chemgineering

Quality Oversight

Part II

Metrics & KPIs – a Case Study:

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From Metrics to Quality Oversight

So we implemented all boundary systems

- Compliance
- Tools
- Awareness
- (MIS)

→ let's start measuring & feeding the MIS

→ let's start getting Oversight

Why not simply use Management Review?

MR might be somewhat static
have a low frequency
be non-quantitative
be dis-connected from daily business

→ need “continuous” information flow, visualization, a “cockpit”
→ need connection through the management (review) ranks
→ need information aggregation
→ Design more quantitative and aggregative KPIs / Metrics
→ Implement tighter monitoring / control

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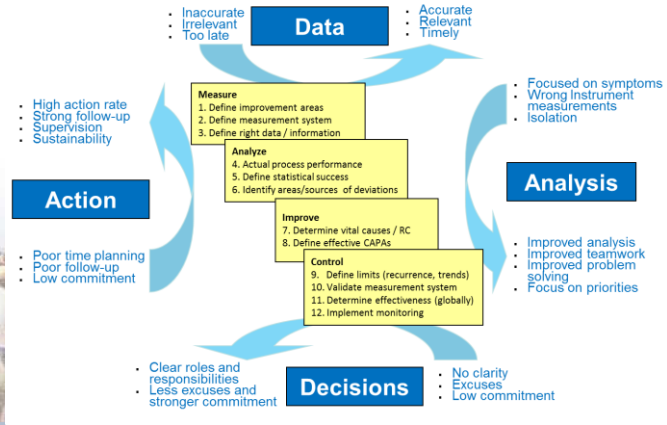
In a nutshell

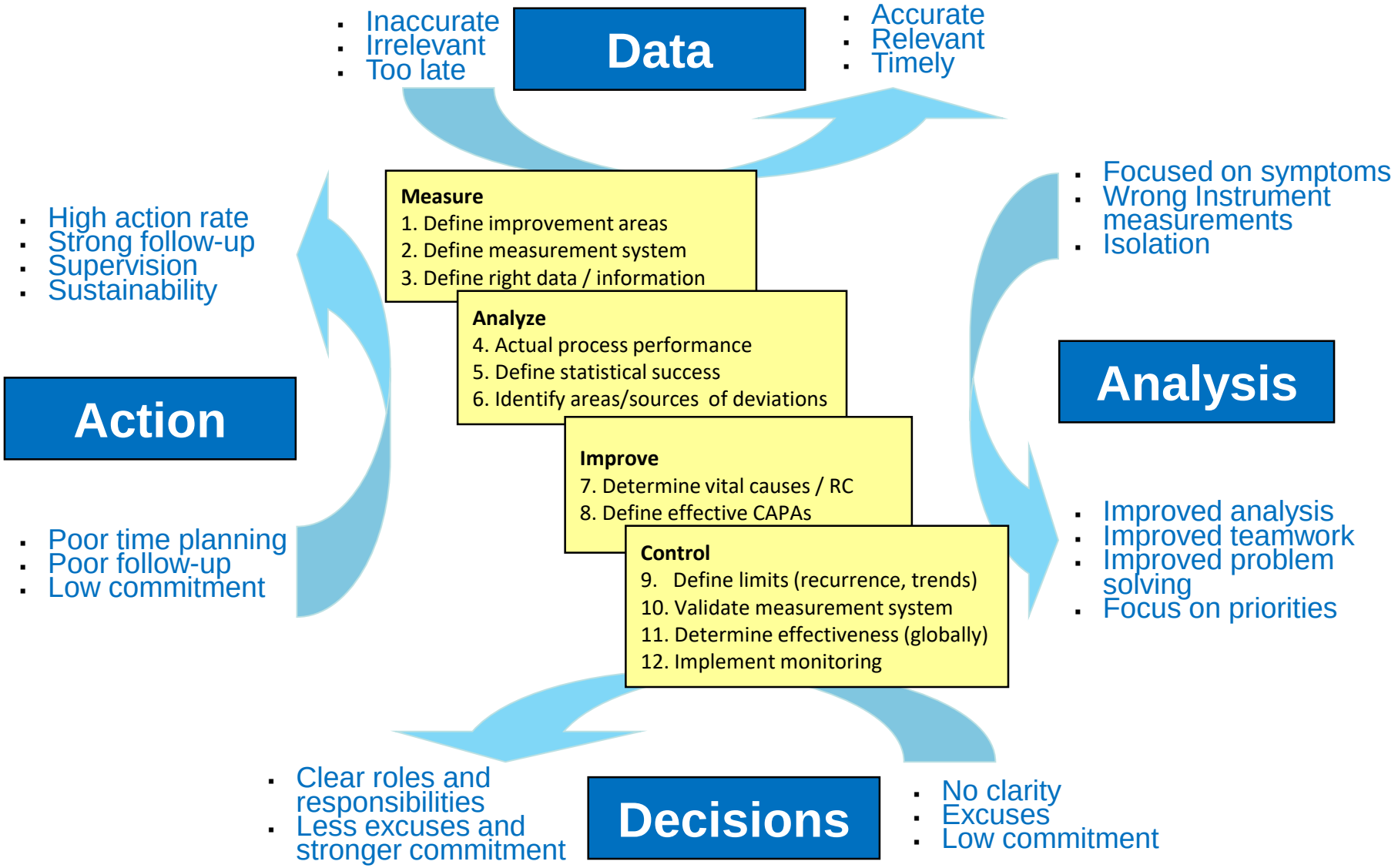
Quality Oversight means

- timely availability of true, representative data for
- sound analysis of the situation,
- resulting in adequate decision taking
- leading to the right, sustainable (remediation) actions

→ continuous state of control



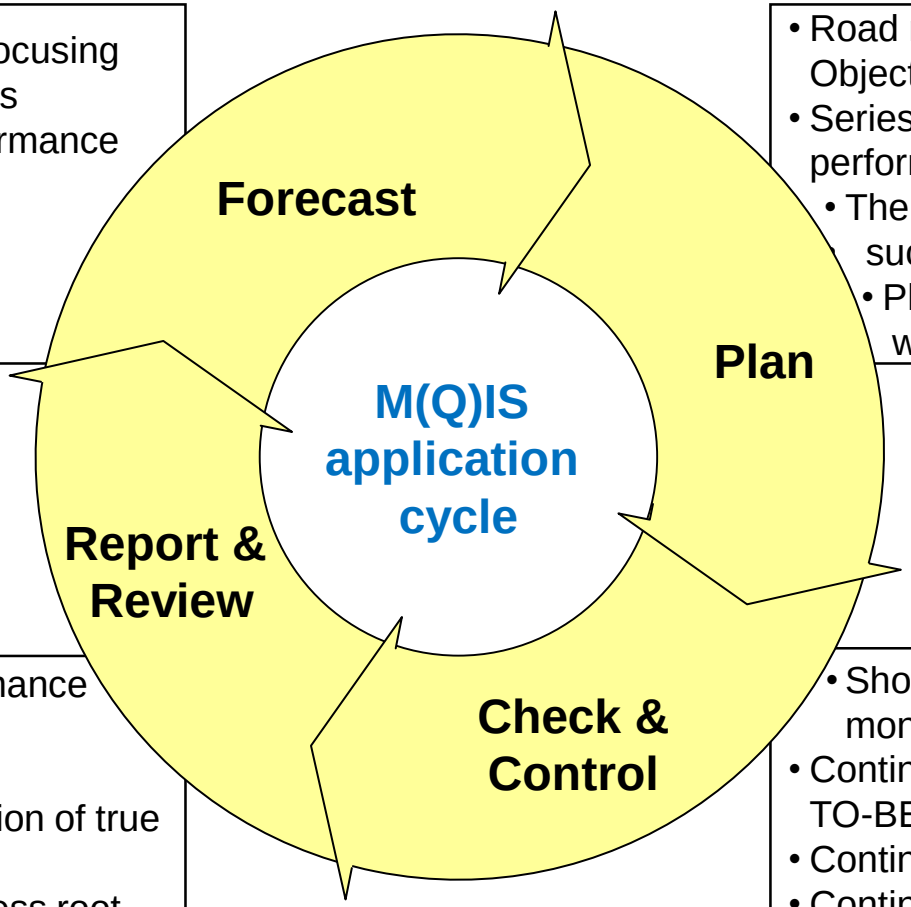
Idealized situation for a Management Info System



We need consolidated data → KPIs / metrics

Implement KPIs into M(Q)IS: Forecast – Plan – Control – Report & Review

- Projections and targets focusing on Business Q-Objectives
- Connection of past performance with a plan to improved performance
- Usual timespan of 6 – 12 months

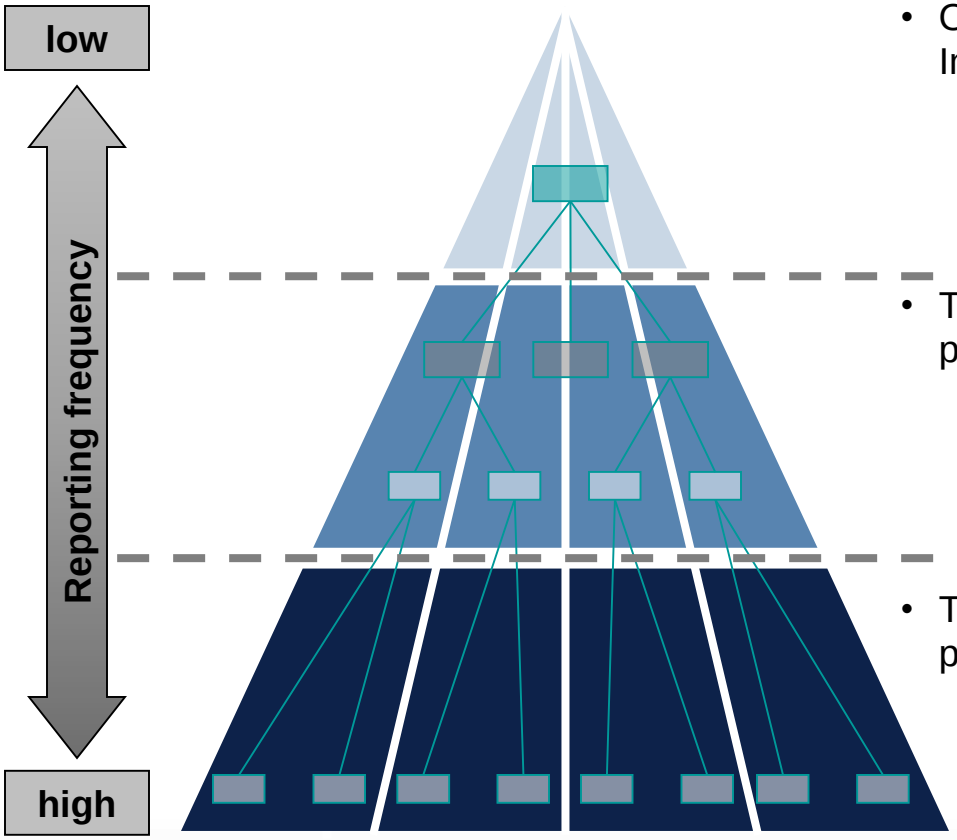


- Road map to achieve Business Q-Objectives
- Series of actions to reach required performance level
  - The plan is the baseline for success control
  - Planning frequency: weekly/monthly/yearly

- AS-IS *vs*. TO-BE performance
- Clear accountabilities for performance
- Extracting and identification of true root causes
- Deciding actions to address root causes
- Usually weekly / monthly → yearly

- Short interval control – weekly / monthly
- Continuous review of AS-IS *vs*. TO-BE
- Continuous focus on variances
- Continuous corrections
- Data recording of causes for deviation/variance

KPIs / metrics need sound aggregation



- On the top level the condensed Key Performance Indicators (KPI) are defined for:
  - All information at one glance
  - Goals and status control
  - Trends and strategic evaluation
- The mid level consolidates indicators to tactical parameters:
  - target/status - divergence
  - BU / site -specific information
  - Allows for trends visualization & tactical measures
- The basic level uses true operative indicators / parameters:
  - Detailed informations on status of quality events and systems; processes
  - Allows for control & optimization

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Using Quality Metrics for Quality Oversight

Distinction Quality Metrics *vs*. Q-Oversight:

- Metrics (amongst other) needed for Oversight
- Oversight & Quality „trusted“ if specific Metrics ok

→ What kind of Metrics are there?

→ How to pick and use “right” Quality Metrics?

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Using Quality Metrics

Some Metrics are desired by FDA / might be enforced in future
- like Quality Metrics Initiative (Pharma) with ISPE

Some “Metrics” are already required
- APR (FDA – *connects to Q-Metrics*) & PQR (EU) data
- contin. PV data (for new processes)
- Management Review & PQS parameters (EU GMP Chapter 1 & part III, ICH Q10; 21cfr part 211.180 f)

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FDA & ISPE metrics

FDA & ISPE initiatives [UCM455957 (& UCM456211 & UCM374192)]

- **Lot acceptance rate** [# of lots attempted & # of lots rejected]
- # of lots reworked or reprocessed
- # of lot release tests conducted
- Oos rate [# of Out of Specification Results (# of lot release tests failed)]
- # of lot release results invalidated because of laboratory error/anomaly
- **Product quality complaint rate**
- **Invalidated out-of-specification rate**
- APR or PQR on Time Rate
- Stability Failure Rate
- # of recalls

Special/other metrics, e.g. aseptic production

- Right first time rate; process capability
- Media Fill failures; Environmental Monitoring events
- Trainings on time; Revalidations on time, Calibrations on time
- inspections passed-ratio; critical / recurring complaints

Other sources: PDA (*Melissa Seymour*); Xavier University/PWC

Using Quality Metrics

Various other (types of) Metrics and applications, “metric-like” parameters, and supportive systems, e.g.

- control charts / SPC → contin. Process Validation
- PQR/APR data
- “5S” tools & systems

Some “Metrics” are simply needed/useful for good oversight:
→ Combination of product- and process-specific metrics with QMS metrics

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Metrics on site level

- “classic” metrics, like deviations, oos, complaints, changes, CAPAs , stability samples….: opened / closed / overdue… trends, runtimes…
- Internal effectivity checks: deviation/oos/complaints recurrence – good clustering parameters necessary, Pareto tool possible
- Internal effectivity checks: CAPAs reopened due to ineffectiveness

- „Dynamic“ KPIs can be issued and adapted depending on situation to remediate the situation. Remove KPI once situation solved.
- Mitigation should be designed already on site level, e.g.: examining “waste” streams/tasks and permanently eliminating recurring deviations through engineered solutions (instead of “*retraining*”)

- 5S method (incl. walk-throughs / self-inspection) is a good tool to quality

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Metrics - What can we learn from the ISO world?

- Management Review a long time established topic for e.g. Medical Devices (ISO 13485)
  - Audits / Inspections
  - Complaints / Customer Feedback
  - Process capability and product conformity (~ deviations)
  - CAPA status
  - Follow-up of previous reviews (CAPAs)
  - Changes
  - Recommendations for improvement
  - Impact of changed/new regulation

Metrics - What can we learn from the ISO world?

Quite some similarities in contents, but clearer system framework, better incorporated into general SOP- and Q-system:

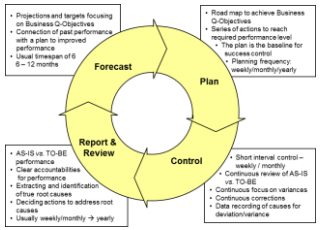
- Clear **SOP, annual plan** and **predefined agenda**
- Good documentation (**standardized report**) expected
- Hint to importance of **meeting structure**
- Clear outcome and **actions** expected regarding
  - process and product improvements
  - resource requirements

KPI requirements on site- or BU- level

- BU / site management is responsible to implement corporate policies
- Especially on the level above the site / production block, monitoring becomes important
- Some type of „Q-council“, aggregating and cross-connecting events:
  - Compare and cross check, general
  - Some benchmarking possible
  - “challenge” site info & measures
  - Overview and disseminate info on issues; deviations; complaints; Audit results, CAPAs at other sites / between sites
  - Monitor & analyse CAPAs reopened due to ineffectiveness, check, compare and verify CAPA effectiveness measures
  - Discuss “engineering solutions” for recurring issues
  - Trends may be more informative than plain numbers, also trends can have acceptance limits

Typical tasks on corporate level

- Define / Authorize Corporate structures
- Define / Authorize Policies / SOPs and initiate translation to site level
- Generate (annual) Q-Plans & Reports
- Generate Internal corporate audits system
- Generate communication / visualization system

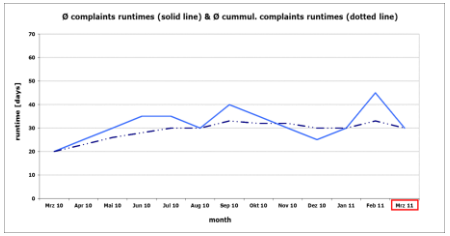


- KPIs / Executive Dashboard - Objectives
  - Visualization rather than numbers
  - Trends rather than absolute numbers, or thresholds
  - Escalation numbers & events

- Define own corporate KPIs and objectives/targets, e.g.:
  - Q-staff numbers to overall / OPS staff to SKUs
  - Resource use and efforts
  - Number of Q-staff per level
  - Evaluation of results of analysis on Issues / CAPAs at various sites

How to pick the right Metrics & KPIs?

How do we define and agree on „good“ KPIs?



→ Workshop on KPI definition
  → Peek at FDA /ISPE/PDA Metrics
  → Invite different levels of the Q-reporting chain
  → Propose indicative KPIs to (corporate) management and get input / feedback
  → Meeting with representatives of all affected sites

→ Assess getting help of external coach/mediator

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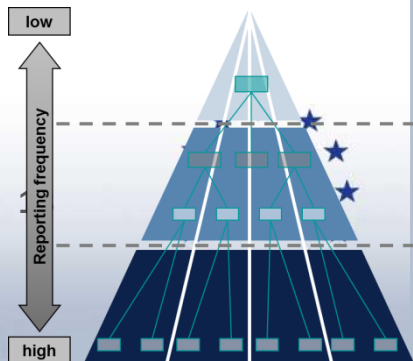
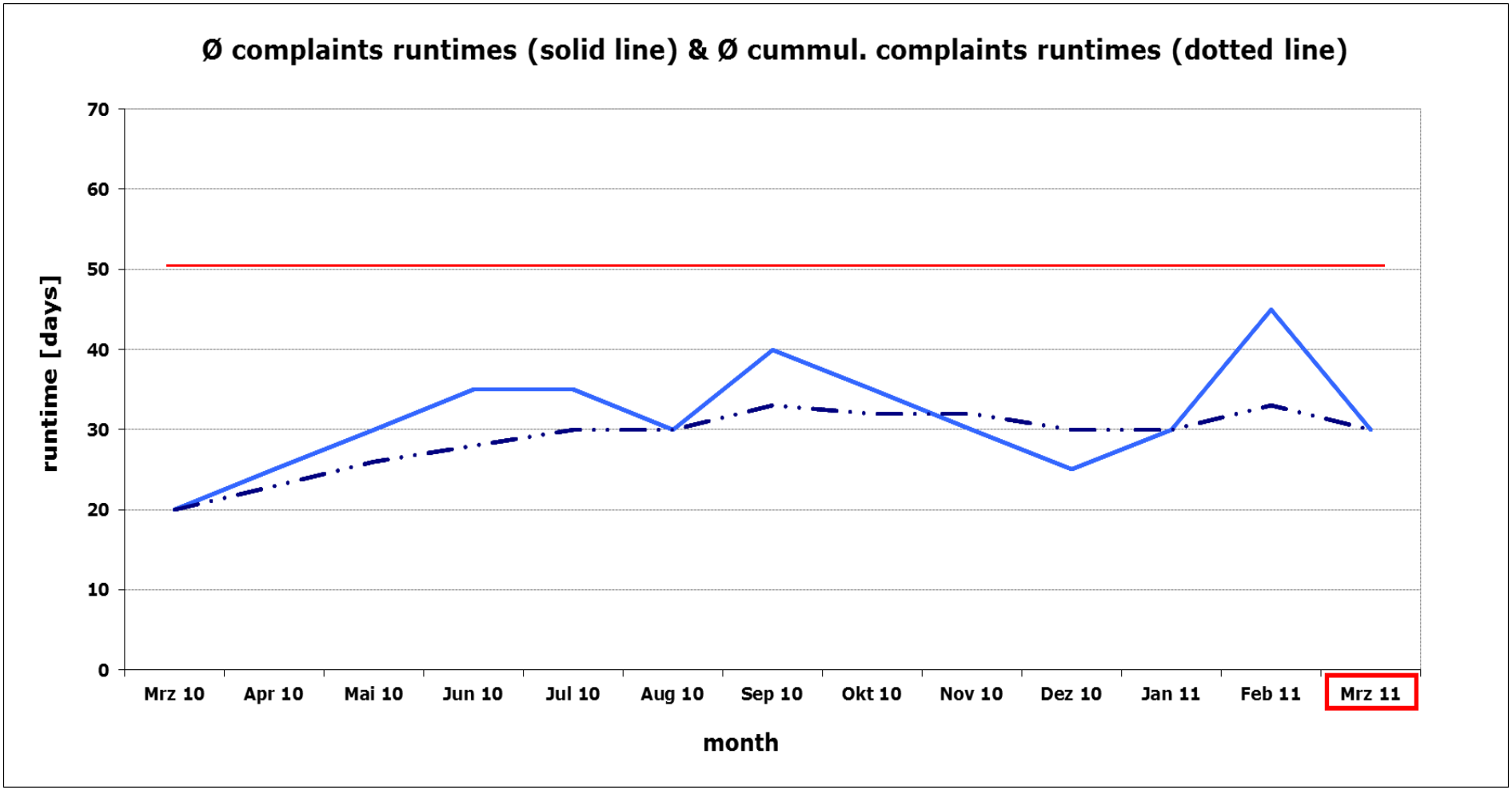
Give Metrics & KPIs their framework

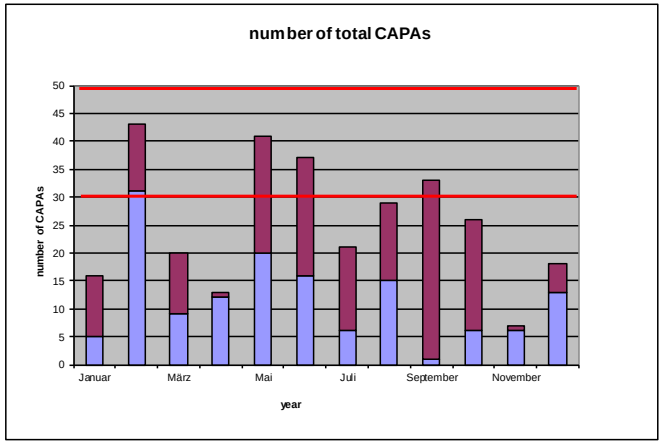
- Generate SOPs on how exactly to define, measure and report KPIs (incl. frequencies)
- Describe how KPIs connect to Q-Plans and other Q-tools / GMP systems (cPV, PQR, Management Review)
- Describe how to act upon pre-defined events / numbers / trends for certain KPIs
- Cross-link to Meetings: Output of one level (meeting) becomes Input of next (higher) level meeting
- Generate reporting tools; Excel, Sharepoint etc.



Quality Metrics – Example

1	KPI	**Ø complaints run times**
2	Calculation	Ø complaints run time = Σ (Date complaint closure – Date complaint intake) / Σ obtained complaints Cummulative: cummulative over 13 months



Metric	Number of total CAPAs
	Target (Q-Unit and operational)
	few open CAPAs, relatively high number of closed CAPAs no target on opened CAPAs
qualitative description	*Total number of CAPA is the sum of closed & opened & still open CAPAs in particular month*
Formula	*total CAPA in period = opened + open + closed open = existing open CAPAs in DB - opened in particular period*
Metric Unit	*number (pieces)*
prerequisites and rules for metric calculation	*A CAPA is deemed opened once it obtains an ID number and is entered into the DB. A CAPA is deemed closed once QA has set the status to closed due to verified completion. Ineffective CAPAs will be reopened.*
Data Source	*CAPA Database*
capture method	*extract from CAPA DB, monthly intervals*
Graphic result	
Metric responsible	*CAPA process owner*
reporting frequency	*monthly*
reporting form	*grafically by chart and table; resolution: monthly Alert Limit & escalation specification for open CAPAs*
target for metric (alert)	*open: nmt 30*
escalation spec	*open: nmt 50*
escalation / control responsible	*Head QA*
notes	

KPIs definition in SOP

- **General approach in SOP**
- **list of metrics and definitions in Annexes for easier adaptation**

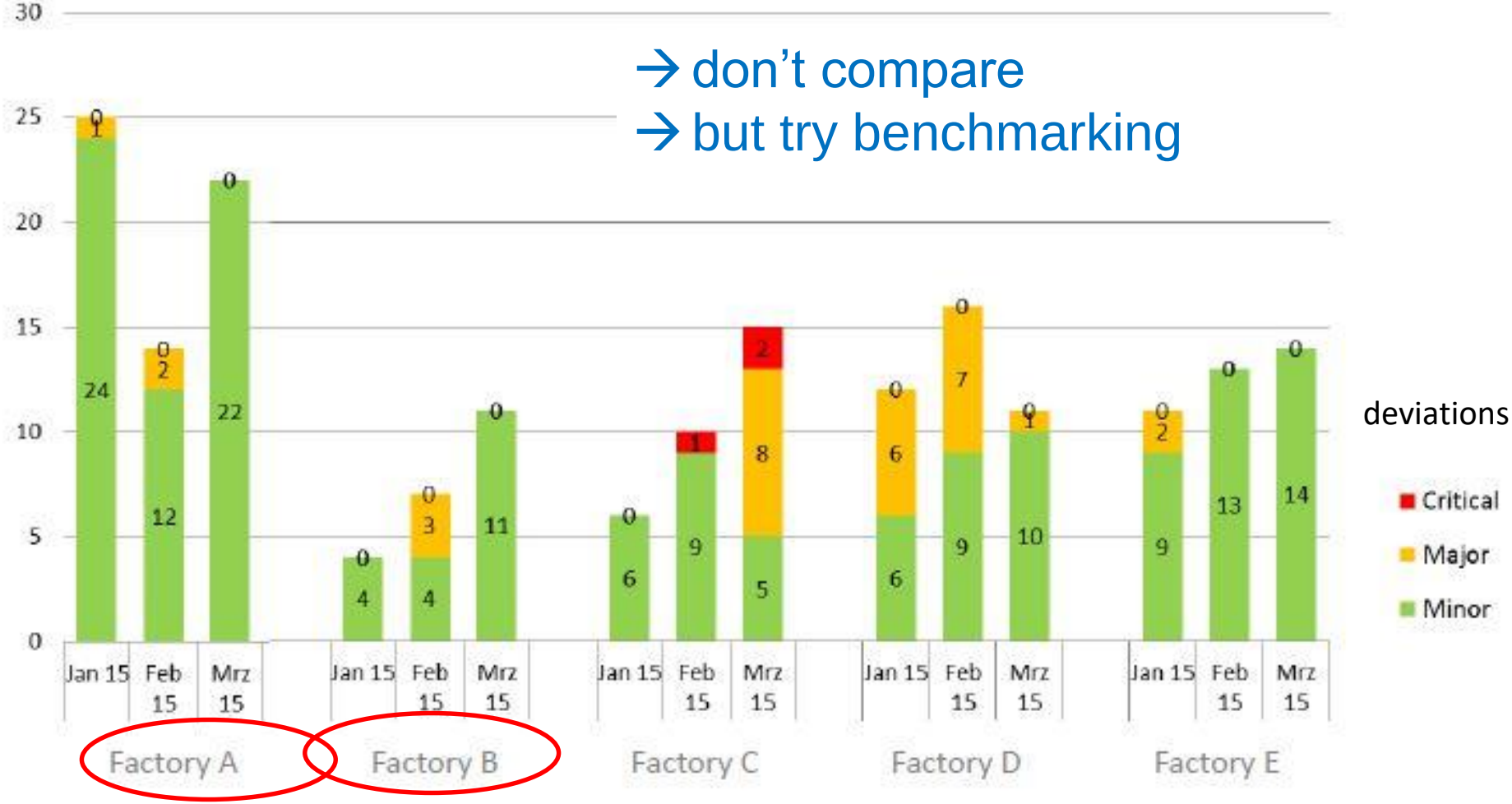
- **Non-GMP trial phase, Pilot**

- Assembling will need SOP / Manual with good description.
- Also possible to include in Excel sheet(s)

WS “Tools” – KPIs - aggregation

„comparison“ – overview rather – of e.g. sites, incl. trends

→ don’t compare
→ but try benchmarking



Source: Dr. König, Aenova Group

Ombudsman program – “Whistleblowers”

Ombudsman programs provide direct access between any company employee and a neutral third-party that takes reports of suspected conditions or activities that are illegal, unethical, or against company policy. Employee concerns about cGMP compliance fall into all of these categories and should be included in the program along with other areas such as finance, safety, and human resources. In order to preserve confidentiality and engender openness, the Ombudsman program should be managed independently by a third-party and coordinated by a neutral group such as the legal department. The quality officers and their respective quality councils will have a role to play in investigating and responding to reports.

John E. Snyder

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Quality-Oversight – Case Study

Mid-Size European Pharma Manufacturer, various dosage forms
Aim:

- Implement Q-Oversight & KPIs for corporate assessment of sites
- **5 sites**, across EU
- Consolidate data
  - “horizontally” (monthly into annual → efficiency) &
  - “vertically” (sites to corporate)
- Allow **use for site** and **corporate**, replace existing reports

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Case Study: step 1: definition of reporting units

- What is a reporting unit / level?
  - line, plant, site?
  - by product or by location?
    - Problem: large volume vs. small volume products

→ For Q-Oversight, the **site level** was chosen
  → Site-internal reporting possible
  → Internal metrics consolidated to site level KPIs
  → Special products and issues (variable KPIs) can be reported separately
    → Report templates have **variable parts** in addition to **fixed parts**

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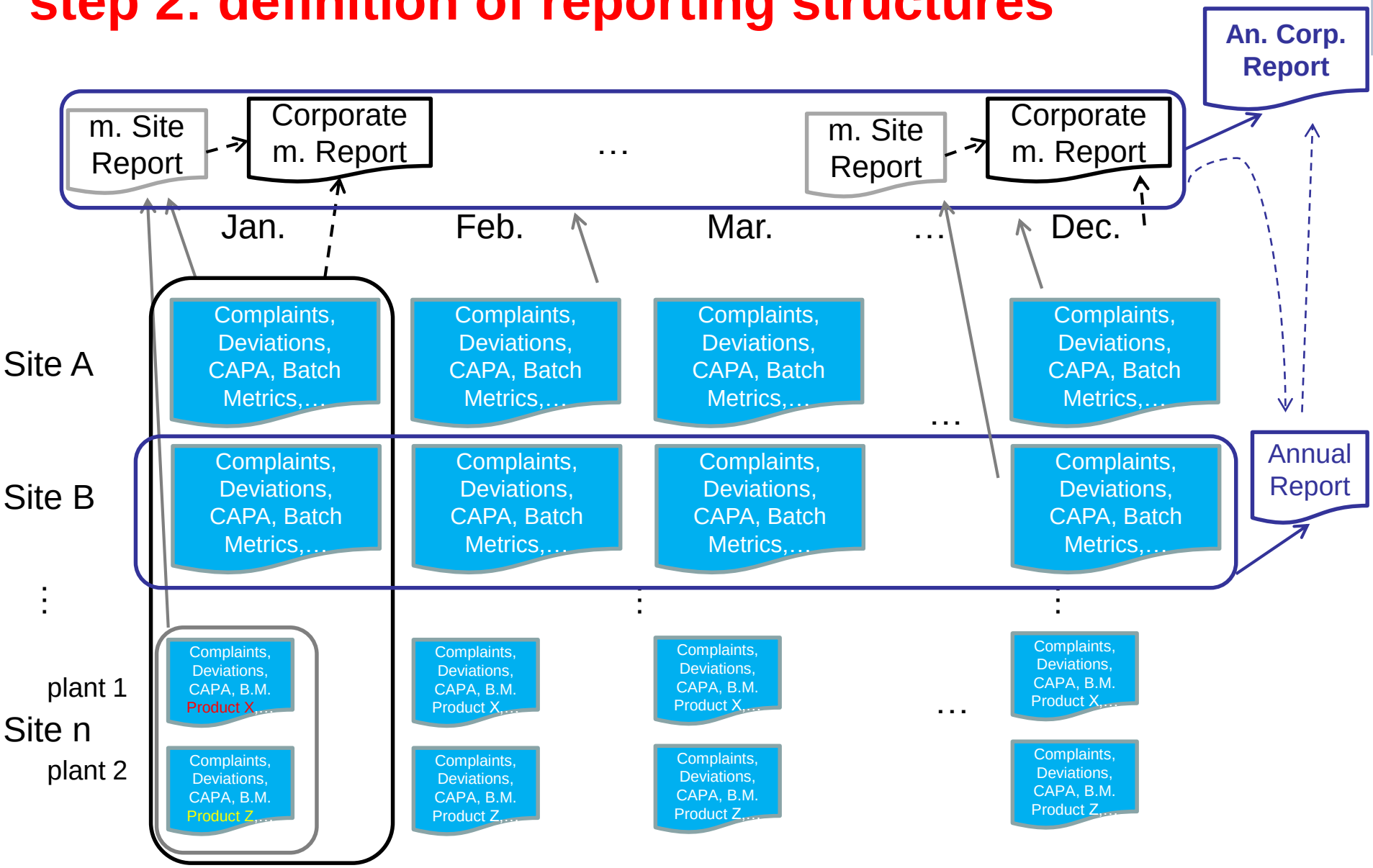
Case Study:
step 2: definition of reporting structures



Case Study: step 3: defining metrics/KPIs

- Initiator: corporate Q-Unit, “task force”
- Face to Face meeting with (QA-) representatives of all sites
- Explaining goals and concept
- Proposing first KPIs
- Check vs. existing KPIs/metrics
- Evaluating ease of KPI generation → tools, (e-) systems

→ Results: first set of agreed KPIs
→ Consolidation of used templates (Excel sheets)
→ Identification of tools-gaps & KPI-generation problems
→ Assess change of KPI (generation) or implementation of tool
→ Costs for corporate / site

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Case Study: Results step 3: KPIs

- Monthly & Quarterly
  → *no 2 Reports, rather add quarterly parts to routine monthly*
- „product“-related and „Q-system“-related (divided to monthly/quarterly)
  → *not necessarily required in my opinion*

- Product Complaint Rate (per released units)
- Number of Deviations / Batch Deviation Rate / Batch Rejection Rate
- Invalidated oos-Rate (*QC-performance measurement*)
- CAPAs: opened / closed / overdue
- Complaint timelines
- Investigation timelines
- Change Control timelines
- PQR and Self Inspection accomplish rates

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Case Study: step 4: building templates & tools

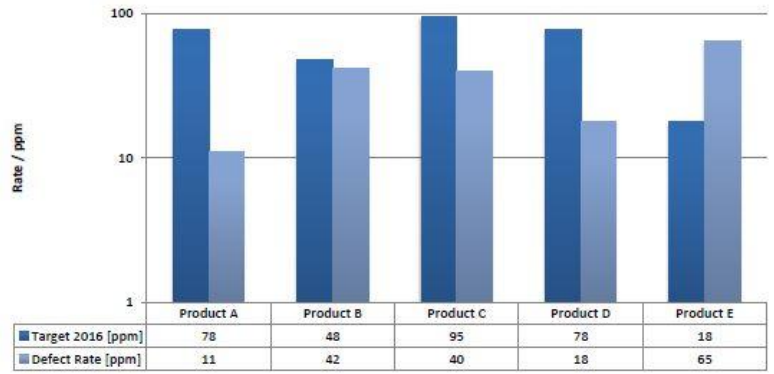
- Agreed metrics have to be translated to Excell Sheets
- All metrics one Sheet, several Tabs
- Basis: **tables** with content. Each Tab can have its **graph** (*not mandatory*)
- Front page "**Dashboard**": visualization: graphs but also tables

- ➢ Manual input of data is too laborious
- ➢ Transfer within Sheet should be automated (Macro)
- ➢ Input should be automated: programming of interfaces required: SAP, Trackwise etc.!
  - ➢ readout of specific cells / containers

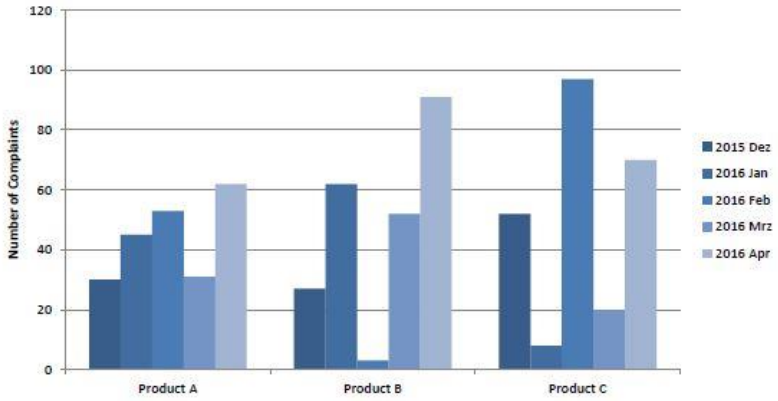
Monthly Quality Report
Production Site Niceview
May 2016

Site	
Reporting Month	5
Reporting Year	2016

Complaint overview



	Product A	Product B	Product C	Product D	Product E
Target 2016 [ppm]	78	48	95	78	18
Defect Rate [ppm]	11	42	40	18	65



	2015 Dez	2016 Jan	Feb	Mrz	Apr
Product A	30	45	53	31	62
Product B	27	62	3	52	91
Product C	52	8	97	20	70

Case Study:
step 5: Workshops at sites - preparation

Design of preparatory Questionnaires, e.g. ca. 50 questions, to allow for knowledge consolidation and assessment of existing and planned system:

Questionaire				
1.	Review of existing meeting and reporting structure			
1.1	Meetings	1	2	3
1.1.1	Describe the current quality related meetings incl. quality circles.	monthly Q-Meeting	weekly (Q-&) Mngmnt-Meeting	mothly Site
1.1.2	Who is the owner of the meeting?	Ms. Nice (Head QA)	Mr. Cool (Head OPS)	Plant Manager
1.1.3	How often are the meetings held?	monthly	weekly	mothly
1.1.4	Who is involved in the meetings?	Q-Team	core Q-Team & Management	SME & Managers (cy. 30p.)
1.1.5	Which departments/ products/ units are covered?			
1.1.6	What are inputs for the meetings?	monthly Q-Report	monthly only: Q-Report annually: Mngmnt Review	ppt from Olga's Excel & SAP
1.1.7	What is the scope/ subject of the meetings?		1h, Q-KPIs, monthly	info rather, KPI sharing
1.1.8	What are the outputs of the meetings?			no minutes
1.2	Reports	1	2	-
1.2.1	What quality reports and trend analysis/ monitorings are generated?	Quality Status QM	Mangmnt Review Report	Monthly Q-Report Pharma
1.2.2	How often are the reports generated?	monthly	annual	monthly
2.	Feedback on new reporting templates for internal (site) use			
2.1	Do you see redundancies between other established internal reportings and monthly quality reporting or quarterly process review?			

Case Study:
step 5: Workshops at sites - preparation

- Send Metrics-Tool & Templates (Report Templates) to sites
- Request to check for data availability and collection options
- Request a preliminary template execution test

- Send questionnaires for primary assessment

- Communicate visit plans, agenda, etc.

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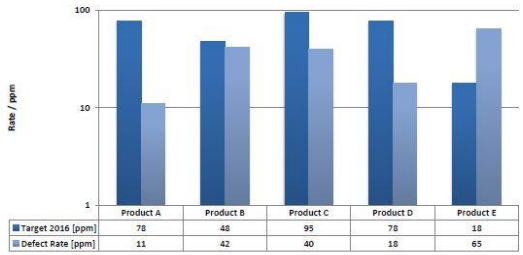
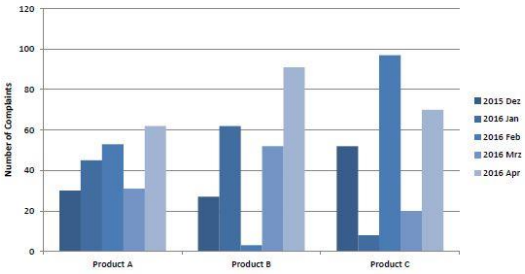
Production Site Niceview
May 2016

Site	
Reporting Month	5
Reporting Year	2016

Complaint overview





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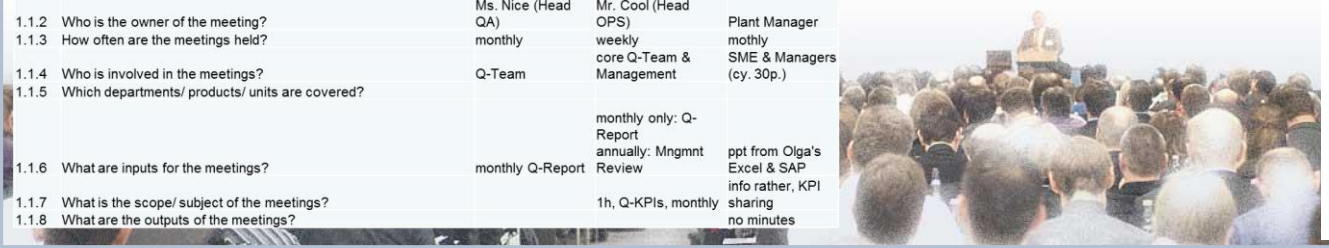
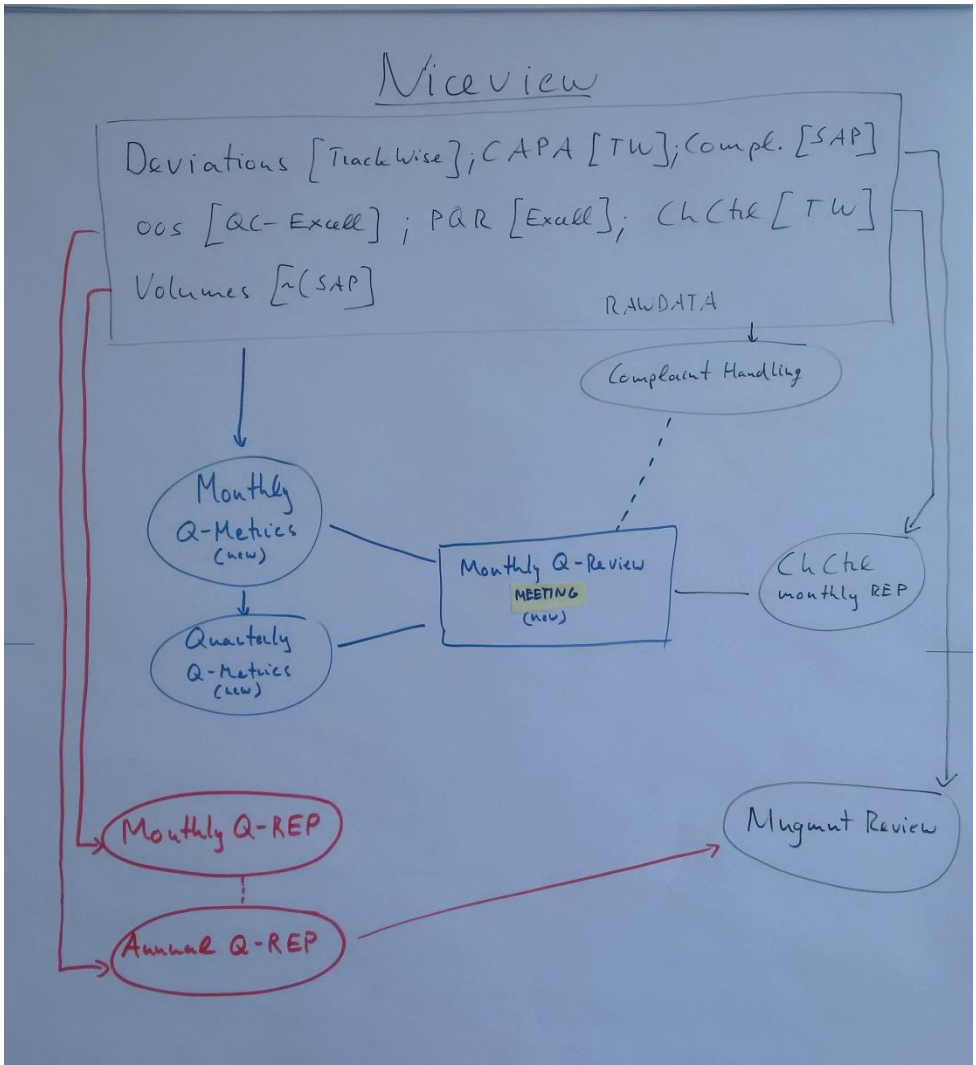


Case Study: step 5: Workshops at sites

Perform Sites Workshops
→ 2 days
→ team of 2 (corporate) + QA, Q-SMEs, others
→ Info site management, emphasize improvements:
- reduce redundancies
- get Oversight ⇨ improve quality & efficiency

Visualize Reporting & Meeting structures

Get Feedback,
Consolidate current system / situation and willingness & ability to install Q-Oversight



Case Study: step 5: Workshops at sites

Results:

Feedback & Knowledge on site situation, capabilities, culture/openness

Input for improved and adjusted Metrics & Templates

(e.g.: for some management overviews/summaries, tables (*with e.g. automatic highlighting*) might still be better than graphs)

First Dataset for agglomeration

Consent of sites, QA and Management

Comparison between all sites

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Case Study: step 5: Workshops at sites

Problems to be solved:

- Definitions: units produced / released
- Time range: moving, fixed year
  → can ERP/SAP generate that numbers?
  → who gets the numbers (sales?)

- Reporting timing: when are numbers available? → relates to reporting due date to corporate

- Deviation Rates:
  - „significant“ only?
  - Identification of Batches with Deviation?
  - Count of several deviations in one batch?
  - Merely *all deviations* divided by *all batches*?

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Case Study: step 6&7: consolidate results & aggregate KPIs for corporate

- Refine definitions, define tools & interfaces (TrackWise, SAP, …)
- Adjust reporting templates to consolidated KPI list, include site-individual metrics
  - → *Lots of thinking and programming and testing work!*
  - → *Software experts needed (Excel, TrackWise, ERP/SAP)*

- Define agglomeration of data: how to condensate data and keep it meaning full?
  - → *Remove site-individual information*
  - → *Concentrate on critical events, escalation thresholds*
  - → *Link to Forecast and Q-Planning (improvement projects, resources)*

- Monthly / Quarterly / Annually
  - → *Try to use same data, only to be accumulated / summarized*

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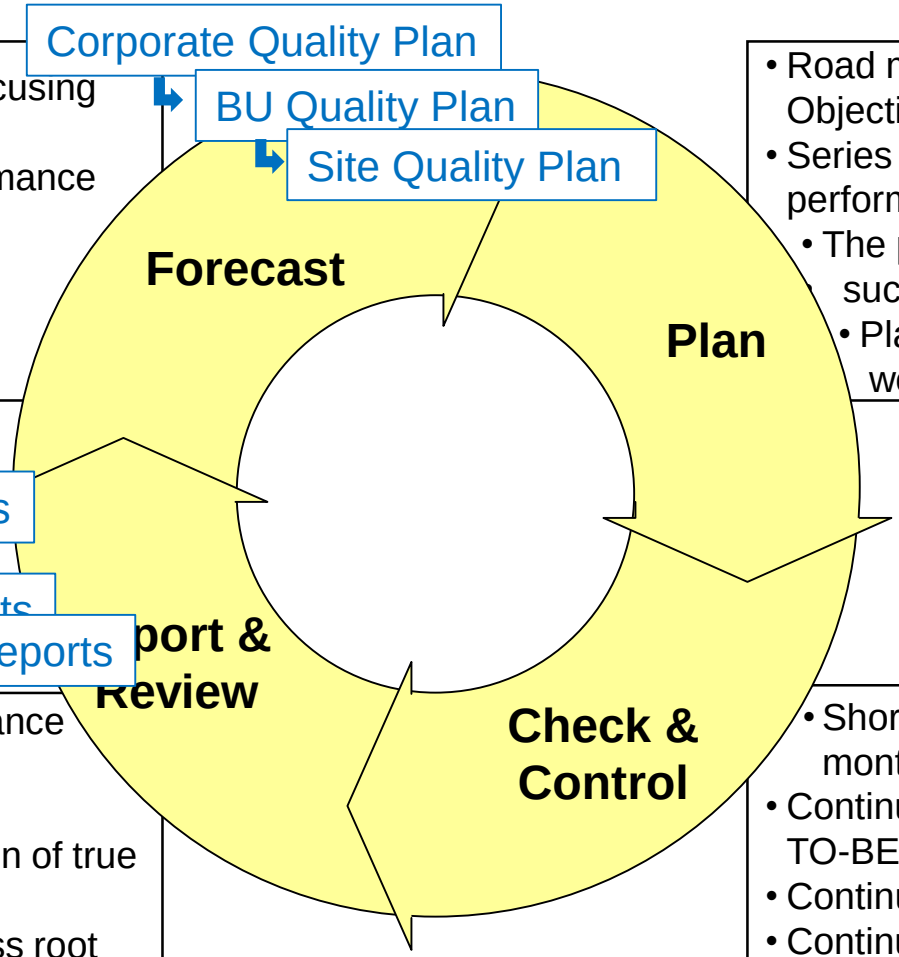
Case Study: Fit with theory?



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- Clear accountabilities for performance
- Extracting and identification of true root causes
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- Continuous review of AS-IS *vs*. TO-BE
- Continuous focus on variances
- Continuous corrections
- Data recording of causes for deviation/variance

Staying in Control: Checks & Feedback Loops

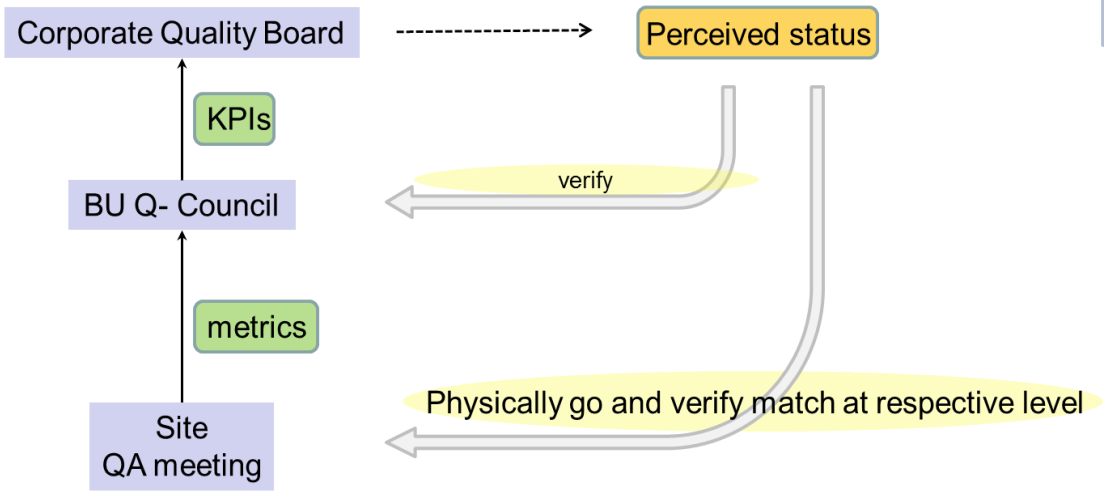
- The QM- and Q-Oversight Systems need regular checks and monitoring/review of their functionality

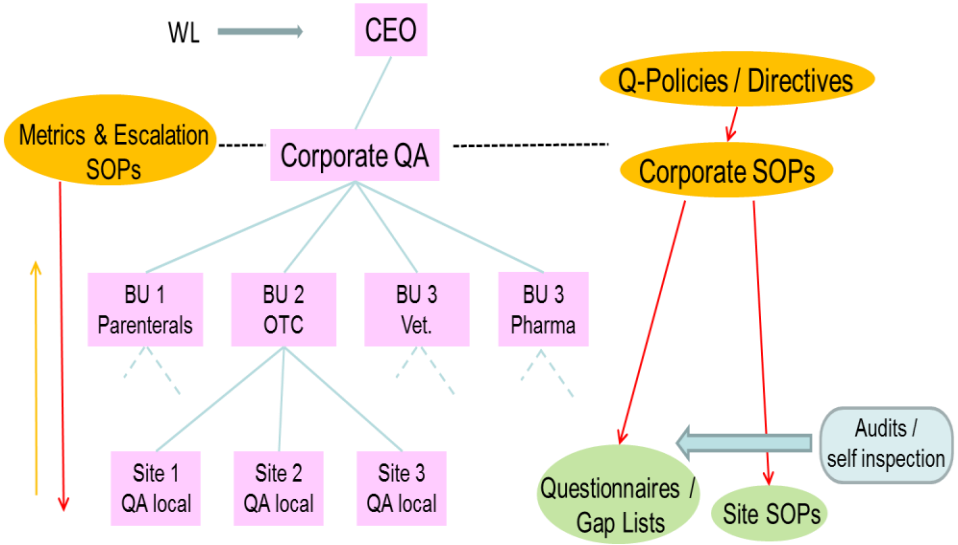
→ Retrospective control of variances and trends
→ Prospective anticipation of potential issues

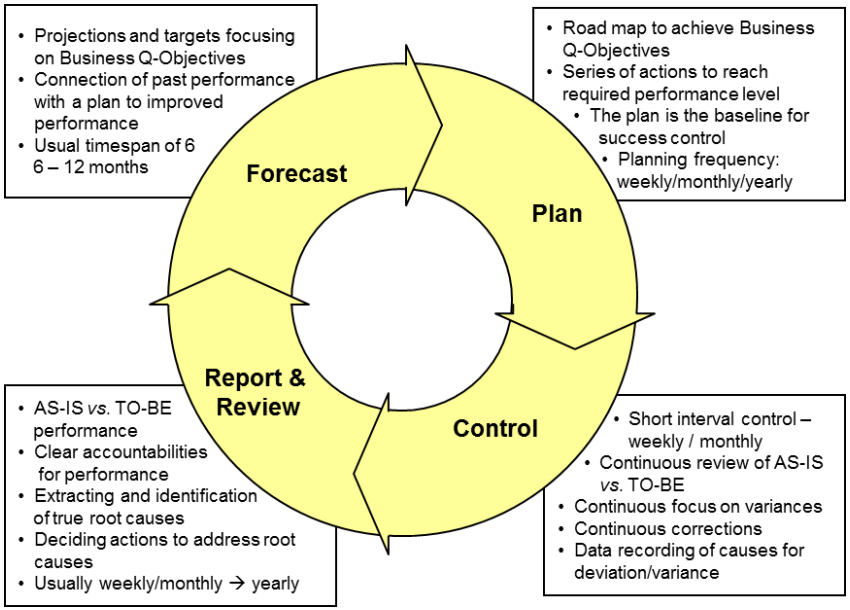
- Requires right **frequencies** for metrics review, typically

  - **Weekly** monitoring of metrics at the lowest Q-level (site, block)
  - **Monthly** data collection and reporting to site management and next Q-level (BU) and aggregated to division / corporate
  - Monthly management review of Pharmacovigilance (recalls, adverse effects)
  - Review of quality status by management in Quality Review and Management Review meeting(s) **throughout the year / once a year**

Feedback Loops

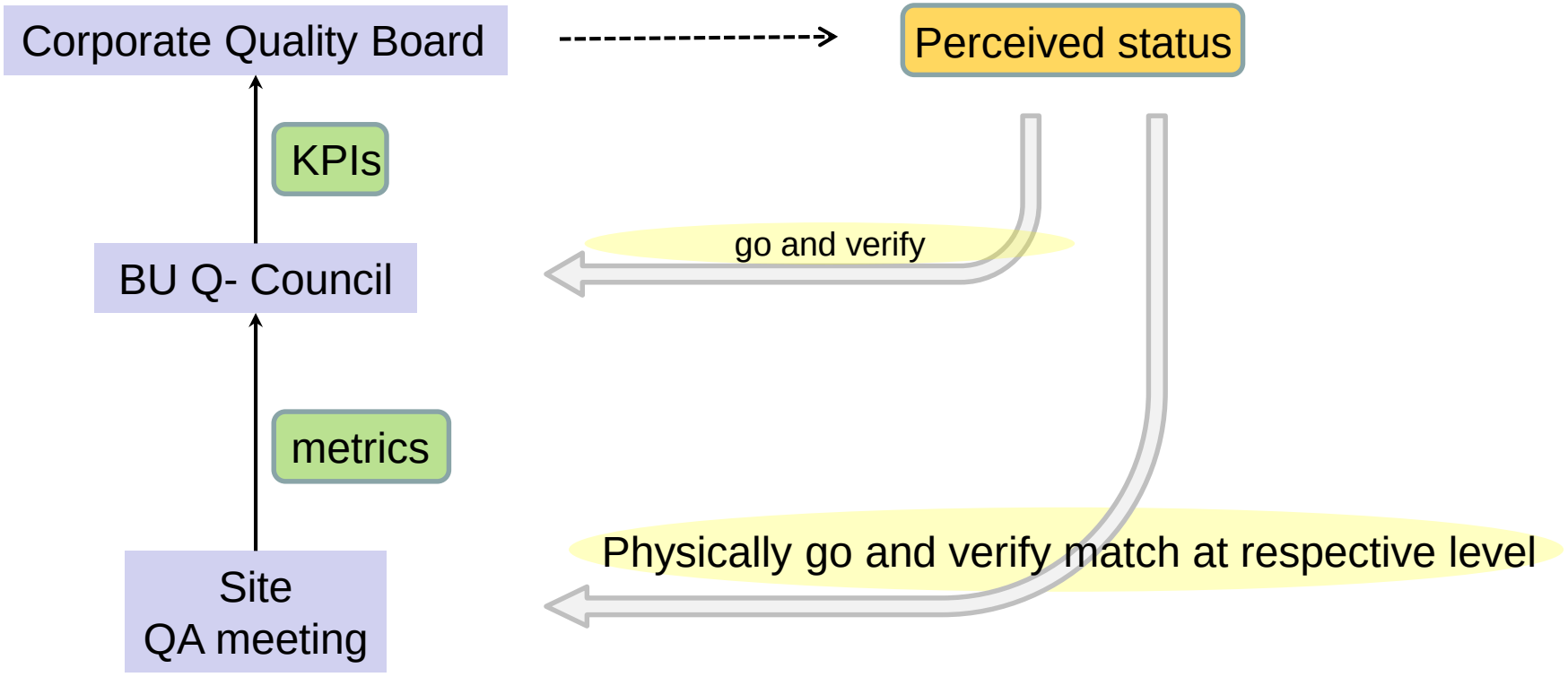






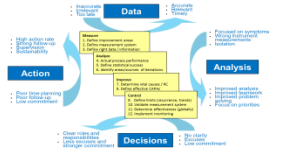
Verifying functionality of Q-Oversight

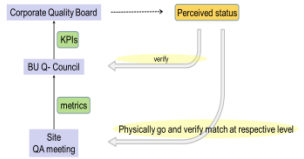
At least during Implementation Phase the validity of Q-Oversight results needs to be checked and monitored (physically on site, by a Q-Team)

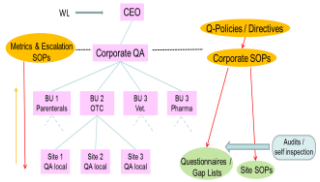


Feedback Loops

- Quality planning (Q-Plan) and completion control – M(Q)IS
  - on corporate level but also BU, site
  - Measure – Analyse – Improve – Control
- Effectiveness checks from higher Q-level (e.g. Q-council)
- Verification of match of true status vs. aggregated KPIs
- Internal corporate Audits
- CAPAs from Management Review, & Report
- Prioritization of actions by management







No news is bad news

Lessons Learned

- What are the „right metrics thus?
  - „indicative“ of situation/status
  - not too many, especially at beginning
- Good aggregation is important, visualisation and trends
  - Site comparisons (“grades”) are difficult, use benchmarking rather

- A lot of Oversight is based on awareness, responsibility, ownership; efficient tools (Q-events admin) and structures (meetings, reporting)

- Quality culture, resources and skills / training (e.g. sound RCA) are essential

- Required capture and reporting tools are very complex and need good IT support and accessibility of corporate Software interfaces

ECA ACADEMY

Thanks for your attention – Questions?

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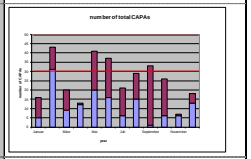
Metric	Number of total CAPAs
	Target (Q-Unit and operational)
	few open CAPAs, relatively high number of closed CAPAs no target on opened CAPAs
qualitative description	*Total number of CAPA is the sum of closed & opened & still open CAPAs in particular month*
Formula	*total CAPA in period = opened + open + closed open = existing open CAPAs in DB - opened in particular period*
Metric Unit	*number (pieces)*
prerequisites and rules for metric calculation	*A CAPA is deemed opened once it obtains an ID number and is entered into the DB. A CAPA is deemed closed once QA has set the status to closed due to verified completion. Ineffective CAPAs will be reopened.*
Data Source	*CAPA Database*
capture method	*extract from CAPA DB, monthly intervals*
Graphic result	
Metric responsible	*CAPA process owner*
reporting frequency	*monthly*
reporting form	*grafically by chart and table; resolution: monthly Alert Limit & escalation specification for open CAPAs*
target for metric (alert)	*open: nmt 30*
escalation spec	*open: nmt 50*
escalation / control responsible	*Head QA*