KPIS AND THE REGULATOR: I'M LOOKING FOR QUALITY METRICS, MANAGEMENT REVIEW AND CONTINUAL IMPROVEMENT

by Rachel Carmichael

Interviewing an ex-MHRA inspector on the importance of KPIs provides us with some interesting insights.

"Generally, I will ask to see the metrics that are used to confirm the performance of the quality system and then I will watch the blood drain from the faces of those present.

Then we will waste the next few minutes explaining that it is a requirement to have management review, that they need to be able to demonstrate continual improvement and that this is, and has been, an inspectable part of their processes since 2013 when EU GMP chapter 1 section 1.6 was updated."

There should be periodic management review, with the involvement of senior management, of the operation of the Pharmaceutical Quality System to identify opportunities for continual improvement of products, processes and the system itself.

SO WHAT SETS APART THE COMPANY THAT USES KPIS WELL FROM THOSE THAT APPEAR TO BE DRIVING IN THE DARK WITH NO HEADLIGHTS ON?

"If it is a good company and confident that it has identified appropriate performance metrics with appropriate actions coming from the management reviews, then there is no drama in letting a regulator see the metrics. Equally it is important for regulators to remember that just because a company blocks visibility of information it does not actually mean that the information will be poor. But it does mean wasting the regulator's time and it leads to a feeling of discomfort with regard to their knowledge and understanding of the requirements of EU GMP and the requirements for disclosure.

Vital to an inspector would be the overall picture of performance. There may be areas of weaknesses but if actions can be seen as being allocated and delivered as a result of the identified weaknesses, then that is a demonstration of a well-managed company."

IN YOUR EXPERIENCE, HOW WOULD YOU REACT TO INDICATORS THAT ARE EITHER GOOD OR SHOW ROOM FOR IMPROVEMENT?

"The inspection of the management review and the associated metrics should not constitute a large proportion of an inspection – probably no more than 15 to 20 minutes – which would include a quick look at the procedure and then a review of the output of the meetings over a year or so to make sure meetings are being held at the time points committed to and delivering the review dictated in the procedure.

If there are indicators which are showing weaknesses, it will influence the focus points of the inspection, though 'good performance' will also require verification during inspection.

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A management review and quality metrics which fail to identify weaknesses are a waste of everyone's time and indicate a lack of management oversight of the quality system."

IS THERE ANYTHING THAT IS OUT OF SCOPE OR IRRELEVANT TO THE REGULATORY INSPECTOR?

"As a regulator, I'm not particularly interested in the productivity metrics. My focus needs to be on the quality metrics such as documentation 'right first time', overdue quality actions or repetition of deviations. I will try and ignore the metrics that are focused on speed of change over or time for line clearance or equipment utilization. One company I inspected attributed a cost to every activity including the cost of writing, reviewing and approving the deviations. Although it is essential that companies are well managed and understand the impact of non-compliance, having such a driver can encourage people to cut corners and not report events."

WHAT ARE THE TYPICAL NON-CONFORMANCES IDENTIFIED WHEN INSPECTING THE MANAGEMENT REVIEW PROCESS AND KPIS?

"The inspection of the management review and the KPIs related to it tends to have a limited number of outcomes. The typical deficiencies include:

- No management review takes place or is late
- The review does not cover the full site operations
- The KPIs the company chose do not include sufficient focus on the quality management system
- The KPIs chosen have the potential to drive the wrong behavior. For example, a measurement of the number of deviations is likely to lead to a lack of reporting or reclassification of events so that they are no longer captured within the deviation system
- The review process lacked actions for improvement
- The review is ineffective since it has not identified the issues that the inspectors have, during the course of the inspection, found on the site"

IF THERE WERE ONLY THREE KEY MEASURES THAT YOU'D SEE AS INSIGHTFUL, WHAT WOULD THEY BE?

"The metrics that you want to see depend on the type of site that you are in. If it is a sterile or low bioburden formulation, then the performance of the environmental monitoring and the performance of the water system will be key. If the results demonstrate a completely perfect output, then I would be worried about the accuracy of the data and I would spend more time in the microbiology laboratory.

My personal metric of choice throughout my time inspecting with the MHRA was a review of the number of procedures past due for review and what percentage of the overall procedures this represents. A quality unit that is in control will be on top of the review process, there will not be a significant number of procedures past due date and the ones that are past due will be a matter of months, not years. If the company is failing to manage the operation and if there are insufficient staff, then this aspect of the operation is the one which seems to be a good indicator of the state of control.

I would be looking at the performance of the deviation system and the complaints system (perhaps in tandem with the CAPA system when possible). However, we can't have a discussion about KPIs without mentioning the fact that the U.S. FDA is seriously looking at a

standardized set of metrics as part of its vision for the future announced last summer. The metrics would be the same for each site, enabling the regulator to identify supposedly good and poor sites and increasing operational flexibility. The first set of proposals indicated that the four core metrics that the FDA will require are:

- Lot acceptance rate
- Product quality complaint rate
- Invalidated out of specification rate
- Product quality reviews on time

Optional metrics cover senior management engagement, CAPA effectiveness and process capability/performance. Those with good performance could be rewarded through less frequent inspections or less time on site. The vision is one report per product and one report per source of API, generated by the sites and electronically submitted. Facilities would have to register and the quality unit at each site would be expected to develop the report. Overseas sites would be encouraged (but presumably not required) to report. The metrics proposed are the logical conclusion of the regulated environment. There has been quite a robust response from many aspects of industry, and a company would be naïve not to take these metrics into consideration at the current time."

ABOUT THE AUTHOR

Rachel Carmichael has over 20 years' experience of pharmaceutical manufacture, control and quality management including nearly 11 years as a GMDP Inspector for the UK Competent Authority, the MHRA. This includes serving as the lead inspector representative within the MHRA for the transition from the Medicines Act to the Human Medicines Regulation, SI 2012 1916.

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