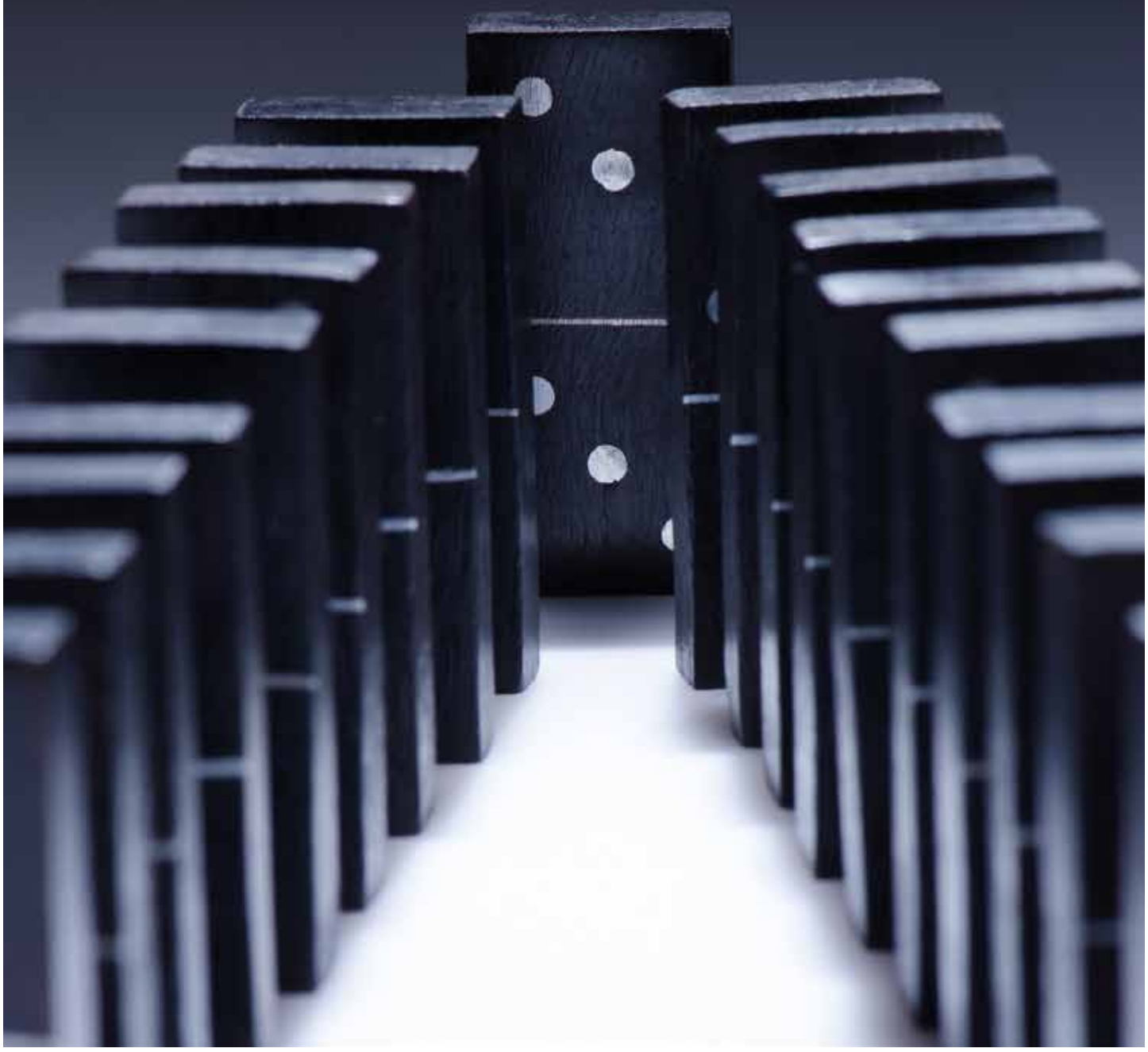
Causes of Effects – What Should we Measure?

KATARINA EGHAN AND ANDREW WADDELL

Quality issues arise from many sources. Audit, inspection, monitoring, quality control and customer comments are some of the most obvious.



It is always highly desirable (and sometimes mandatory) to summarise, trend and otherwise manipulate and present audit and other data generated from quality issues where they comprise more than just a few data points. How otherwise would a busy operations director or a head of a monitoring function of a large pharmaceutical company or a transnational contract research organisation negotiate the information provided to them and more importantly make sense of it? What story do the data typically generated from quality issues tell and what is the purpose of their provision to management (assuming that aggregate data are presented to management for appropriate analysis and decision making)?

Quality issues are often categorised as 'critical', 'major', 'minor', 'other' or some combination of these. Other types of categorisation include whether the finding represents an actual deficiency or a risk ('near miss') or the area from which it originates (such as 'data recording', 'study files', 'protocol compliance'). These categorisations often reflect effect rather than cause, with categorisation by cause being less common but more important. Let's explore why categorisation of effects rather than causes is more prevalent and look for possible alternatives.

'Categorisations often reflect effect rather than cause, with categorisation by cause being less common but more important.'

Selecting Appropriate Data

If we look at some of the definitions of quality and compliance evaluation activities such as audit and monitoring, it is no wonder that effects (symptoms) i.e. observations, near misses, etc. are the ever popular choice for summarising per categories and trending. For example, ISO 19011, guidelines for auditing management systems, defines an audit as a 'systematic, independent and documented process for obtaining audit evidence and evaluating it objectively to determine the extent to which the audit criteria are fulfilled'[1]. In other words, audits look for objective evidence confirming audit criteria have been fulfilled and if not, generate documentation of deficiency, non-compliance or variance (and rightly so!). Hence, auditors typically generate written reports containing quality issues that indicate a variance from requirements which are recorded as 'findings'.

It has become commonplace for organisations to utilise tools to gather these findings in a central place (audit database, clinical trial management system, spreadsheets, etc., depending on the requirements of the organisation's quality management system). Therefore, naturally, quality departments such as quality assurance summarise the data that they have at hand (i.e. findings) and present these to their customers such as an organisation's management (hopefully at predefined intervals and with concrete outcomes following appropriate assessment of the presented information, but debating these points is perhaps best left for another article). The findings tend to be grouped into categories according to their source, such as 'informed consent', 'source data', 'investigational medicinal product (IMP)', etc. and may be further sub-divided into sub-categories such as 'informed consent process', 'informed consent documentation', etc., depending on how granular the organisation wishes the presented data to be. We are of course talking about data metrics and the associated act of trending the data over time with the view of hopefully seeing improvement (e.g. less findings) as the time progresses. However, what does this categorisation and trending tell us and are there alternative ways of dicing and slicing[2] the quality data?

Alternative Approaches

Findings lead to correction but that should not be the end of the matter. Progressive companies that are committed to improvement will wish to use findings to look at the 'bigger picture' and put a corrective and/or preventive action, aka CAPA plan, in place. Not every finding requires a CAPA however, sometimes correction is all that is necessary but stopping at correction misses the opportunity provided by the finding (or multiple findings of the same sort) to identify and remove the cause of the problem or anticipate and prevent similar problems occurring in the future. We produce metrics for audit findings but how often have you seen root causes and/or CAPAs being categorised, summarised, trended and evaluated and the resulting information used for appropriate decision making? We tend to track audit findings and CAPAs so it should not be too difficult to also track root causes.

For instance, a common response following the identification of quality issues in a clinical setting is 're-training', presumably the root cause of the issue at hand being inadequate training to start off with. If you have been in the quality field for some time you may have seen this countless times! Now imagine presenting a dataset to management where instead of the usual six findings relating to 'informed consent', five relating to 'IMP management' and X relating to Y other types of issues, findings broken down by their root causes would (also) be presented (e.g. nine findings where the root cause was inadequate training and three where the root cause was unclear protocol wording) and/or by the associated corrections and/or CAPAs. Would the quality data be looked at differently and would the quality and compliance improvement efforts be perhaps more streamlined and focused, with more resource being allocated as a result in an attempt to address the root causes in a more rational fashion?

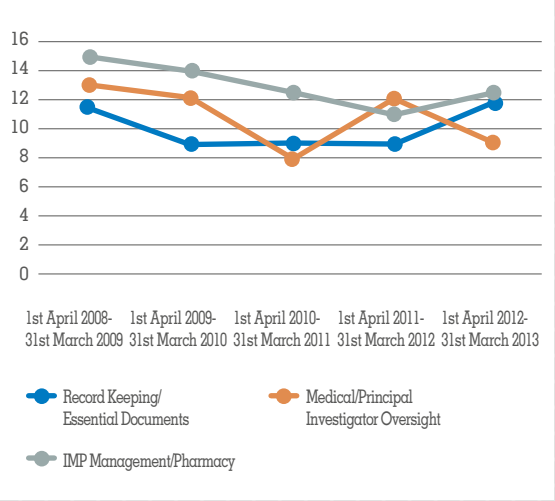
Ultimately, we should be asking why inspection metrics do not show marked improvements in the quality and compliance levels of organisations and identify why there are repeated issues uncovered during reactive quality verification activities such as monitoring, audits and inspections. For example, compare a sample of the UK Medicines and Healthcare products Regulatory Agency (MHRA) Good Clinical Practice (GCP) inspection metrics from 2008 to 2013, where the mean and maximum number of findings per inspection (of commercial sponsors – routine systems, study specific and triggered) were more or less the same or look at the trends in percentage of 'any' findings (critical, major and other) for three randomly selected observation categories from UK investigator site inspections (Figures 1 and 2).

Figure 1. Metrics from Inspections of Commercial Sponsors (Routine Systems, Study Specific and Triggered)[3-7]

Metrics Period	No. of Inspections	No. of observations*					
		Critical		Major		Other	
		Mean	Maximum	Mean	Maximum	Mean	Maximum
1st April 2008-31st March 2009	22	0	1	3	8	7.5	14
1st April 2009-31st March 2010	32	0	1	2.2	7	6	12
1st April 2010-31st March 2011	30	0	1	2	8	6.5	11
1st April 2011-31st March 2012	27	0	1	2	5	6.5	11
1st April 2012-31st March 2013	19	0	1	1.5	6	7.5	13

*Approximate figures used

Figure 2. Trends in Percentage* of Any Findings (Critical, Major, Other) for Three Categories from UK Investigator Site Inspections[3-7]



*Approximate figures used

"Lessons learned' should be sought at a higher level and appropriate actions taken to eliminate (or if not possible at least mitigate) the root causes of detected deficiencies.'

Shifting Paradigms

Only if individual processes and systems are perused as an interlinked web forming an entire organisation and by looking at often complex interfaces may the overall root cause of the individual 'smaller' causes be identified. It is not enough to look at issues in an isolated manner and within functional areas or per trial i.e. work in 'information silos'[8]. 'Lessons learned' should be sought at a higher level and appropriate actions taken to eliminate (or if not possible at least mitigate) the root causes of detected deficiencies. After all, receiving 'the site has been re-trained' as CAPAs to audit observations loses its novelty value after some time.

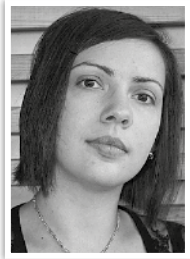
'Quality by design' and 'data mining' are the buzz words of today. With resources allocated to quality being scarcer and scarcer and with ongoing efforts to streamline the monitoring and auditing activities, quality professionals need to inspect what influence they have on the state of their companies' overall compliance. The optimal data need to be scrutinised by the optimal people at the optimal times in order to reach optimal decisions so as to assure optimal levels of quality and compliance.

Quality data metrics rightly form part of a robust quality management system. However, care should be taken that data are not summarised and trended for the sake of summarising and trending them. To truly build quality into processes and systems, one must first fully understand the characteristics of each process and system and the desired attributes of the associated outputs. Once deployed, the underlying reasons for any underperformance of such systems and processes should be looked at, not just the symptoms of underperformance.

REFERENCES

1. The British Standards Institution. BS EN ISO 19011:2011 Guidelines for auditing management systems (ISO 19011:2011). London: BSI; 2011.
2. Business Intelligence.com. Dictionary Term - Slice and Dice [Internet]. Business Intelligence.com [cited 11 Aug 2014]. Available from: http://businessintelligence.com/dictionary/slice-and-dice/
3. MHRA (UK). GCP Inspectorate GCP Inspections Metrics Report Metrics Period: 1st April 2008 to 31st March 2009 [Internet]. MHRA; 12 Mar 2013 [cited 11 Aug 2014]. Available from: http://www.mhra.gov.uk/home/groups/is-insp/documents/websiteresources/con249665.pdf
4. MHRA (UK). GCP Inspectorate GCP Inspections Metrics Report Metrics Period: 1st April 2009 to 31st March 2010 [Internet]. MHRA; 04 Mar 2013 [cited 11 Aug 2014]. Available from: http://www.mhra.gov.uk/home/groups/is-insp/documents/websiteresources/con249666.pdf
5. MHRA (UK). GCP Inspectorate GCP Inspections Metrics Report Metrics Period: 1st April 2010 to 31st March 2011 [Internet]. MHRA; 14 Mar 2014 [cited 11 Aug 2014]. Available from: http://www.mhra.gov.uk/home/groups/is-insp/documents/websiteresources/con395220.pdf
6. MHRA (UK). GCP Inspectorate GCP Inspections Metrics Report Metrics Period: 1st April 2011 to 31st March 2012 [Internet]. MHRA; 24 Mar 2014 [cited 11 Aug 2014]. Available from: http://www.mhra.gov.uk/home/groups/is-insp/documents/websiteresources/con396992.pdf
7. MHRA (UK). GCP Inspectorate GCP Inspections Metrics Report Metrics Period: 1st April 2012 to 31st March 2013 [Internet]. MHRA; 24 Apr 2014 [cited 11 Aug 2014]. Available from: http://www.mhra.gov.uk/home/groups/comms-ic/documents/regulatorynews/con409290.pdf
8. WebFinance, Inc. Information silo [Internet]. WebFinance, Inc. [cited 11 Aug 2014]. Available from: http://www.businessdictionary.com/definition/information-silo.html

Biographies



Katarina graduated from the MSc in Quality Management in Scientific Research and Development in 2013 and presently works with TMQA, a quality assurance consultancy providing support across all the GxPs located in Edinburgh, UK, where she is responsible for their Central European operation based in Bratislava, Slovakia. Previously, she held the position of a clinical quality auditor at Janssen, Pharmaceutical Companies of Johnson & Johnson. She started discovering clinical research and quality assurance within Phase 1 commercial Contract Research Organisations. She has been a member of RQA since 2008 and currently serves on RQA's Education and Training and Publications Committees.

KATARINA EGHAN

Andrew is the Director of TMQA and a past Chairman of RQA. Before setting up TMQA in 2001 Andrew was the Head of Quality and Training at a major international Contract Research Organisation and a Lecturer in Pathology at the University of Edinburgh Medical School. He joined the RQA (then the 'Quality Assurance Group') in 1980. He helped to develop and deliver the first RQA training course in 1982 and continues to contribute regularly to conferences and training courses.

ANDREW WADDELL