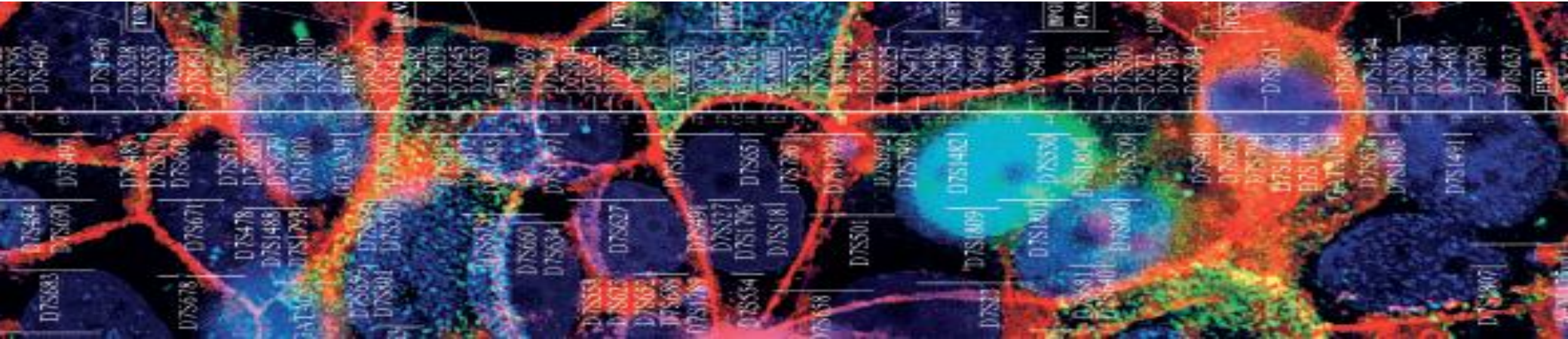


Principles of Quality Risk Management

SESSION I: Principles for Building Quality into Clinical Trial Development

CTTI Workshop on Quality Risk Management: Making Clinical Trials Fit for Purpose

*Beat Widler, Clinical QA and Risk Management Expert
August, 2011 – Bethesda, US*



Setting the Scene



Ultimate Goals of Quality Management Principles and Goals in the World of Health Care

Patient Safety, Rights and Integrity

in all clinical trials and post-marketing activities

*The
Focus*

Data Integrity

of data created in these clinical trials and post-marketing activities

What is Quality?



What is Quality?



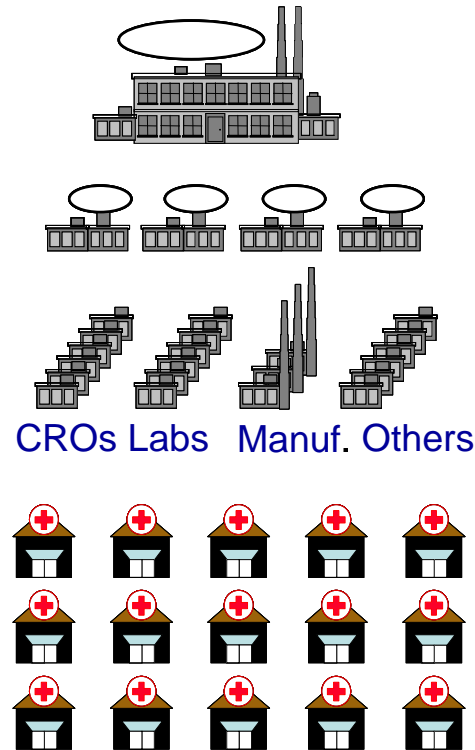
The numbers are against us, for example, *Audits cover only about 2% of clinical-related activities*

Main Risks

Safety Processes

Data Integrity

GCP & Pharmacovigilance Entities



Audit Coverage

250
Audits

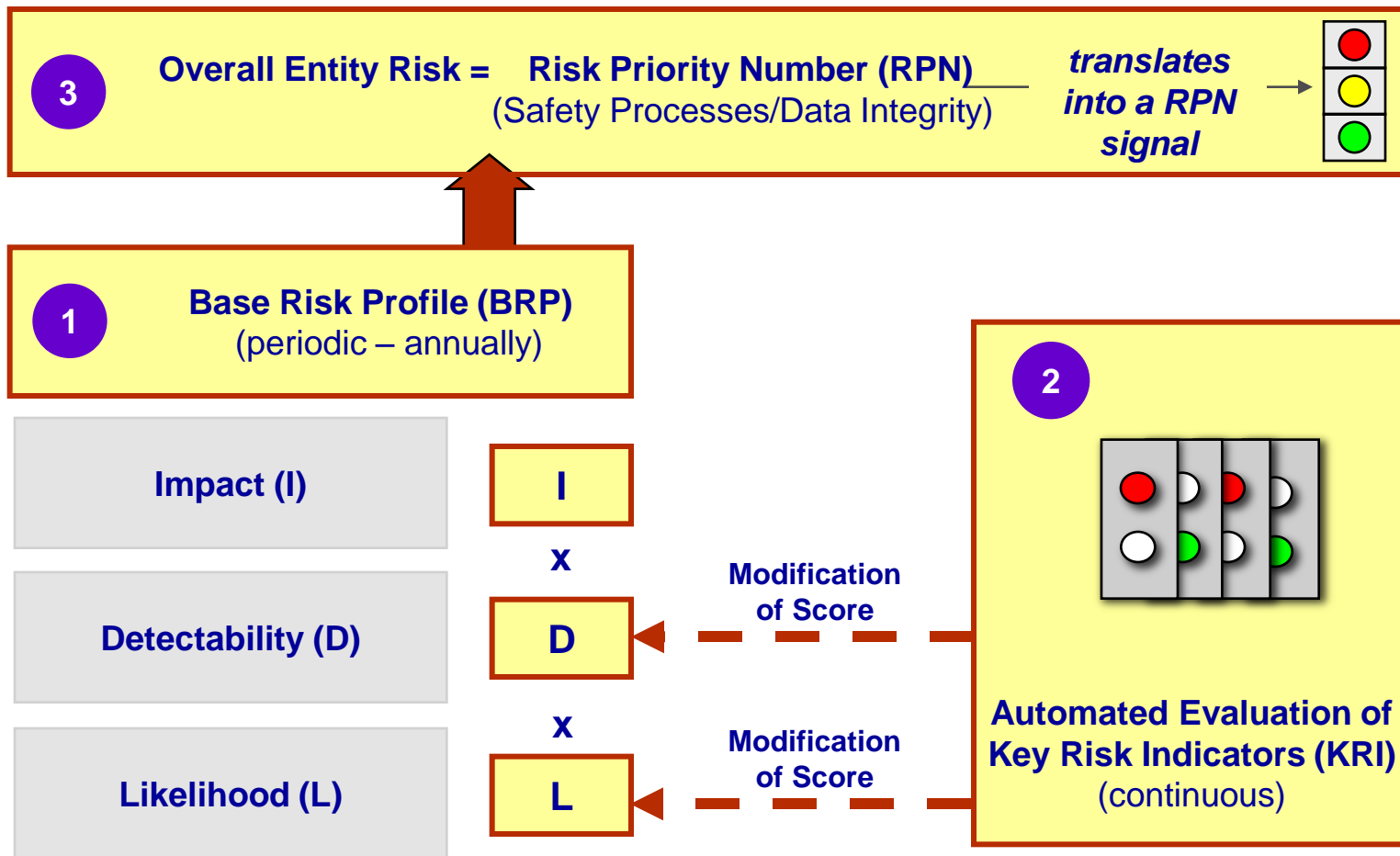
~ 20,000
Entities

=

< 2% Audit
Coverage

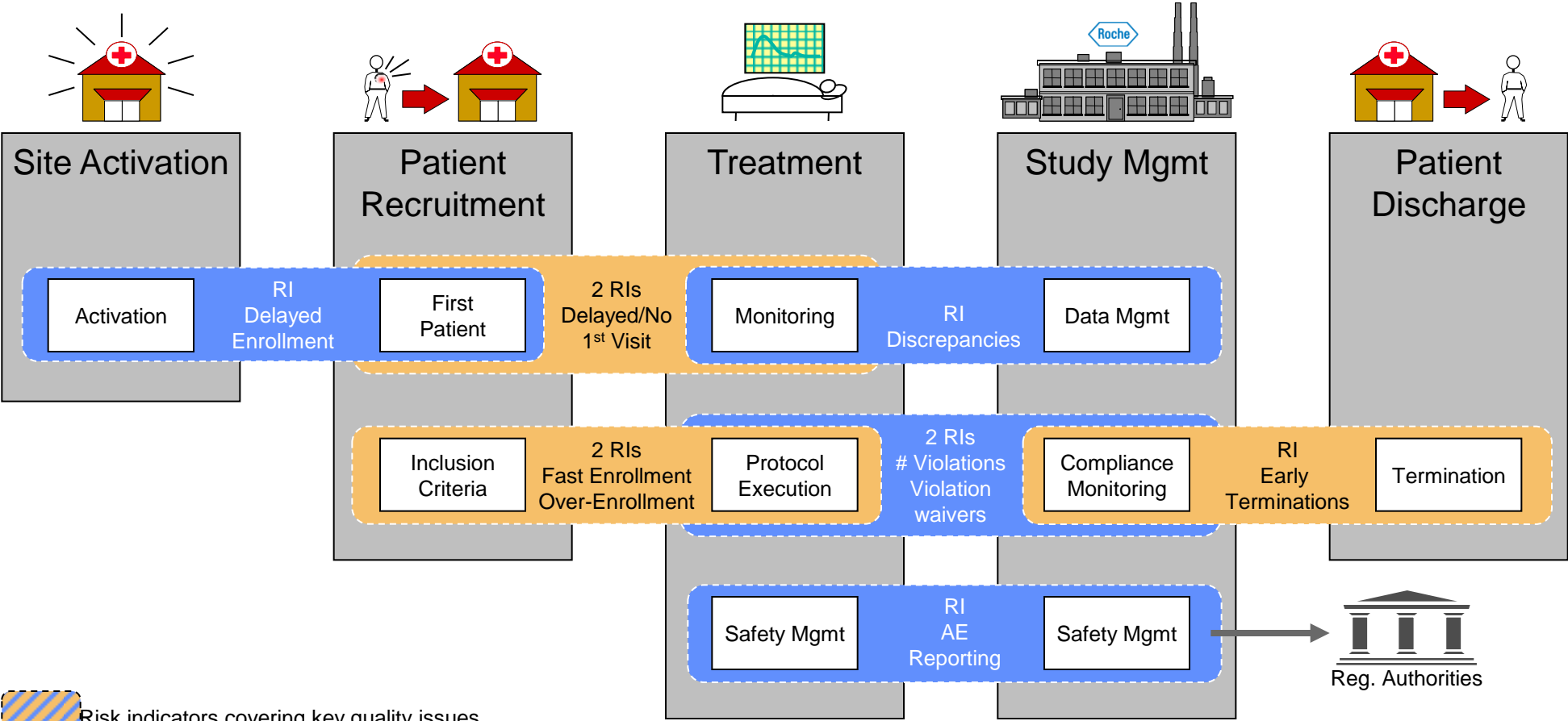
Continuous Risk Evaluation:

Three core steps



QRM “risk indicators” are designed to detect these issues early before they become problems

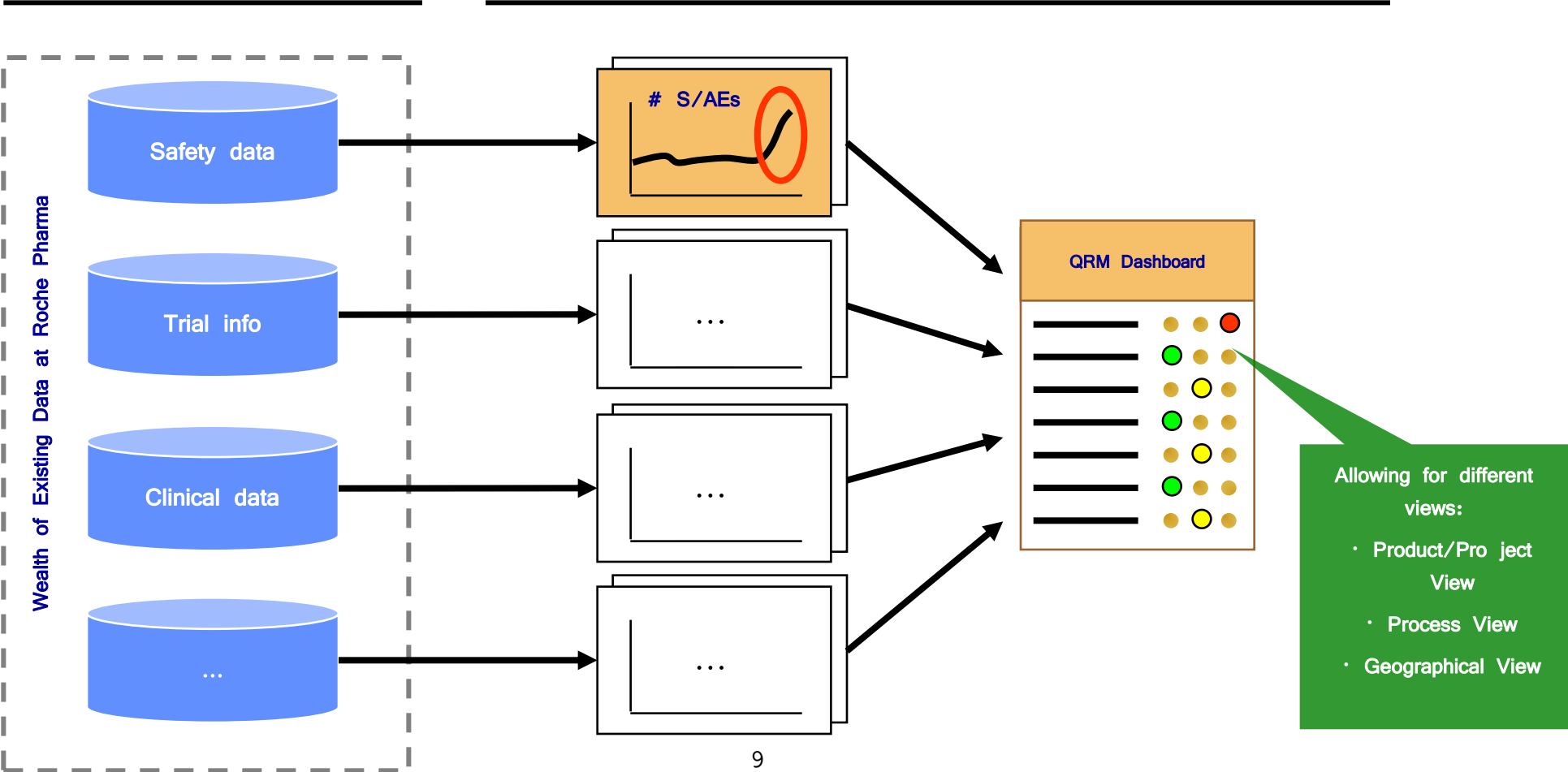
Risk Indicators Along the Trial Management Process



Continuous Risk Evaluation based on *automatic Analyses of existing Data*

Use existing data...

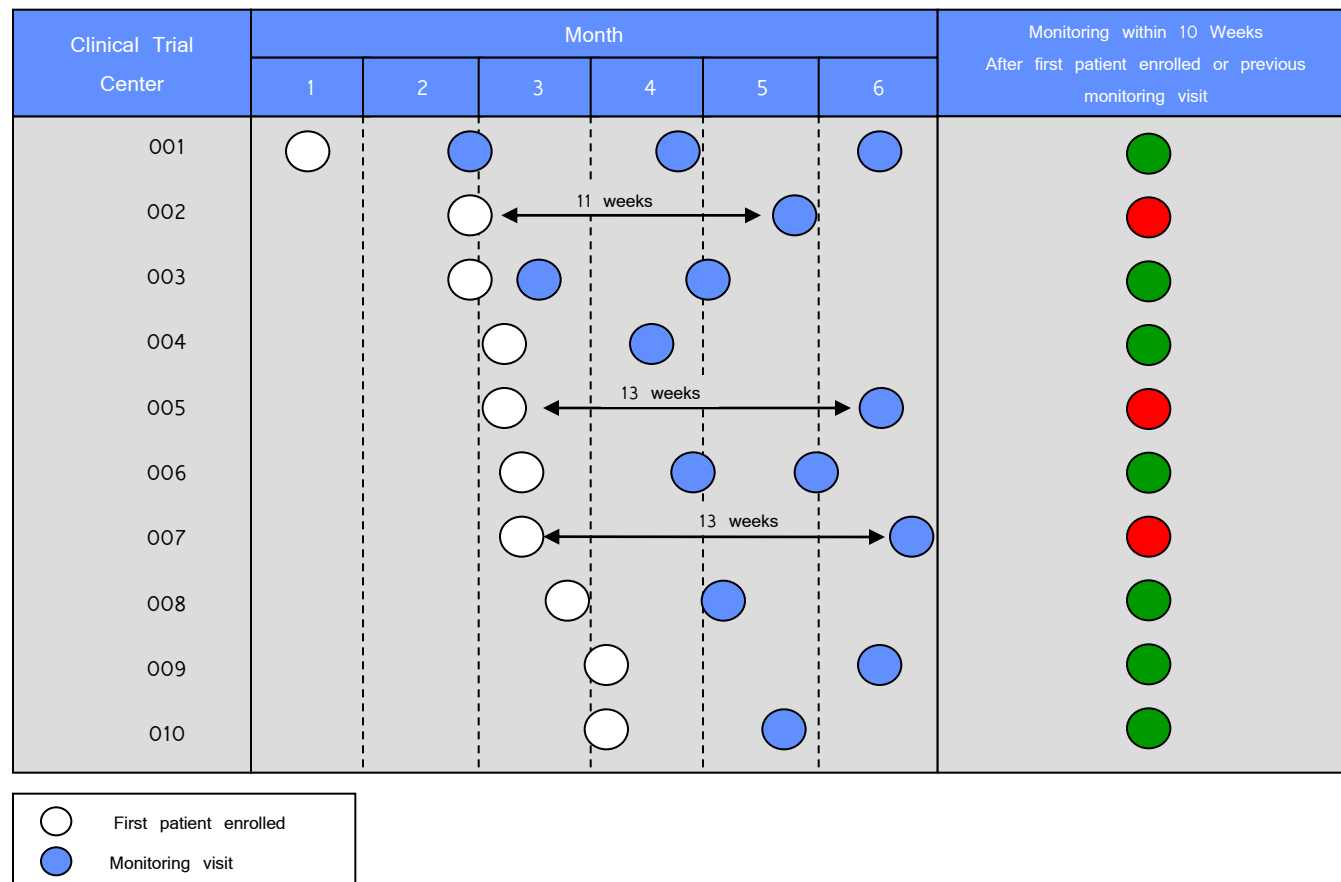
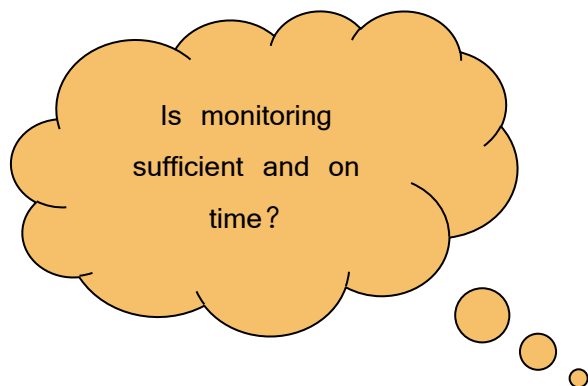
... to identify areas with increased quality risks



Example: *Monitoring visits delayed*

Study: XYZ

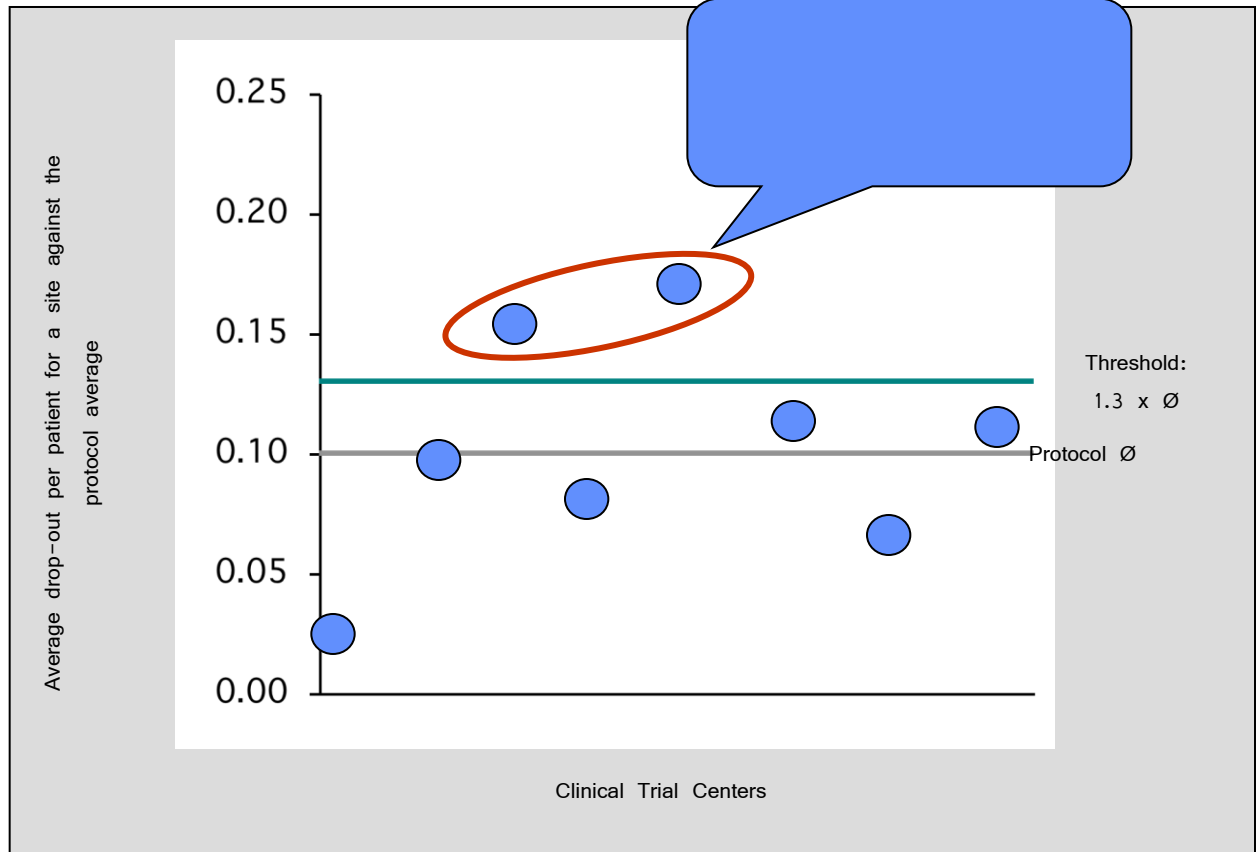
Risk Indicator: Delayed Monitoring



Example: *Premature terminations above protocol average*

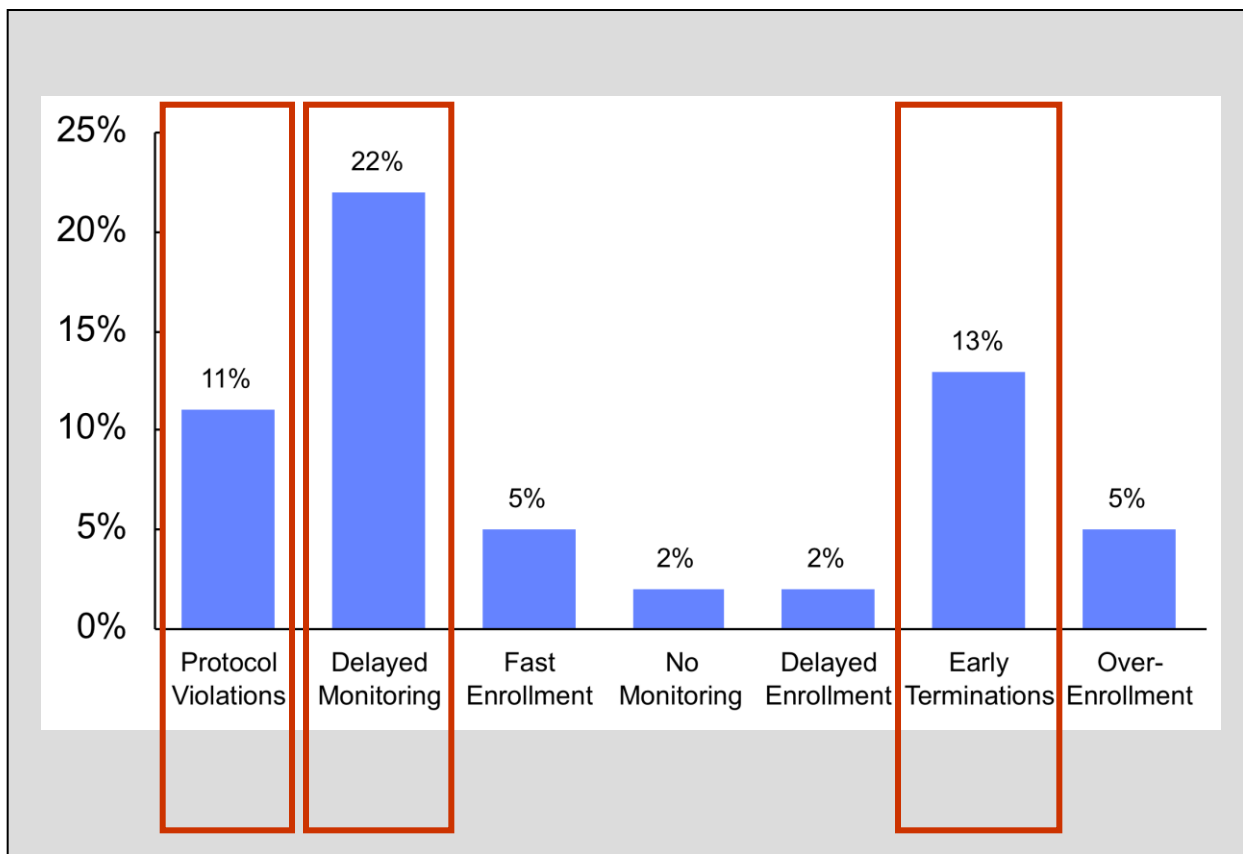
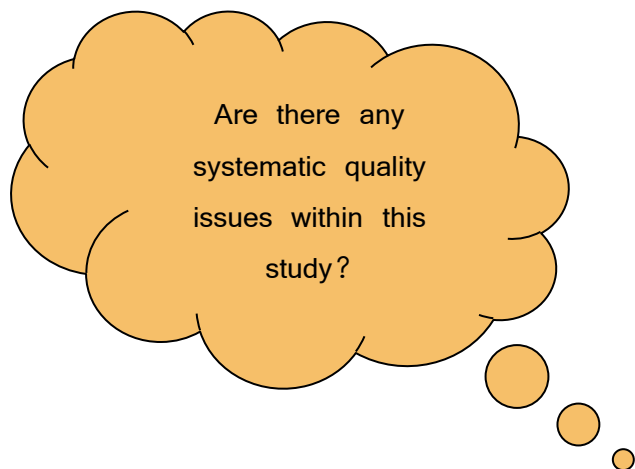
Is there an unusually high rate of unexpected drop-outs at any site?

Risk Indicator: Premature terminations of patients¹



QRM to detect systemic issues

Share of Clinical Trial Centers with Red RI Signal in Country A



Protocol Violations – QRM tracks the data over time, which allows for addressing the issues as in this case: KRI Value drops

Microsoft Excel - CTC_PROTOCOL_WA16855_2008_SEP(1).xls

File Edit View Insert Format Tools Data Window Live Meeting Help Adobe PDF

Type a question for help

Imago 10 B I U %

A124 fx

Months: Sep-2007 - Aug-2008

	Sep-07	Oct-07	Nov-07	Dec-07	Jan-08	Feb-08	Mar-08	Apr-08	May-08	Jun-08	Jul-08	Aug-08
KRI Signal							●	●	●	●	●	●
KRI Value							24.21	17.36	15.47	15.33	4.03	2.54
Threshold							> 3.00	> 3.00	> 3.00	> 3.00	> 3.00	> 3.00
Number of patients enrolled per site							6	6	6	6	6	6
Number of protocol violations per patient visit per site							0.02	0.02	0.02	0.01	0.04	0.04
Number of protocol violations per patient visit per protocol							0.00	0.00	0.00	0.00	0.01	0.01

Risk Assessment all CRTNs / ... / CRTN 34050 / CRTN 34051 / CRTN 34052 / CRTN 34053 / CRTN 34054 / CRTN 34055 / CRTN 34056 / CRT

Ready

The number of violations increases: an alert for the study management team

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Type a question for help

80%

Imago 10 B I U

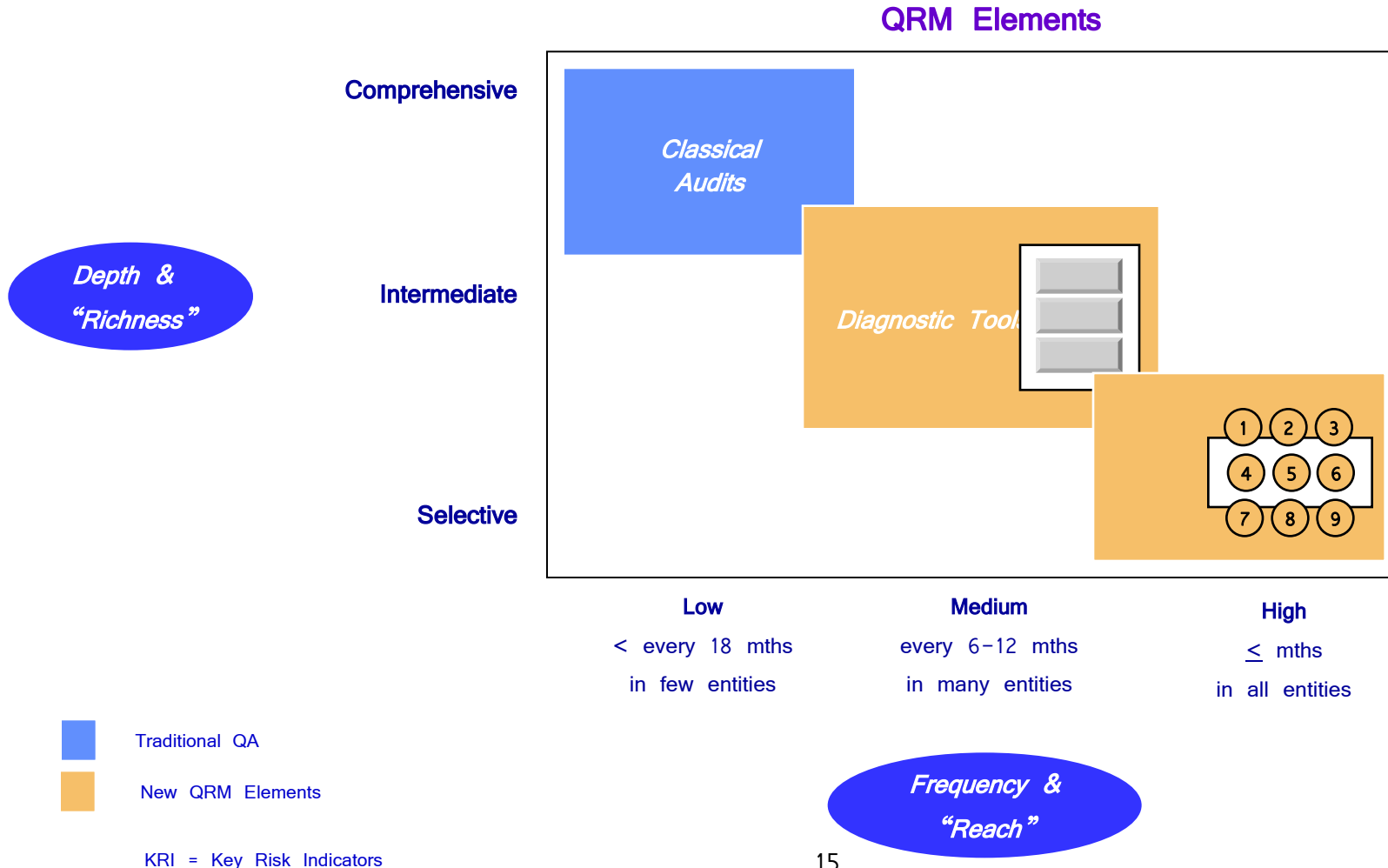
A124 fx

	Sep-07	Oct-07	Nov-07	Dec-07	Jan-08	Feb-08	Mar-08	Apr-08	May-08	Jun-08	Jul-08	Aug-08
KRI Signal							●	●	●	●	●	●
KRI Value							0.00	0.00	0.00	0.00	3.88	4.54
Threshold							> 3.00	> 3.00	> 3.00	> 3.00	> 3.00	> 3.00
Number of patients enrolled per site							4	4	4	4	4	4
Number of protocol violations per patient visit per site							0.00	0.00	0.00	0.00	0.04	0.06
Number of protocol violations per patient visit per protocol							0.00	0.00	0.00	0.00	0.01	0.01

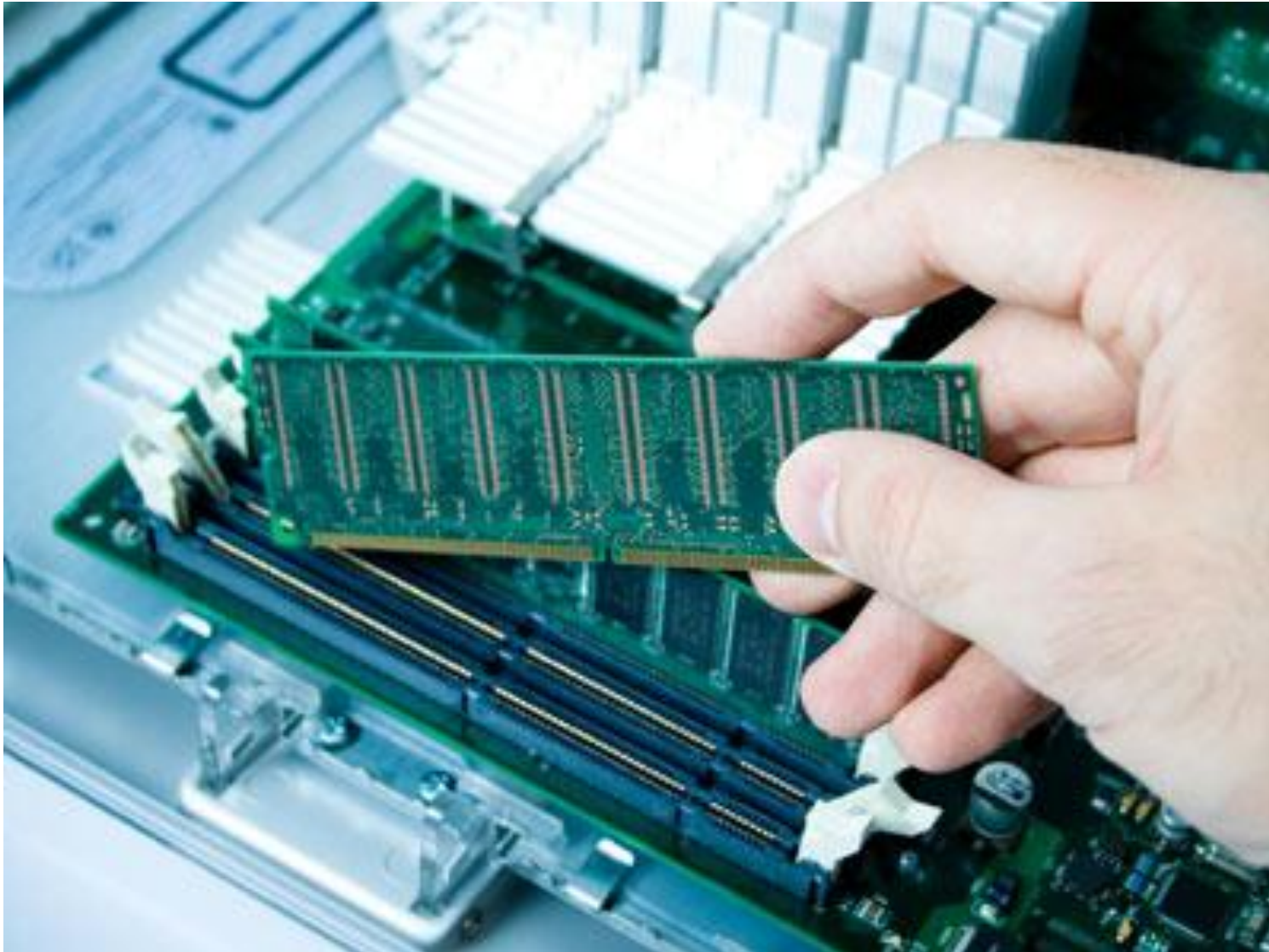
● Red signal ● Green signal ● KRI turned off ■ No Data

Ready

Integrated Quality Management Approach



Automated QRM Tools Enhanced



Impact of QRM on “traditional” Compliance & Quality Activities



Impact of QRM on “traditional” Compliance & Quality Activities



The Reward for Quality by Design and Quality Risk Management



Errors “that are understood”, do not matter!

Taking Quality beyond Compliance

The QRM & QbD Twins



A lesson from the US Navy



A Wind of Change



**The Cost of
Accepting Work-
arounds
or
When Murphy is
the Engineer**

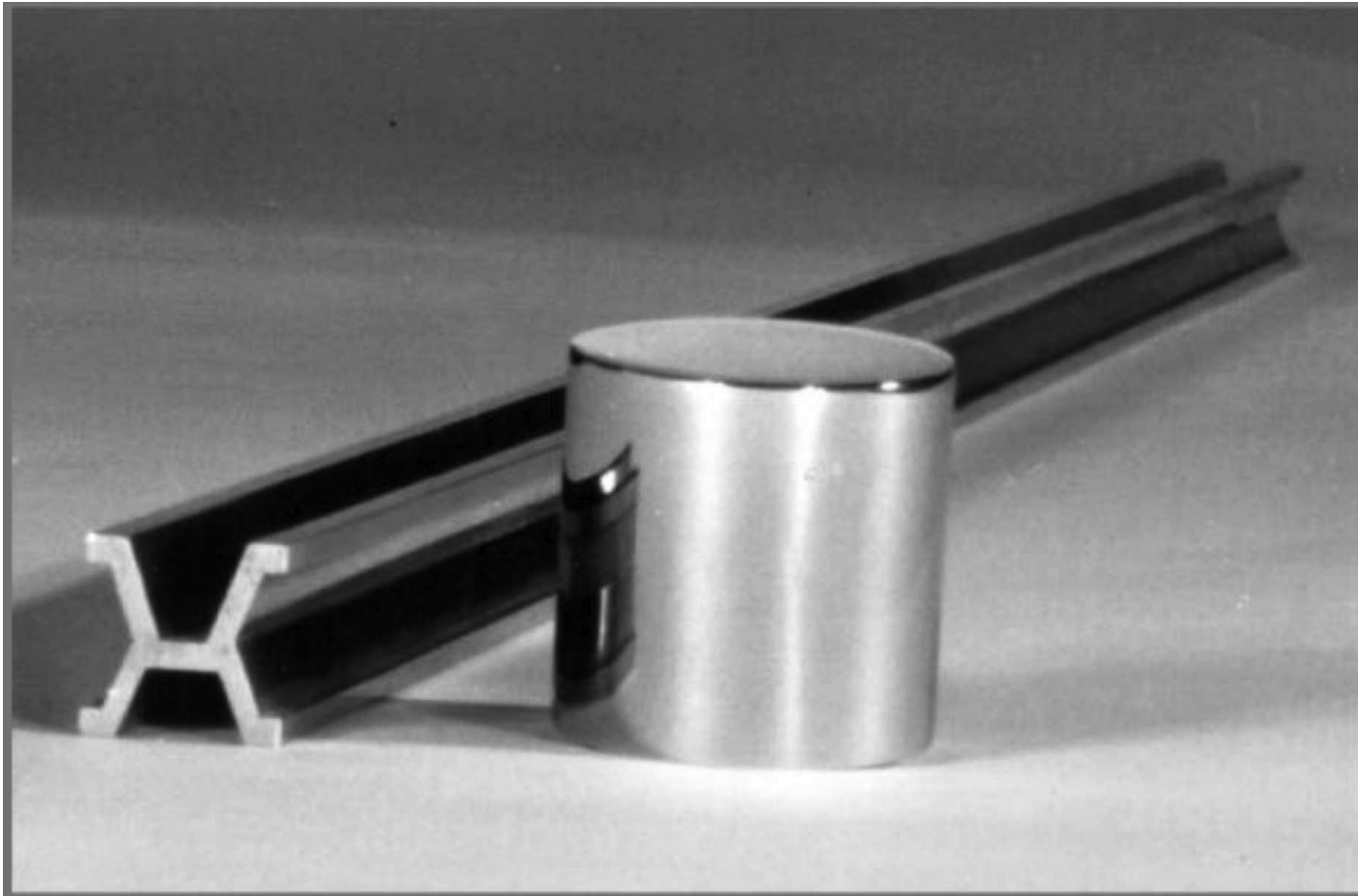


Taking Quality beyond Compliance

What needs to be done



Essential Elements to drive Quality by Design in Drug Development



**Essential
Elements to
drive Quality
by Design in
Drug
Development**



My Contact Details

- ▶ widler.ed@gmx.ch
- ▶ St. Alban Ring 245
CH-4052 Basel