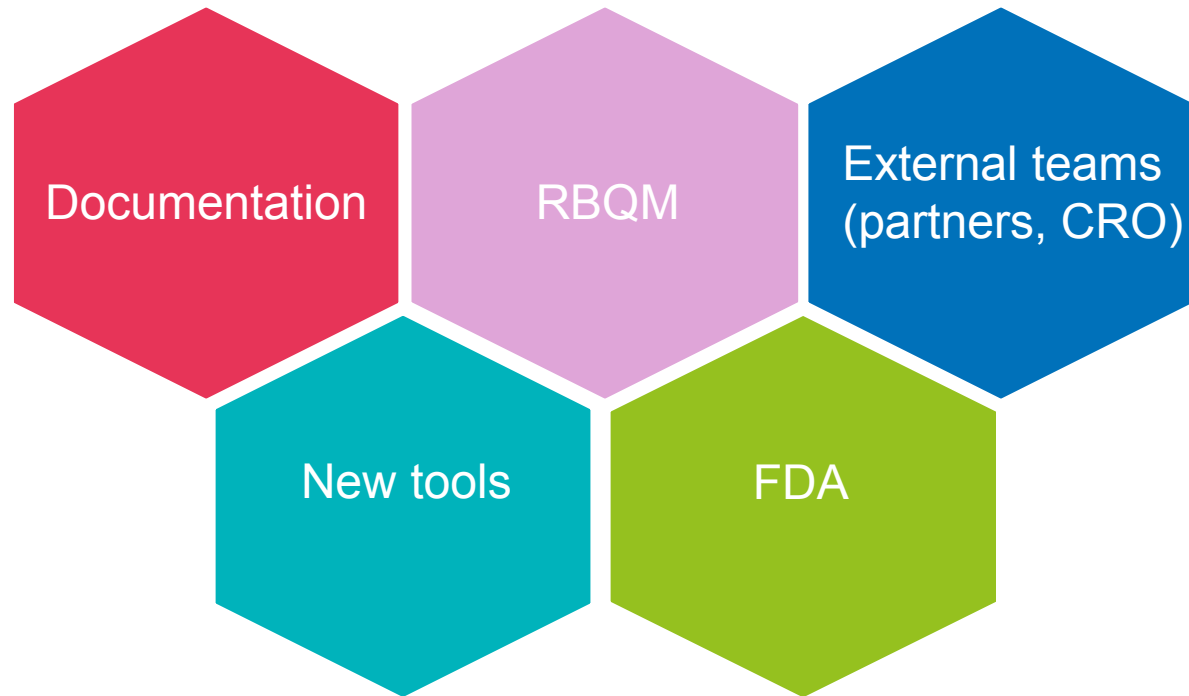


Next Challenges

First feedbacks from FDA inspections



Next Challenges





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RBM

Themes & Questions

Are you currently using RBM?

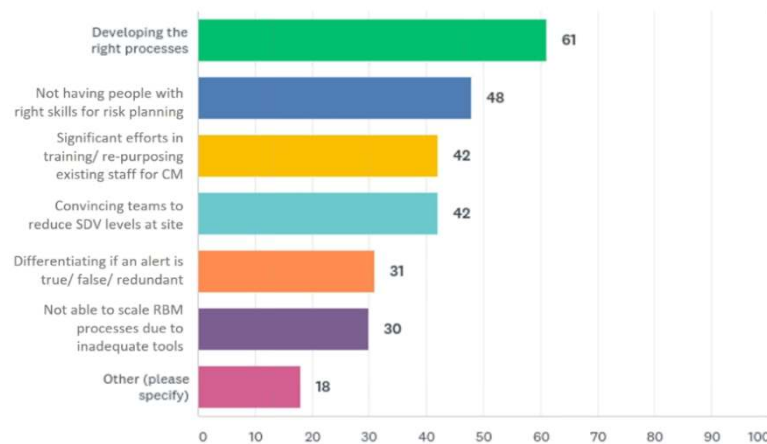
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Themes & Questions

Are you currently using RBM?

- what are the top challenges you face?



RBM&ICH-E2 (R2) adoption
industry Survey – results - July
2018
OmniComm



RBM

Themes & Questions

How do you measure and analyse study performance and risks?

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RBM

Themes & Questions

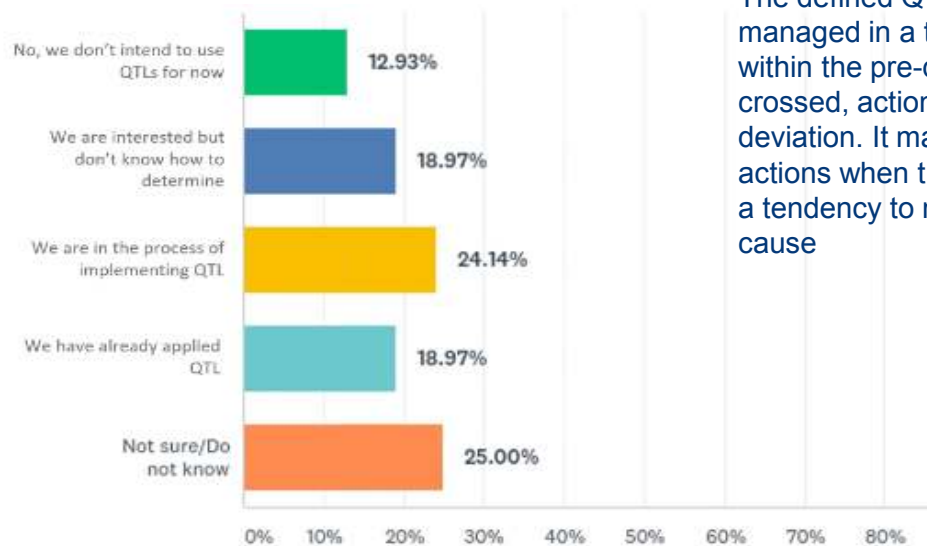
What is your approach to perform central monitoring?

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Themes & Questions

Do you set Quality Tolerance Limits (QTLs)?

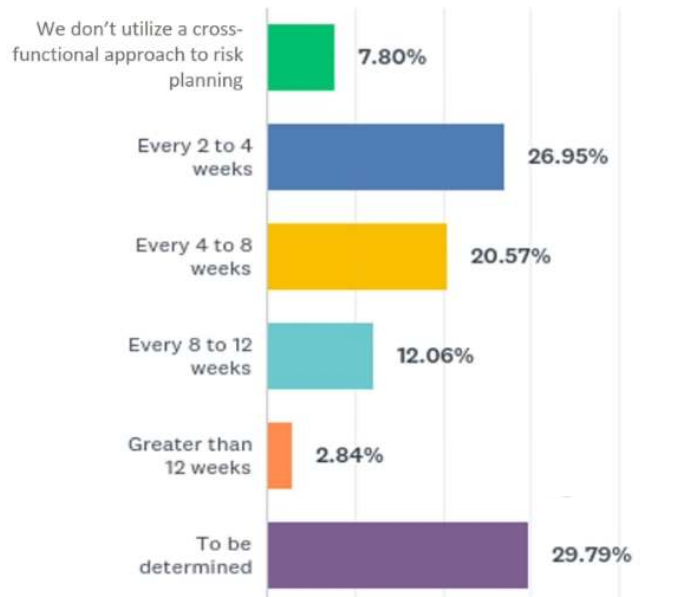


The defined QTLs constitute a limit for the parameters that are managed in a trial. As long as the risk under consideration remains within the pre-defined limit, the quality is adequate. If limits are crossed, actions need to be undertaken to assess the cause for this deviation. It may be advisable to establish secondary limits that justify actions when the identified risk is still in the tolerable range, but shows a tendency to move towards the QTL due to some systematic root cause

**RBM&ICH-E2 (R2) adoption
industry Survey – results - July
2018
OmniComm**

Themes & Questions

How frequently do you review the risk assessment on a study?



RBM&ICH-E2 (R2) adoption
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Themes & Questions

How do you manage issues identified by RIs ?

- Do you have a specific tool? Internal/external?
- Any feedback on the existing tools?

Themes & Questions

How do you manage issues identified by RIs ?

- Is the solution is always increase of SDV/SDR?



RBM

Themes & Questions

What are the impacts of GDPR on RBQM?

13/11/2018

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