TriTiCon

The 3 Tiers Consulting Company

Risk Based Monitoring for Data Management

DADM General Meeting 2017 – January 25

TriTiCon | The 3 Tiers Consulting Company | www.triticon.com
Phone +45 52 19 34 99 | Mail info@triticon.com | Sandvejen 30 | DK 2665, Vallensbæk Strand| Denmark

The road to RBM

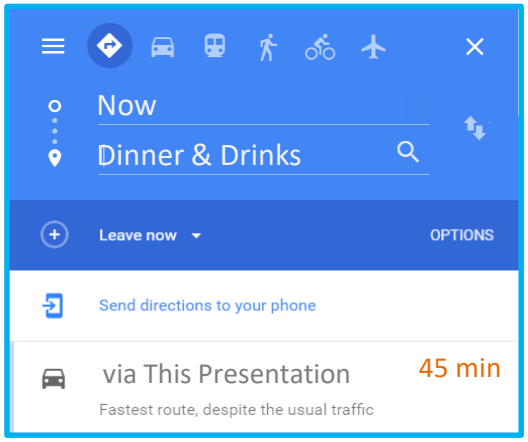
Lonely?

Confusing?

Risky?

The road to RBM

Nice?



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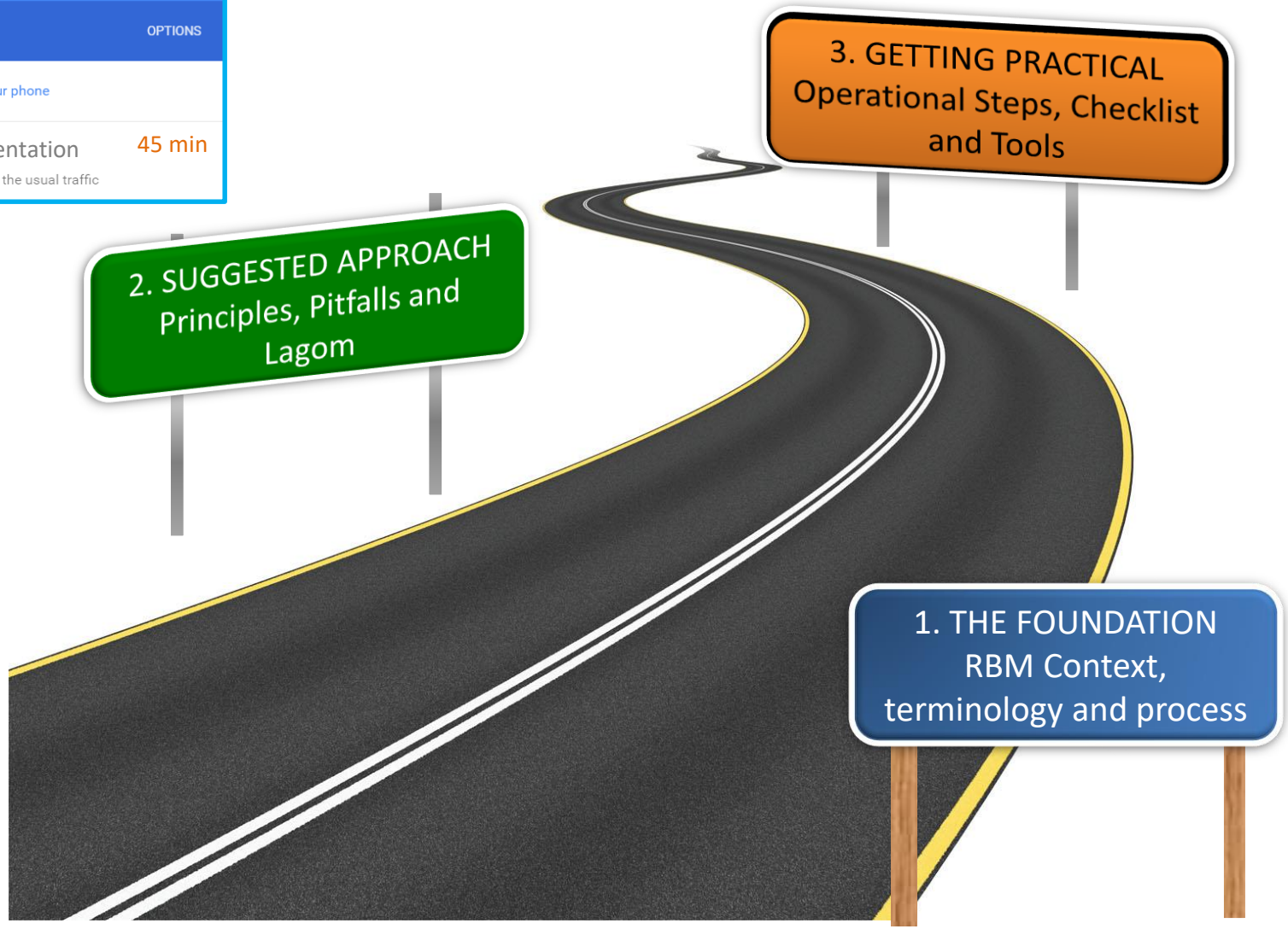

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Where are you ?

1) Company status

- Thinking…
- Piloting
- Doing
- Optimizing ?

2) Company approach

- Clinical
- Cross-functional
- The CRO way

3) CDM Role

- Provide?
- Perform?

4) Company objective

- Quality
- Time
- Money

The next 45 minutes

1) The foundation - RBM Context & Definitions
   - Background, CDM Scope, Basic Process
   - RBM by CDM - The R & B & M and the P
2) Suggested Approach
   - Key principles
   - What not to do – common pitfalls
   - Why CDMs are ideal for RBM
3) Getting Practical
   - A first checklist for CDM risks and monitoring areas
   - Tools (recommendations, examples)
4) Summary

1-4) Discussion, Questions, Opinions

Section 1: Context and Definitions

- Background, CDM Scope, Basic Process
- RBM by CDM - The R & B & M and the P

RBM in Context – Background

FDA

Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring

…strategies for monitoring activities …focuses on critical study parameters…
…combination of monitoring activities to oversee a study….
specifically encourages greater use of centralized monitoring methods

findings should be evaluated to determine whether additional actions….
…quality is an overarching objective that must be built into the clinical trial Enterprise..

EMA

Reflection paper on risk based quality management in clinical trials

…too many trials in which avoidable quality problems arise…
…a more systematic, prioritised, risk-based approach to quality management of clinical trials….
….The quality of information generated should therefore be sufficient to support good decision making. ..
…identification of the risks on a continuous basis for risk-bearing activities throughout the design, conduct, evaluation and reporting of clinical trials. The process should start at the time of protocol design so mitigation can be built into the protocol and other trial related documents …..

TransCelerate

POSITION PAPER: RISK-BASED MONITORING METHODOLOGY

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 subject safety and data quality.

(1) building QbD into trials,
(2) early and ongoing risk assessment,
(3) a focus on Critical Processes and Critical Data,
(4) use of Risk Indicators and Thresholds, and
(5) adjustment of monitoring activities based on the issues and risks identified throughout the study

RBM in Context – Background

Common Key Points

Risk based, focused, prioritized

Strategic, central methods

Adjustment, adaptive, additional actions

Quality is overarching, from design to.., QbD,

RBM in Context – Background

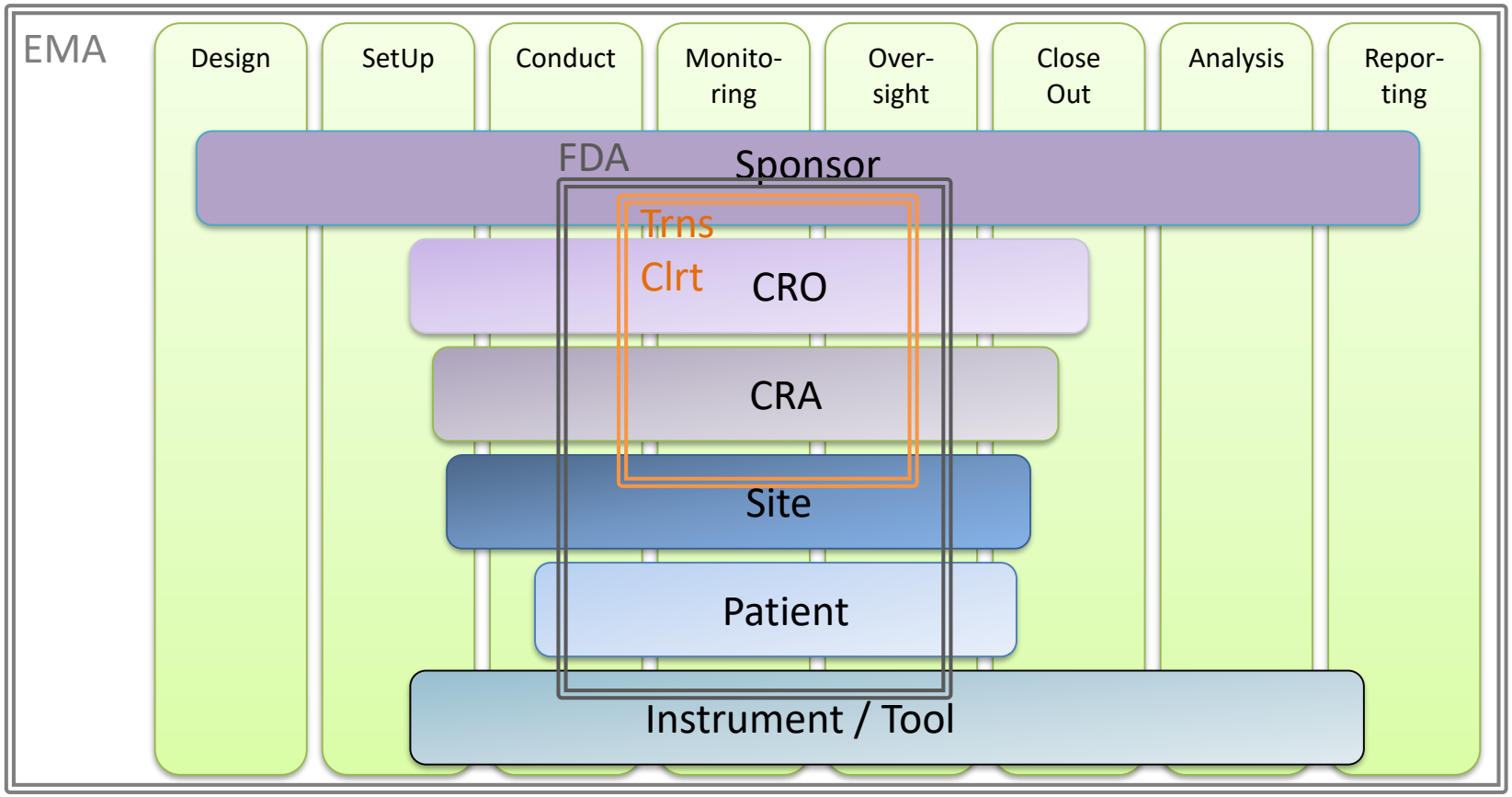
Key Differences

FDA: "...**Approach** to **Monitoring**"
= More general, examples, focusing on monitoring

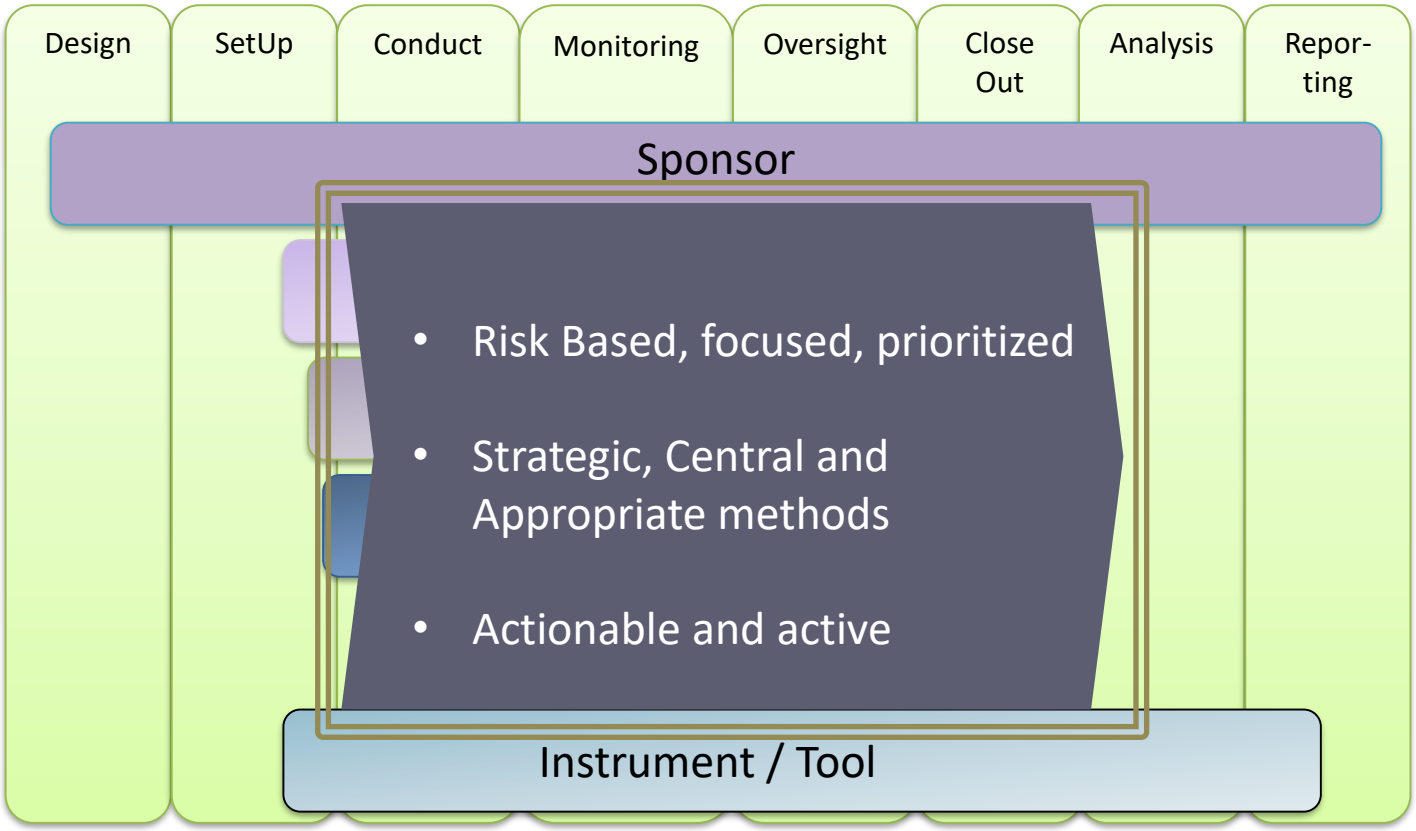
EMA: "...**reflection**..on **quality management**.."
= More methodological, less content, covering end to end quality.

TransCelerate: "..**monitoring methodology**". (+ tools)
= Very operational, focusing on (traditional) monitoring (CRA) activities.

RBM in Context – Process and Scope



RBM in Context – CDM Process & Scope*



* Process and Scope for RBM performed by CDM. In addition CDM might often also provide RBM tools to others.

RBM in Context – Background Summary

Situation

- We have quality a problem..
- Quality must be built in end to end
- Quality = fit for purpose

Solution

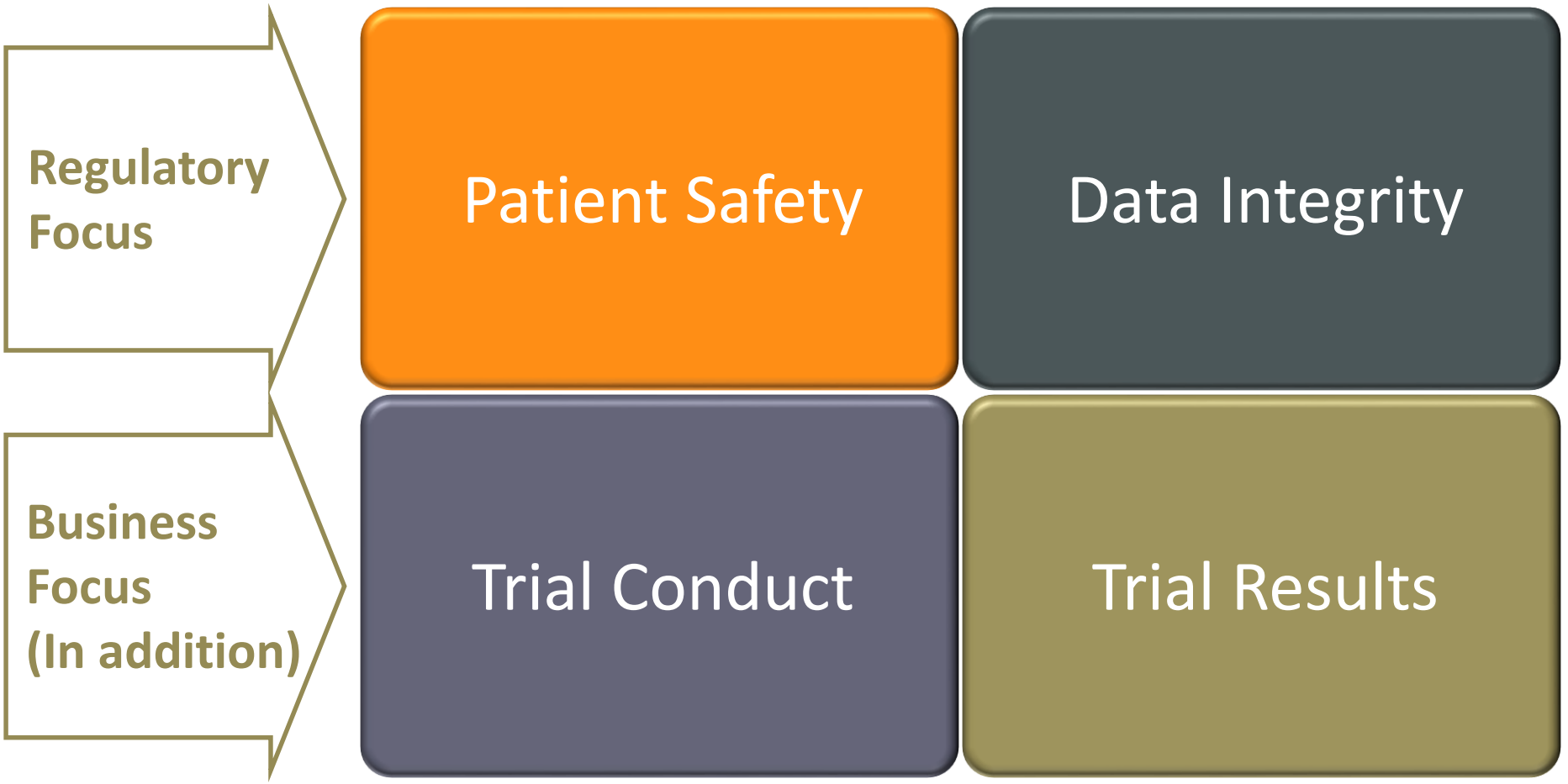
- Monitoring/Management should be: *Risk Based, focused, prioritized.*
- Use *Systematic, Central and appropriate methods*.
- Result in *adaptions and actions*

Benefits

- Improvement in data quality and patient safety for clinical trials
- Reduction in effort expended on low-value activities.
- Cost reductions

RBM is much more than reduced SDV and on-demand monitoring visits..

RBM Definitions – RBM by CDM: The R



RBM Definitions – RBM by CDM: The R

Regulatory Focus

Business Focus (In addition)

(Patient Safety)

Data Integrity

- Data not being trust-worthy or not reflecting the actual "truth".
→ Data not usable by sponsor or not accepted by authorities.

Trial Conduct

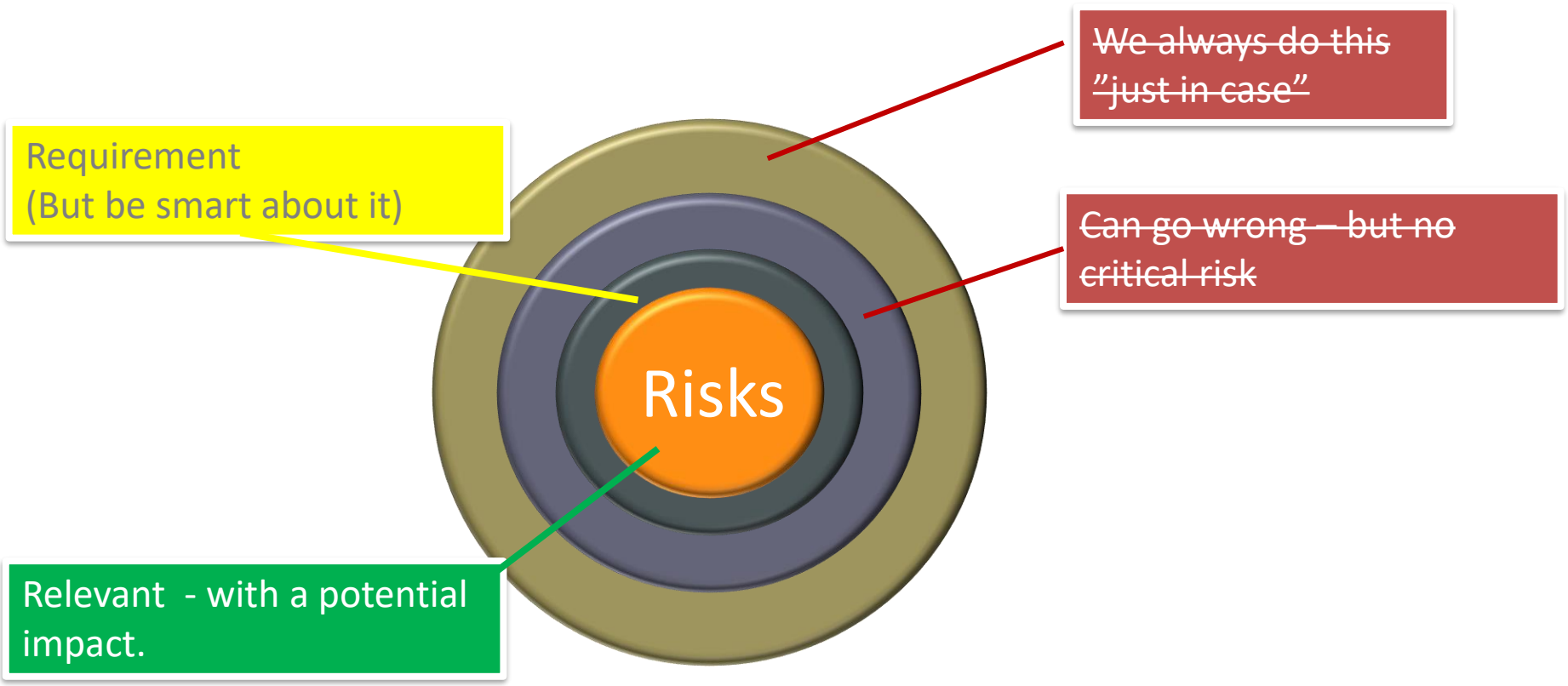
System Quality - System not available or not supporting data quality
→ Lost data, decreased trust and motivation. Delays and poor data quality.

Trial Results

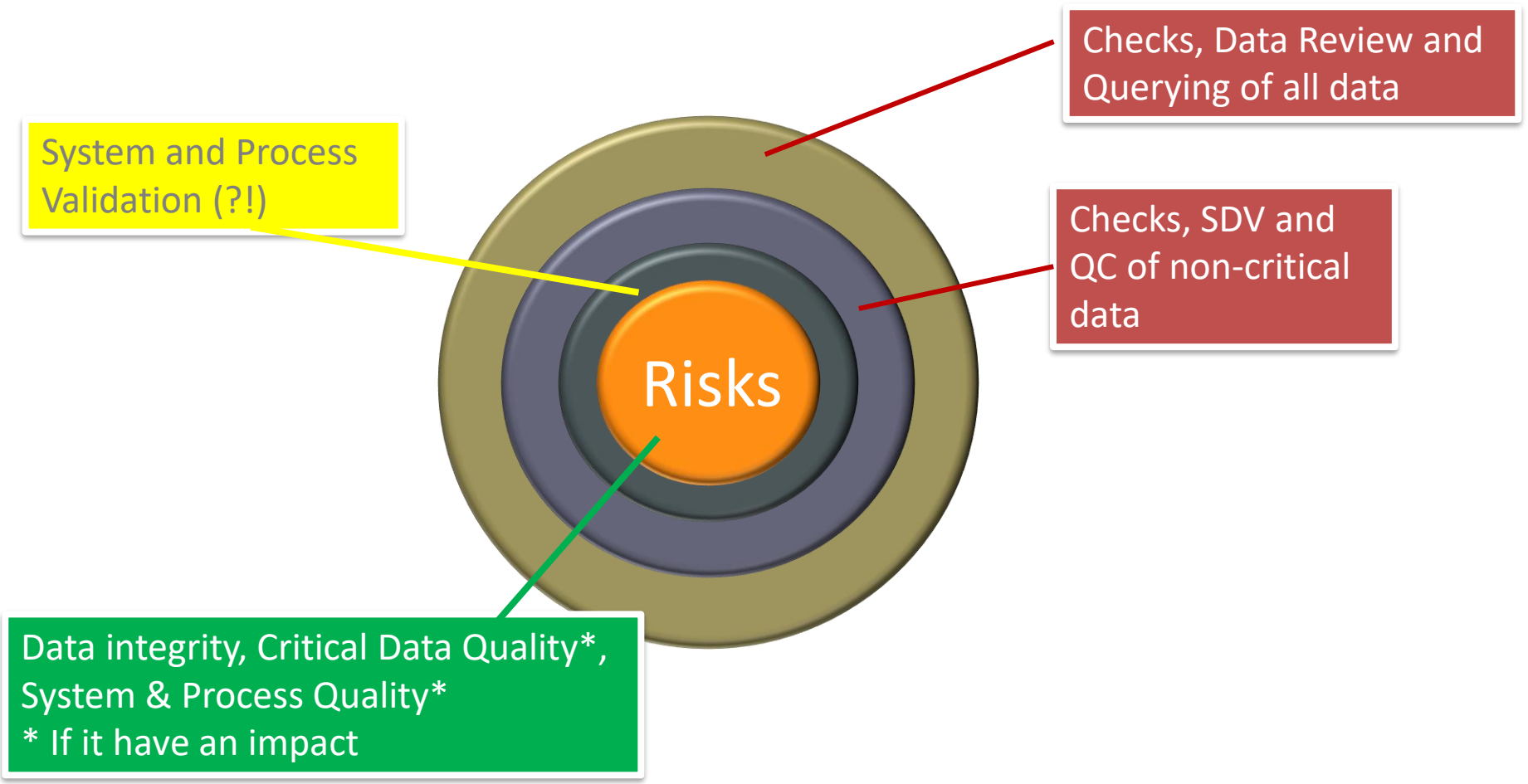
Data Quality (Critical Data) – Incomplete / inconsistent data. Data not according to protocol.
→ Data not supporting analysis/result (failure to prove actual result)

More details later ..

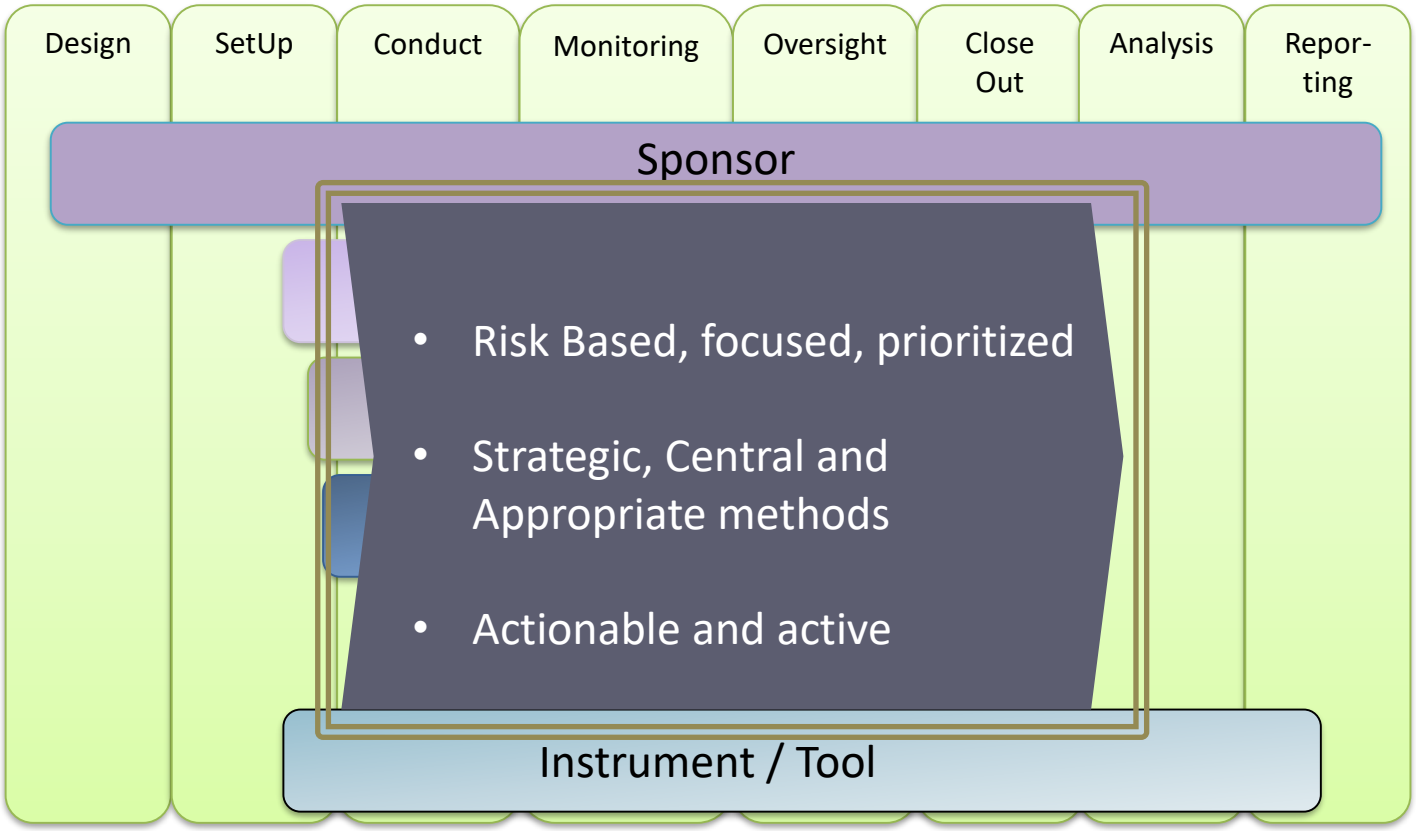
RBM Definitions – RBM by CDM: The B



RBM Definitions – RBM by CDM: The B



RBM in Context – CDM Process & Scope*



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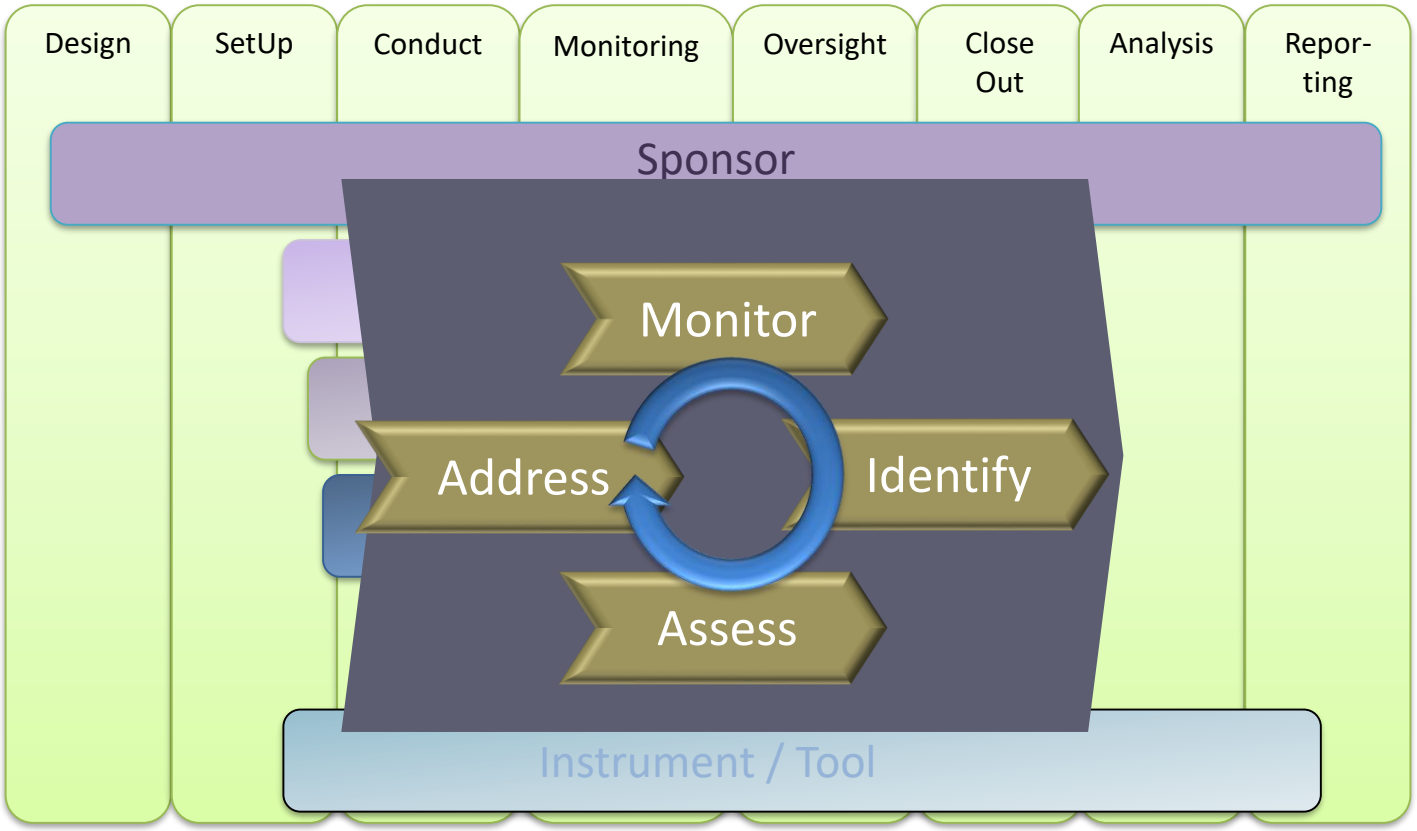
RBM in Context – The M



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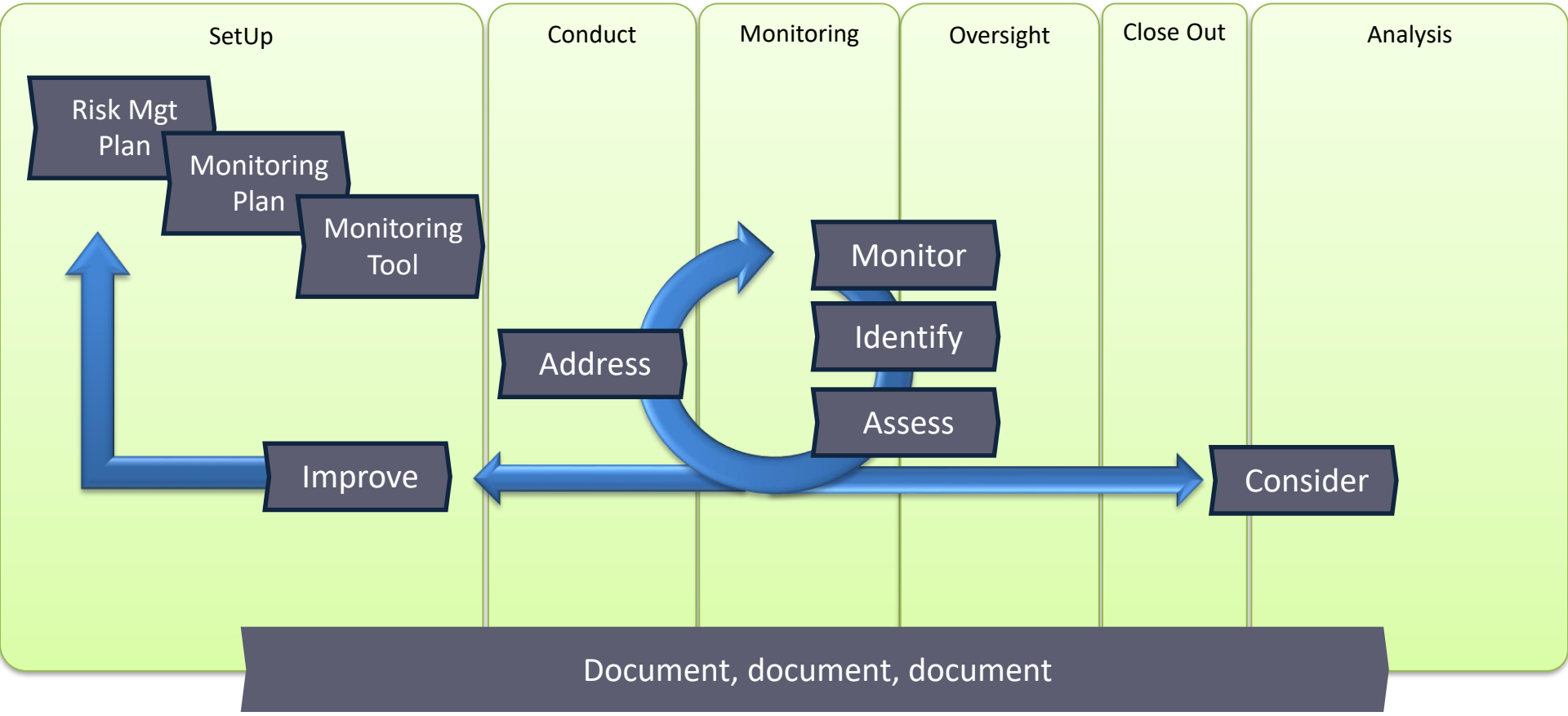
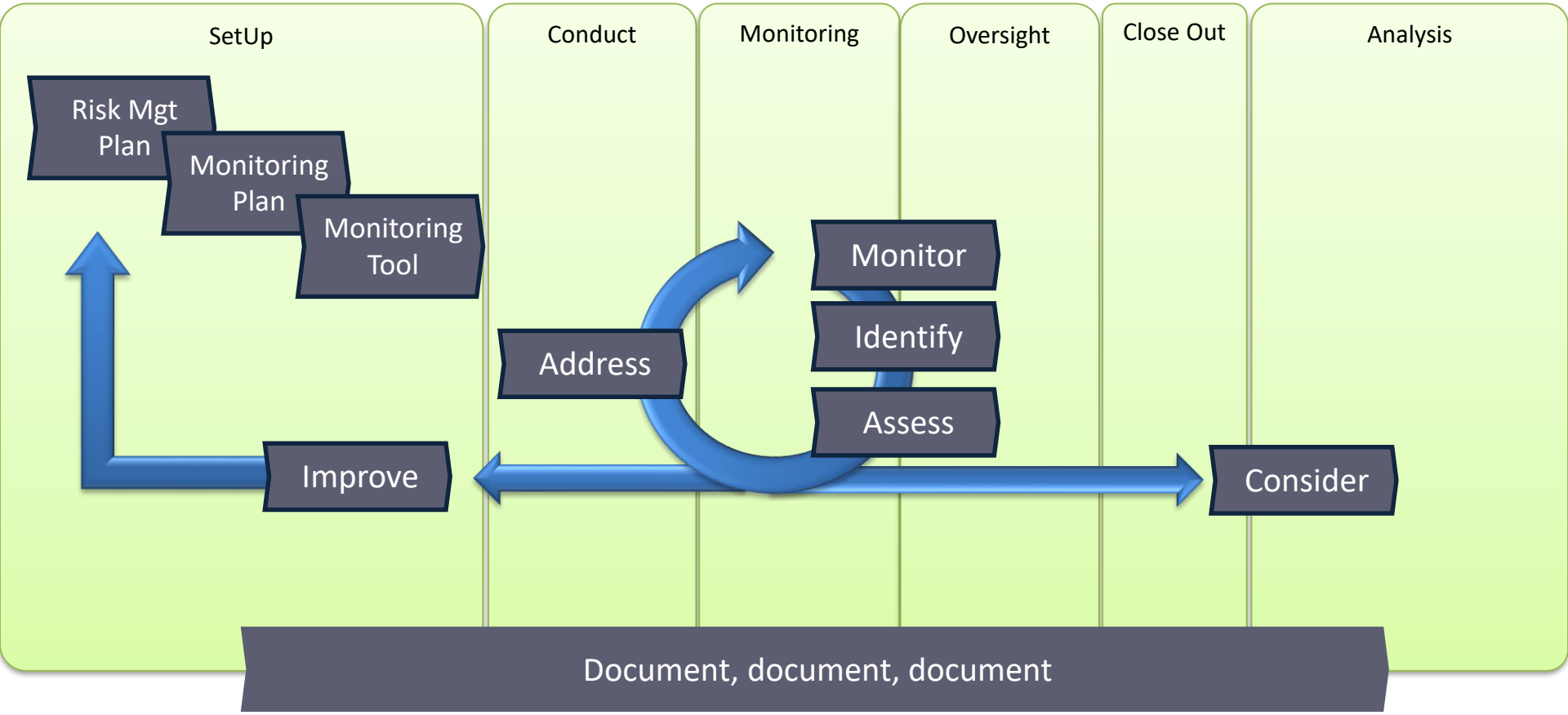
RBM Definitions – RBM by CDM: The M



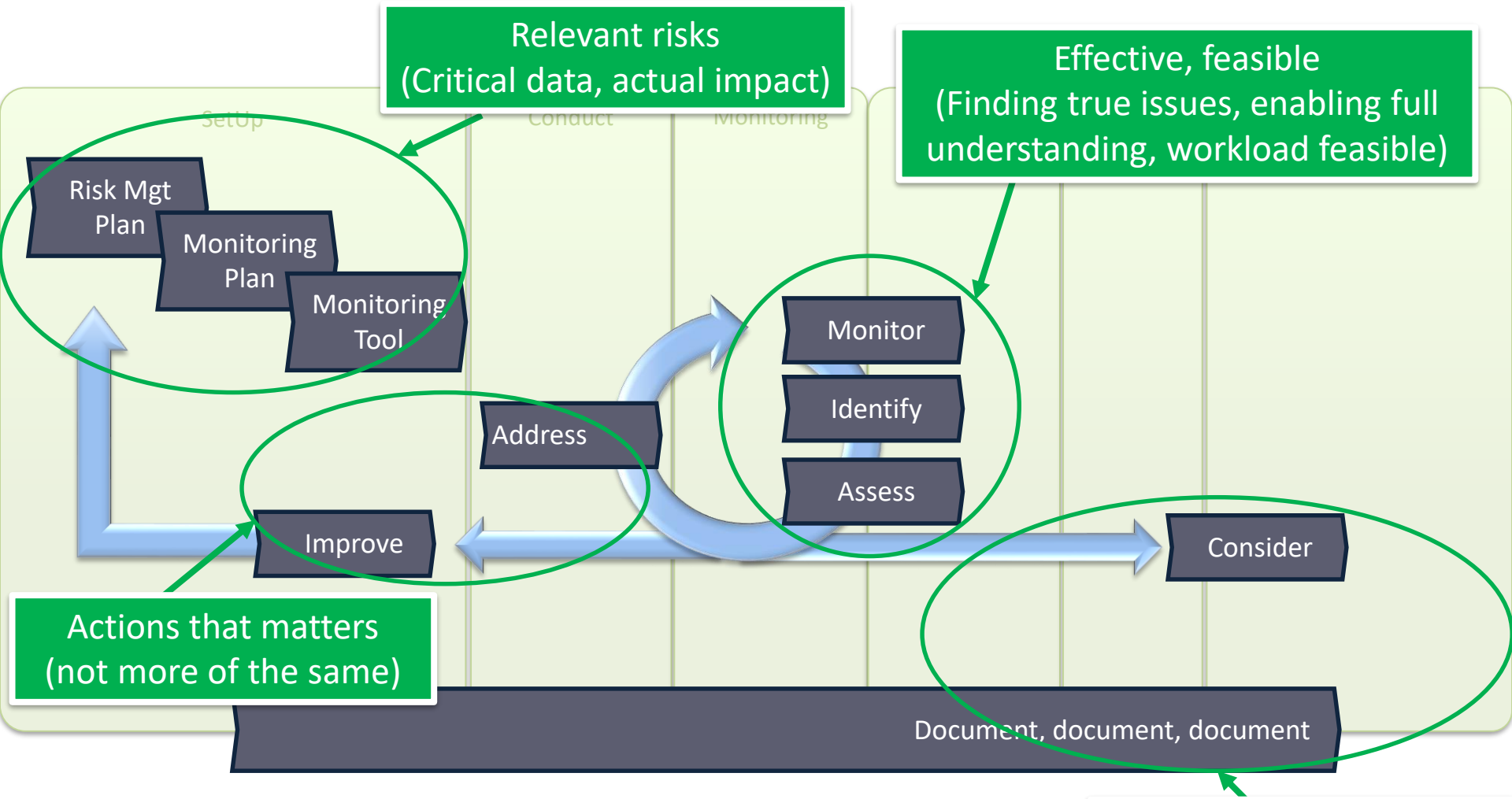
Section 2: Suggested Approach

- Key principles
- What not to do – common pitfalls
- Why CDMs are ideal for RBM

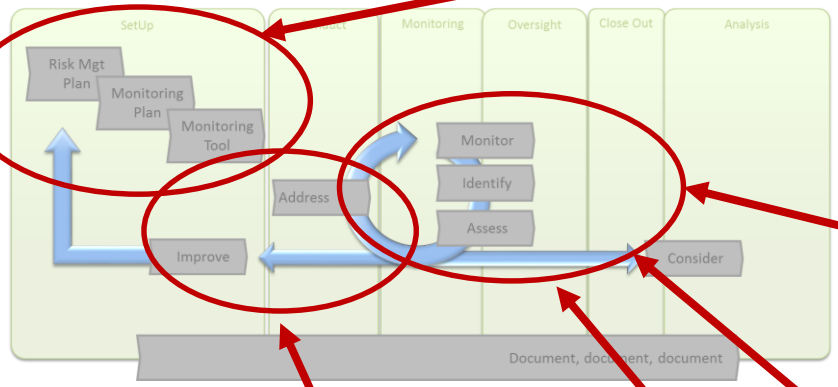
How to do it– Process recap



How to do it - Key Principles



What not to do – common pitfalls



RBM is not considered from the beginning
→ Problem compensation, not risk management.

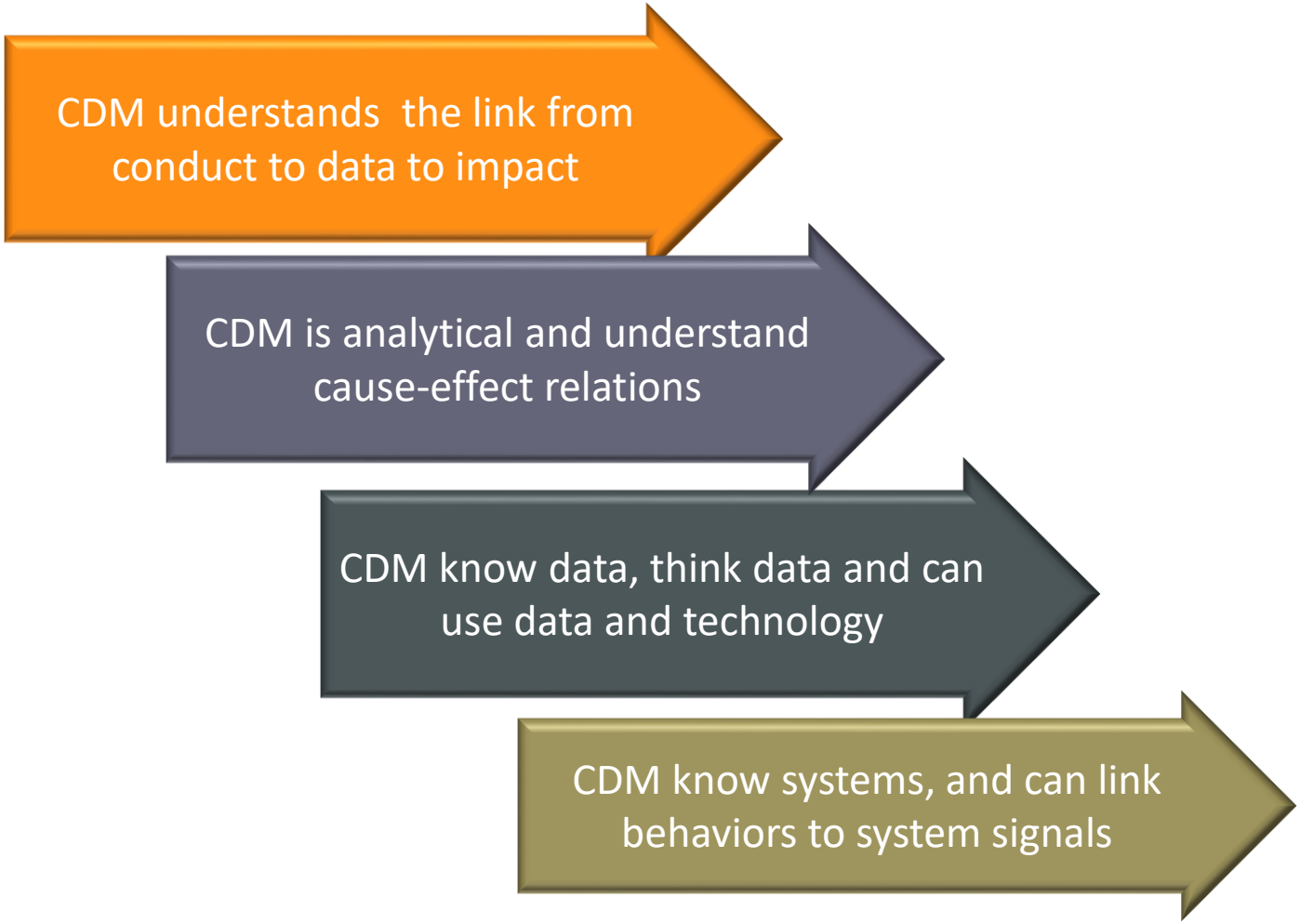
We do what we can, what we have, and what we normally do
→ We KPIs that do not identify risk and do enable actions that matters
We conclude and act – but blindly

We rely on KRIs to find and understand issues
→ We don't find the issues in time, we get false signals .
We don't get the benefits.
We create problems.

We don't define new action paths
→ We do more of the same (witch obviously didn't work in the first place). More SDV, more site visits, repeat the same training.

We want to do it all.....
→ We drown....

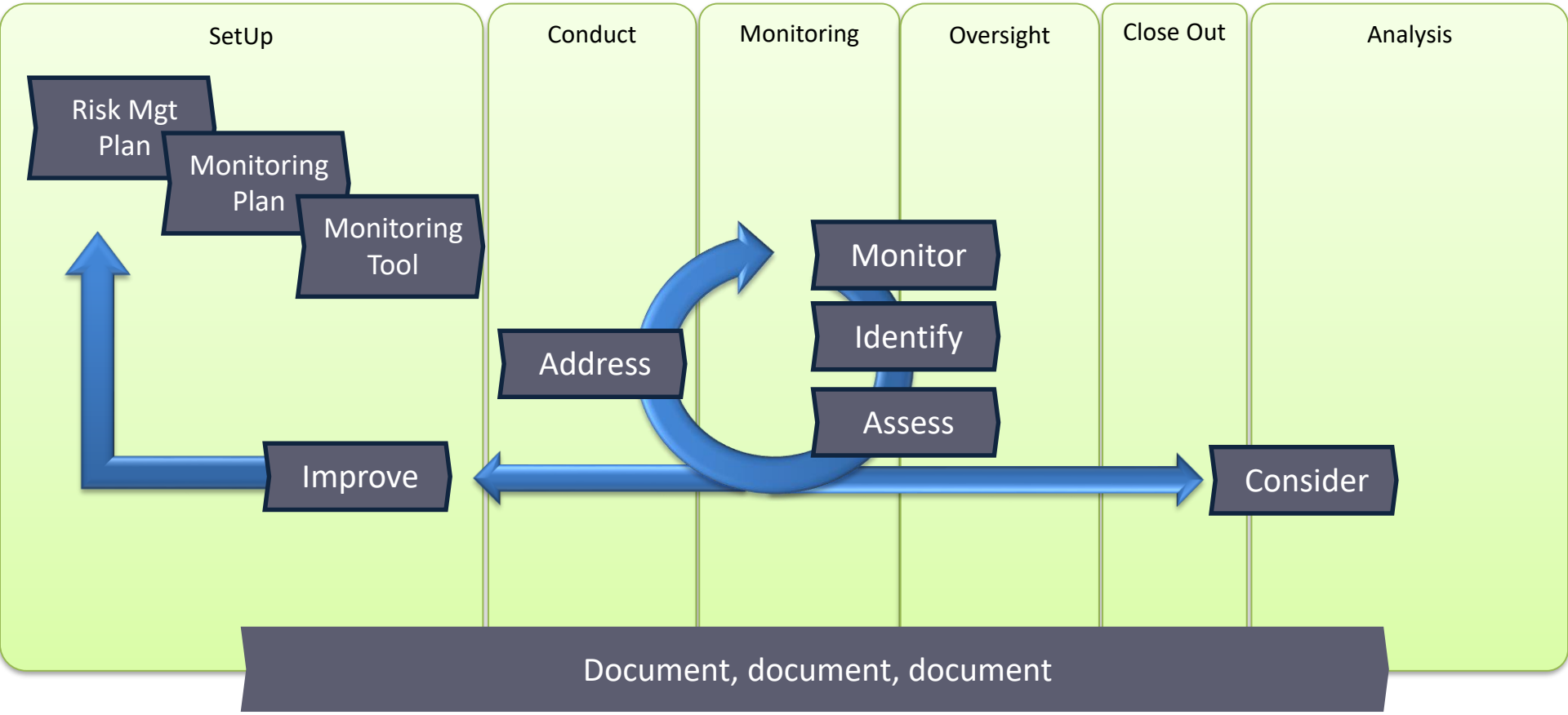
Why CDMs are ideal for RBM



Section 3: Getting Practical

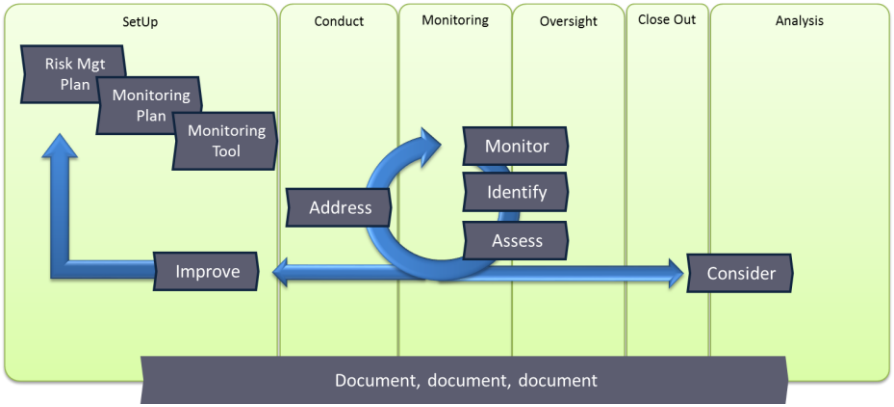
- Practical steps from set up to closure
- A first checklist for CDM risks and monitoring areas
- Tool Examples / Recommendations

Getting Practical– Process recap



Getting Practical- Steps

Design
- Risk input to protocol
- Risk mitigation in contracts etc.
- RBM considerations in protocol



Document
- Performed reviews (even if no findings), identified (potential) issues, considerations and actions.
- Action follow up, conclusions and residuals.

Set up
- Include CDM aspects in RMP* and Monitoring plan*.
- Set up monitoring process and tool

* Or corresponding documents

Conduct
- Analyze and truly understand an issue.
- Agree appropriate actions (cross-functional).
- Follow up / confirm impact.

Close-out
- Report/consider residual issues.
- Assess impact on analysis.
- Other considerations?

Getting Practical– Risk Example/Checklist

Category: Data Integrity. Description: Data not being trust-worthy or not reflecting the actual "truth". Consequence: Data not usable by sponsor or not accepted by authorities	
Area	Risks
Data processing errors	Collection errors (eCRF), transfer errors. Errors in conversions, derivations or mappings.
Non-intended use/behaviour	Data not collected or processed as/when intended.
Security-breaches, misuse	Unauthorized access (EDC or downstream), misuse of user-ids.
Skewing/simplifying/cut corners	Leaving out data or information, not handling exceptions, re-sampling, influencing
Fraud	Fabricated data or patients (by sites or by patients or by company..)

Category: Data Quality Description: Incomplete or inconsistent data. Data not according to protocol. Consequence: Data not supporting analysis/result (failure to prove actual result)	
Area	Risks
Incomplete Data	Expected procedures "not done" or conditional/event data missing.
Inconsistent Data	Data inconsistent, data issues not adequately solved.
Incorrect Data	Data incorrectly registered (entry error, wrong patient, visit or mixed up in other ways)
Data not according to protocol	Protocol procedures not followed (Timings, methods, definitions/rules)

Category: System Quality Description: System not available or not supporting data quality Consequence: Lost data, decreased trust and motivation. Delays and poor data quality.	
Area	Risks
System deviating from protocol	Not matching / supporting protocol - Data not collected according to protocol
System incorrect	Incorrect checks/review reports - False hits/findings, missed hits/findings
System not stable	System issues, down time, poor performance - Lost data, decreased trust and motivation
Poor System usability	System cumbersome to use or difficult to understand - Decreased trust and motivation

Getting Practical - Tools

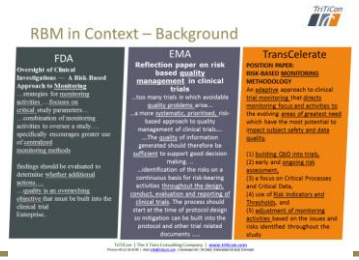
Tools:

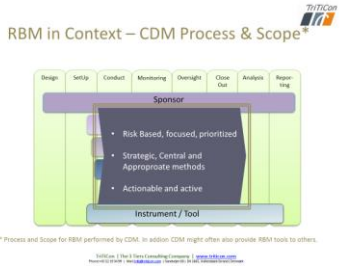
- Visual, Graphical, Dynamic tools are a great benefit for understanding signals.
- KRIs and thresholds (traffic lights) are not enough…(too simplified, too late, too limited, too inefficient)
- Look for Distributions, outliers, patterns, trends.
- Embedded documentation capability is a great help.

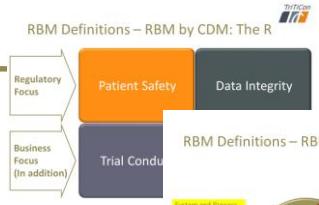
Type	Examples
Business Intelligence Tools	Qlik, Microsoft BI, Cognos, Spotfire
CRO Process Proprietary	Quintiles, etc.
System/Vendor Proprietary	Medidata, Omnicom, Oracle, DSG (Typical EDC+ providers)
Specific CM/RBM/SM software	Cluepoint, Comprehend, SAS JmpClinical

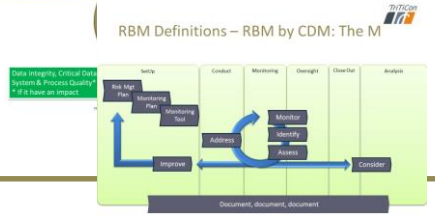
Summary

Background, context

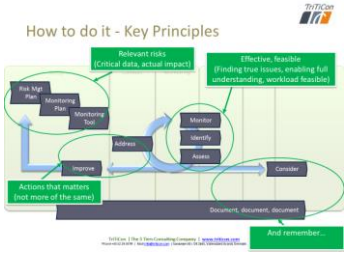


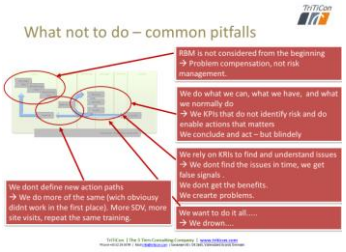


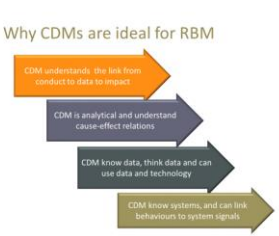




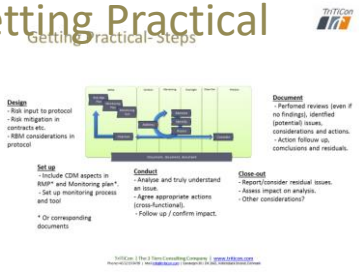
How to do it

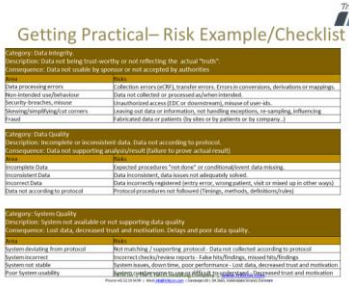


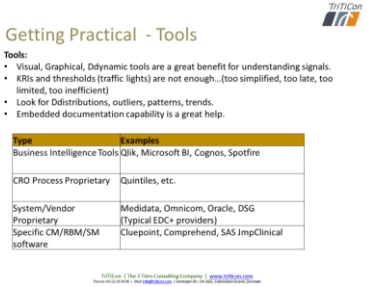




Getting Practical







Thank You!

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The Company – Experience that matters

More than 20 years of industry experience.

Work Experience

Aktivia Science Work,
AstraZeneca,
Astra Hässle,
Clinical Data Care,
Ferring Pharmaceuticals,
H. Lundbeck,
Pharmacia&Upjohn,
Trial Form Support

360° Data Handling

Experts in Clinical Data

Biometrics / Clinical Development Consulting

Health Economic Research

Expert Networking partners

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The Company – The 3 Tiers Methodology

What you need – nothing more, nothing less – and with minimal client effort

Meeting Your Challenge

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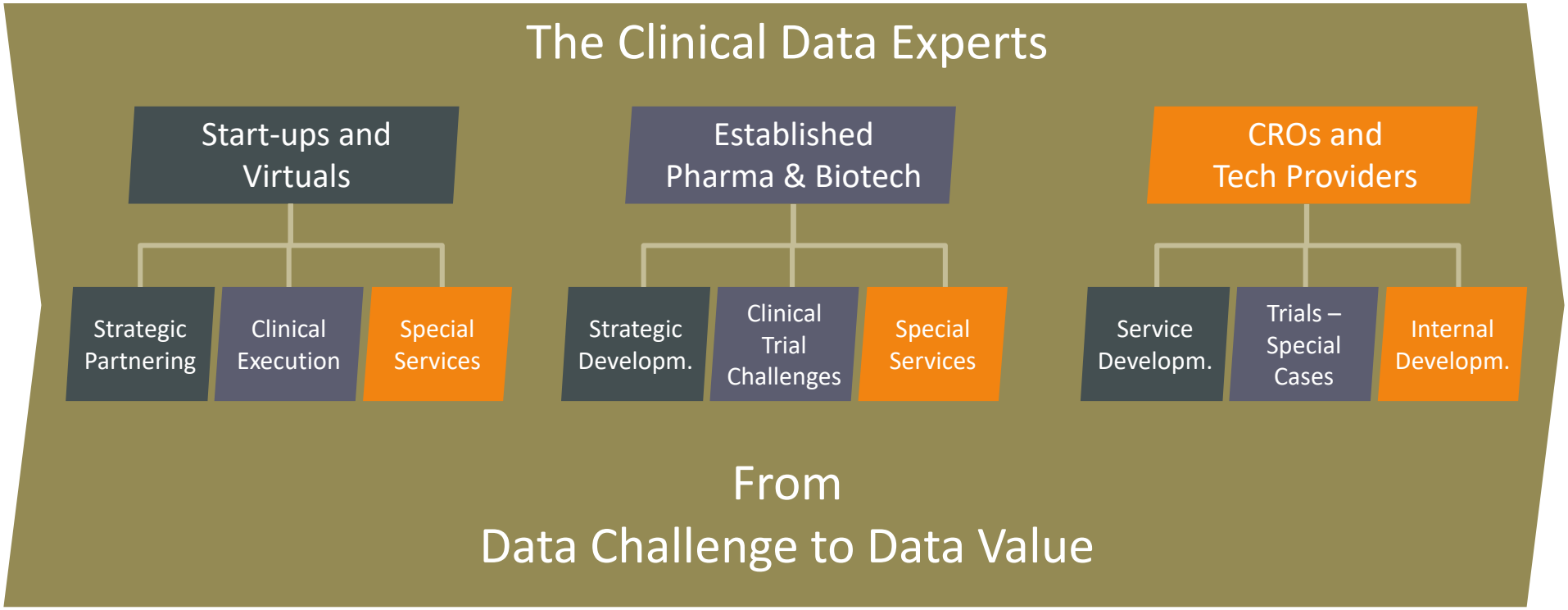
The Services – Overview



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