Monitoring & Centralized Monitoring : a Risk-Based Approach
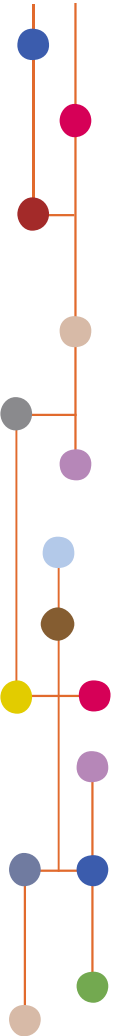
Soazig Chevalier,
Sanofi RBM-PM

DMB Conference - Paris
14th November 2017

- **RBM: General context**

- **Centralized Monitoring and Monitoring at Sanofi**
  - **What ?**
  - **How ?**
  - **Who ?**

- **Conclusion**

Why RBM?

TRADITIONAL APPROACH
On-Site Monitoring
100% SDV performed at regular intervals regardless of site performance

- More Patients
- More Complex CRF
- More Sites

- Time consuming
- High costs
- Data quality not guaranteed

**MHRA
EMA
FDA
ICH
TransCelerate**

ICH
ICH
harmonisation for better health

E6-R2 GCP Guideline
"Quality Risk Management principles and methodologies in clinical development"

HEALTH AUTHORITIES TRANSITION TO RBM
recommends a quality risk-based approach inclusive of RBM

Why RBM?

RISK BASED MONITORING :

An **adaptive** approach to clinical trial monitoring that **directs monitoring focus and activities** to the evolving areas of greatest need which have the most potential to impact **patient safety and data quality.**

(TransCelerate Definition)

RBM Objectives

Improve data quality

Give more added value to monitoring activities

…while continuing to ensure patient safety

Agenda

- **RBM: General context**

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... before RBM implementation :

Study Risk Management Plan (SRMP)
➢ Critical data/critical processes
➢ Risks categorization
➢ Risk assessment

Centralized Monitoring
➢ Medical review
➢ Safety review
➢ Data Review
➢ Data Surveillance (incl. statistical tests for Scientific Misconduct Detection)

Monitoring
➢ Focused and Random Source Data Verification (SDV)
➢ Source Documentation QC
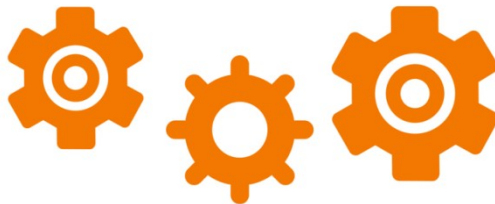➢ Regular Monitoring Visits

3 KEY COMPONENTS TO

RISK BASED MONITORING

An effective RBM approach boils down to three things:

PROCESS
Clear process to execute steps defined in monitoring & data management plan.

TOOLS
Effective tools to optimize performance, distill data quickly and bring the focus to key risks and takeaways.

PEOPLE
Right mix of people to help plan the right approach.

Proactive quality approach

Dedicated tools to identify and anticipate any potential risk or issue

Highly Integrated Clinical Team Effort

HOW

WHAT

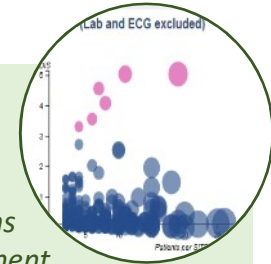**WHO**

RBM – Dedicated tools

Targeted Source Data Verification (TSDV)
Medidata Rave optional module
"For studies using RAVE EDC, the RAVE TSDV module automates and records the SDV performed for a study by selecting the data and the patients for SDV according to preprogrammed setup and randomization algorithms internal to the module."

Data Quality Assessment (DQA)
in CluePoints
(quarterly review)*
Identification of atypical sites or populations for signal detection, tracking and management
Objective & Comprehensive analysis on all data to ensure no stone is left unturned

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RBM dedicated tools =

Automated TSDV
medidata Rave

+

KRI Dashboard
CluePoints
INTELLIGENT STATISTICAL MONITORING

+

DQA
CluePoints
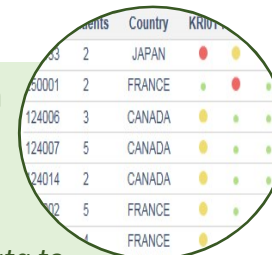INTELLIGENT STATISTICAL MONITORING

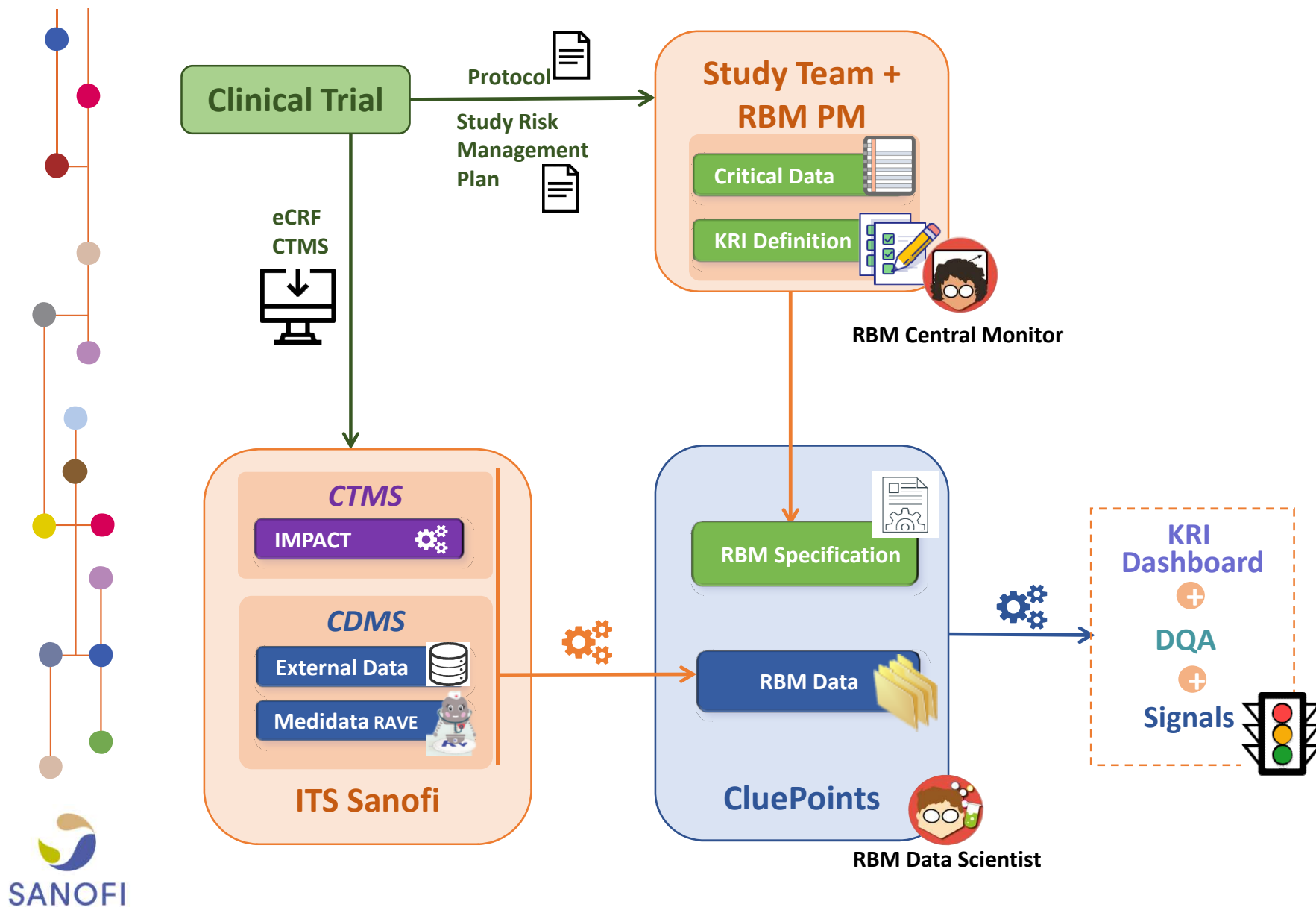**Key Risk Indicators (KRI) Dashboard in CluePoints**
(bi-weekly review)*
Identification of specific signals based on Key Risk Indicators on Operational and Clinical Data to monitor the study conduct
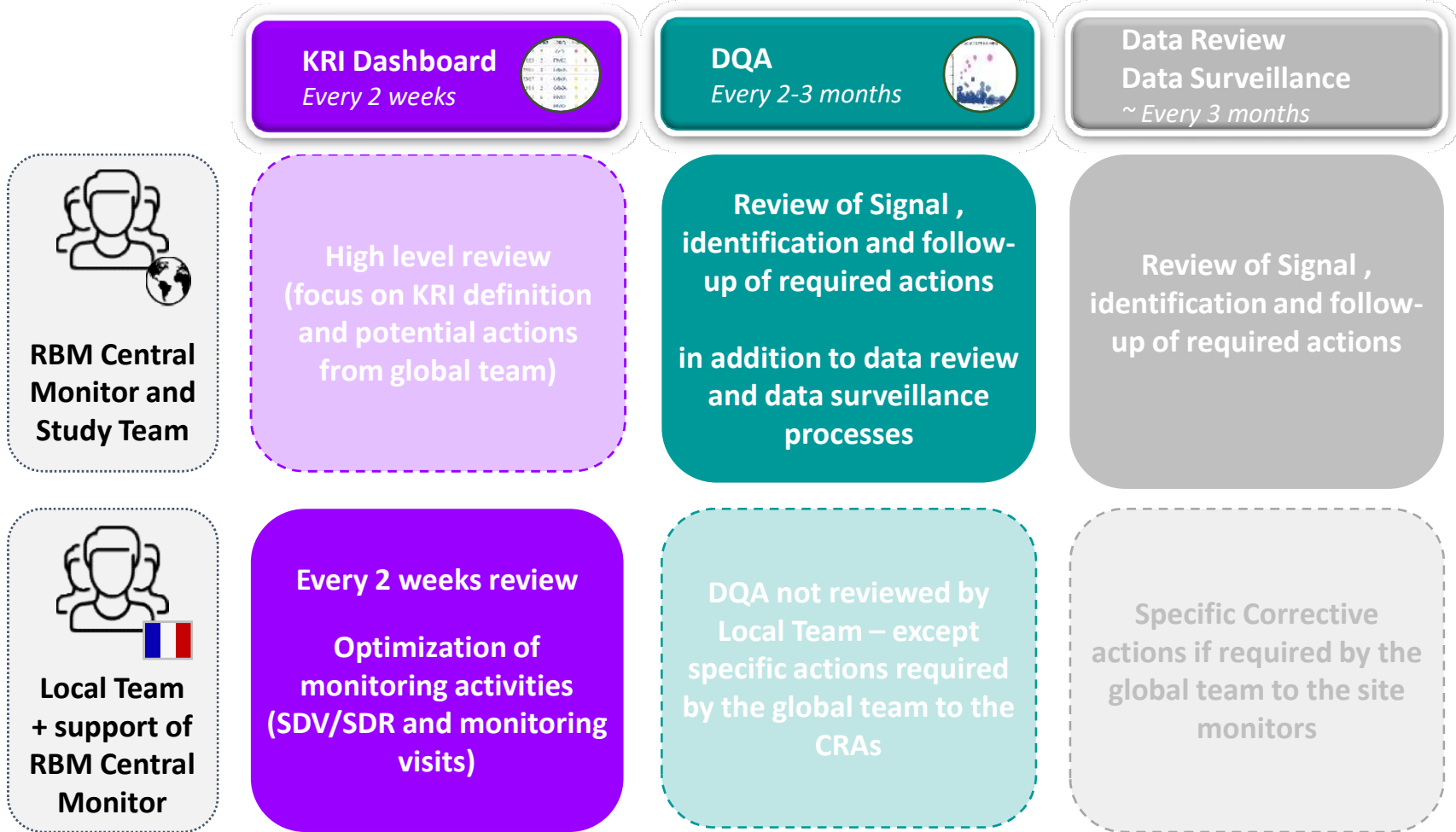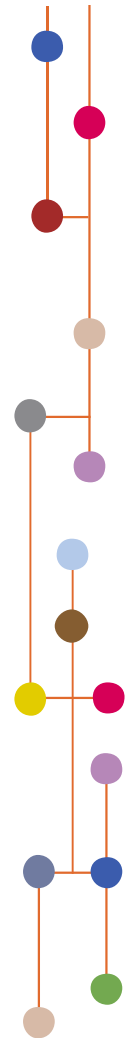
* Based on CluePoints recommendations

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RBM - New monitoring processes

	KRI Dashboard *Every 2 weeks*	**DQA** *Every 2-3 months*	**Data Review Data Surveillance** *~ Every 3 months*
RBM Central Monitor and Study Team	High level review (focus on KRI definition and potential actions from global team)	Review of Signal , identification and follow-up of required actions in addition to data review and data surveillance processes	Review of Signal , identification and follow-up of required actions
Local Team + support of RBM Central Monitor	Every 2 weeks review Optimization of monitoring activities (SDV/SDR and monitoring visits)	DQA not reviewed by Local Team – except specific actions required by the global team to the CRAs	Specific Corrective actions if required by the global team to the site monitors

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RBM - Main Responsibilities

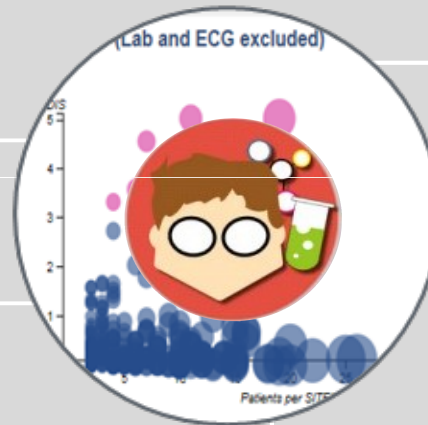| Global study team	Local study team	Site Staff
Global Study Manager, Data Manager, Statistician, Study Medical Manager, **RBM Central monitor**	Site Monitor (CRA), Local Study Manager, Regional Study Manager, **RBM Central monitor**	Primary investigator, Investigator, Nurse, Pharmacist
• Defines critical data and study priorities • Evaluates and mitigates risks at global level • Provides oversight via data analysis • Identifies trends	• Adjusts type & frequency of site engagements based on RBM inputs • Focuses interactions with site on areas of need	• Accountable for site quality • Enters data into eCRF in near real time • Comprehends RBM methodology to ensure subject safety and data integrity

Sponsor

Institution

RBM DATA SCIENTIST
'DATA MODELLER & SCIENCE'

Role
Set-up the KRI & DQA and the Central Statistical Monitoring solution, run data analysis in order to identify atypical sites and improve data quality

Tool box
CluePoints (KRI & DQA)

Skills and Talents
✓ *Statistical methodology*
✓ *Data mining*
✓ *Communication & visualization*
✓ *SAS, SQL*

Mindset
Logical and enthusiastic stats genius, appetite for data analysis

Mission
Program RBM solution and review of DQA for signal detection
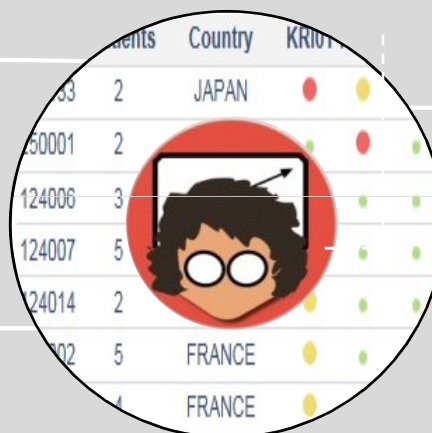
RBM Central Monitor

RBM CENTRAL MONITOR
'DATA DETECTIVE'

Role
Analyze and interpret clinical and operational data; identify specific signals based on Key Risk Indicators

Tool box
CluePoints (KRI & DQA)

Mindset
Intuitive and data lover, curious data wizard

Skills and Talents
✓ *Database systems*
✓ *Leadership and project management*
✓ *Interpersonal Communication*

Mission
Create Site specific Signals and manage Global Signals – Provide interpretation, guidance and support

RBM Site Monitor
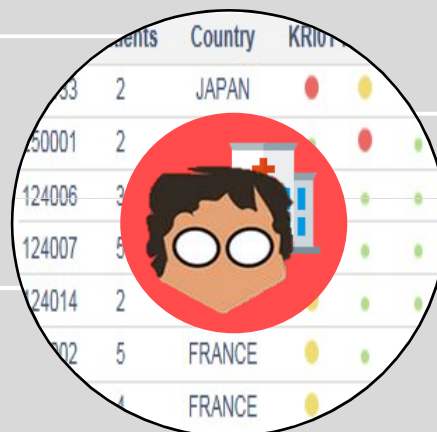
RBM SITE MONITOR
'PROBLEM SOLVER'

Role
Mitigate signals, determine the root cause of alerts, identify & implement appropriate action plan, follow-up & communicate the corrective actions

Tools
CluePoints (KRI), CTMS, CDMS

Mindset
Problem solver, devoted in improving the quality of his data base, closely supporting sites

Skills and Talents
✓ *Scientific, Clinical, & Regulatory knowledge*
✓ *Critical Thinking & Decision Making*
✓ *Technical Skills- Systems/Data/Analytic*
✓ *Interpersonal Communication skills*

Mission
Adapt his monitoring activities based on signals detected

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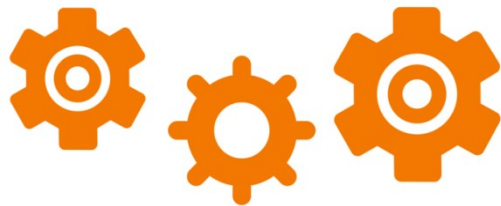- **Conclusion**

RBM Integrated Approach

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Proactive quality approach

TOOLS
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Dedicated tools to identify and anticipate any potential risk or issue

PEOPLE
Right mix of people to help plan the right approach.

Highly Integrated Clinical Team Effort

At Sanofi

New processes at global and local levels: based on the critical data/processes and study risk level with risk management by both local and global teams

- KRI Dashboard
- DQA
- TSDV module in Rave

A new team in China with 2 new roles:
- RBM Data Scientist
- RBM central Monitor

Monitoring and Centralized Monitoring

New components :

Study Risk Management Plan (SRMP)
- Critical data/critical processes
- Risks categorization
- Risk assessment

Centralized Monitoring
- Medical review
- Safety review
- Data Review
- Data Surveillance
- DQA

Monitoring
- Targeted Source Data Verification (tSDV)
- Source Data Review (SDR)
- KRI dashboard
- Low Monitoring Visit frequency

RBM :
Risk based Study Activities

Thank you