LOGFILE Feature 39/2020

Regulatory compliance - issue identification

Excerpt from the GMP Compliance Adviser

5 minutes reading time

by Mark Tucker, PhD

Issue identification is the most critical part of the process and relies on a team of people with high operational and GMP knowledge. All operational and quality areas should be represented and assessed.

The criteria for what is an issue in each area must be clearly defined, and is dependent on the final purpose of the list (see Figure 1.O-2). If this list is destined to be used only for inspection preparedness, you may only want to include issues that would be deemed critical or major by a health authority. If this list is to be used as a quality tool outlining all potential GMP gaps, the criteria will necessarily be much broader. For example, are all discrepancies going to be included on the list, or will only those discrepancies deemed to have a potential product impact be included? In QC, will all Out Of Trend results (OOTs) be included, or only results reported as Out Of Specification (OOS)?

Regardless of how the list will be used, it is imperative that the criteria for inclusion be consistently applied from site to site and from iteration to iteration within a site.

Figure 1.O-2 Some examples of potential risk assessment input values. It is very important to set and understand the boundaries you will use to populate your "risk log", and at what frequency you expect updates.

#	Risk input	Include the issue in your risk assessment if it meets one of the following criteria:	Frequency for assessing this input
1	Regulatory Commitments	· Unmet or past-due post-market commitments related to GMPs	Quarterly
2	QC Testing	· Adverse trend in metrics and assay trending · Use of invalidated method of lack of compliance with validated method · Incomplete or missing documentation related to methods transfer · Incomplete or inadequate sample shipping validation · Insufficient qualification of equipment/instrumentation, including manufacturing test instruments used for in-process testing · Inadequate assay performance, e.g. susceptibility to error or increase in retest rate · Incomplete documentation or inadequate document control · Issues with inventory accuracy and sample chain of custody · Insufficient documentation of rationales for sampling and testing plan · Changes not appropriately filed with health authority agency · Gaps in analyst qualification and training	Monthly
3	Batch Disposition/List	· Multiple lots rejected or terminated for the same reason · A lot (or multiple lots) that were shipped to the wrong destination · Multiple lots impacted by the same investigation · Any lot associated with 3 or more investigations · Any re-processed lots · Any lots in quarantine for >3 months due to Quality issues	Monthly
4	Audit Findings (internal & third-party)	· Critical and major audit findings · Critical and major self-inspection findings · Minor audit observations, recommendations, and comments should be assessed and added to the log if they meet additional input criteria · Overdue audits per schedule and SOP	Within one month of receipt of completed audit report (including final response)
5	Annual Product Reviews/Product Quality Reviews	· APRs/PQRs not completed on time · Inadequate response to Action items · Action Items not identified appropriately · Adverse trend in metrics	Annually per product
6	Final Vial Inspection (Trends)	· Adverse trend in metrics · Changes to action limits (especially if limits became less stringent) · Inadequate documentation of rationale for defect categories, acceptance criteria, and limits · Any lots undergoing multiple re-inspections · Lack of identification of particulate material and acceptable investigation & root-cause analysis · For novel defects, lack of identification or lack of incorporation into current defect library · Inadequate inspection process and inspector qualification process	Monthly

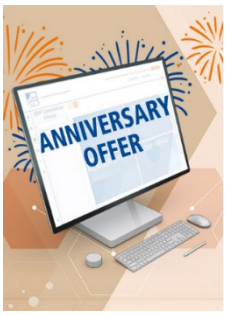
7	Product Complaints	· Adverse trend in metrics
		  · >3 similar complaints on the same or multiple lots
		  · Adverse trends in complaints without adequate follow-up
		  · <95% adherence to the SOP timelines for closure
		· Any product complaint that is confirmed by a production event or investigation
		· Inadequate investigations pertaining to complaints
			Monthly

8	Contaminations	· Any Mycoplasma contaminations · Any viral contaminations (eg., MVM) · Any other unusual contaminations (e.g., yeast, mold "uncommon" isolates) · Any consecutive contaminations on same vessel class (e.g., 20L, 12K)	Quarterly
9	Change Control	· Adverse trend in change control metrics · Any change that requires a regulatory submission as a result of: · Incorrect assessment of changes per GMP/procedural requirements (includes lack of partner notification)	Quartely

Author

Mark Tucker, PhD
Biochemist
Mark Tucker, LLC, Sausalito, USA
Mail: no483@marktuckerllc.com

This text is an excerpt from the GMP Compliance Adviser



The GMP Compliance Adviser is the world's most comprehensive GMP online knowledge portal that successfully combines theory and practice. It is used by more than 10000 professionals in over 50 countries. The GMP Compliance Adviser is divided into two parts:

GMP in practice: "How-to-do" interpretations and knowledge of our renowned industry specialists and according to international GMP rules.

GMP regulations: The most important GMP regulations from Europe, USA, Japan and many other countries (e.g. PIC/S, ICH, WHO, ...).

Anniversary offer! Celebrating 20 years: you only pay for **12 months**, but can use the GMP Compliance Adviser for **15 months**!

>>> Secure your access now!

Don't miss out on the latest news and articles:

Sign up for our free newsletter LOGFILE here!