A tool to harmonize environmental monitoring

"OUR VISION IS THAT, WE WILL KNOW WE HAVE BEEN SUCCESSFUL WHEN AN INSPECTOR VISITS A SITE AND SAYS THAT THEY HAVE SEEN THE MODEL BEFORE AND THAT THEY TRUST IT."

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Ensuring that microbial content does not infiltrate final product is a key concern for all. Procedures to effectively manage risk are in place, of course. However, shortly after its inception three years ago, the Environmental Monitoring (EM) in a Modern Drug Product Facility (EM in DP) workstream identified variations in how contamination risks in manufacturing areas are measured, and insufficient guidelines as a key gap. Since then, the workstream has developed a robust, risk-based standardized process for assessing and monitoring the risk of microbial contamination in modern DP facilities.

The publication of an EM toolkit along with guidance represents an important step forward to harmonize EM across the industry. "When we started this workstream, there were so many representatives from so many different pharmaceutical companies, that it was very hard to find any consensus about what we were trying to achieve," said Manshi Patel, Associate Director of Engineering – Microbial Control at Merck & Co Inc, Kenilworth NJ.

To meet the original objective, of reaching consensus about the right amount of sampling, it was vital to agree a harmonized view on risks.

"After much discussion, we decided to emphasize the importance of using a state of the art standardized risk assessment tool enabling consistent implementation of a risk-based EM program for reducing risks and achieving harmonization across the industry – one size that fits all," said Patel.

Vision

The workstream's vision of standardizing an EM process to contain risk is an ambitious one. "It is complex to put in place an EM program that gives all information needed to understand where potential contamination risks are," noted Patrice Wery, Head of Product Steward, MSAT Secondary Belgium Operations at GlaxoSmithKline Vaccines. "It is frustrating, because if a contamination is detected on a sample, it is difficult to discover the origin of it with only the monitoring program in place. Some tests may support the investigation of the contaminations and some tests may not. Auditors challenge the number of tests that are performed and/or the location of these tests. Despite the fact that risk analyses are based on process, people flow, and material flow, they are mainly based on people knowledge and some subjectivity still exists. Even more frustrating, results are available only after three to five

days of incubation. This makes analysis and root cause investigation more difficult, as people should remember everything that has been done during the samplings."

The workstream agreed an eight-step process for EM. Risk scores are generated based on six different factors and will aid the implementation of appropriate EM strategies. "We really wanted to create an industry standard for selecting meaningful EM sampling points rooted in a risk-based approach," said Sarah Phipps, Principal Microbiologist at AstraZeneca. Members are now testing the toolkit to identify any gaps that need to be filled before its publication.

Standardized toolkit

"The main goal is to have a standardized toolkit that highlights where the risks of environmental excursion are," said Wery. "Actual risk analysis tools (such as HACCP or hazard analysis and critical control points) do not fit well for EM risk assessment. The BioPhorum tool will enable manufacturers to have the right number of sample locations with better objectivity. This will also give a strong degree of confidence to regulatory authorities as the tool should be widely used by different companies."

Collaboration on the toolkit was a pivotal factor for accelerating progress. "If we had done this on our own, we would all continue performing risk assessments using the general regulatory guideline without a consistent approach," noted Patel. "By using a harmonized best practice approach based on industry's collective experience, we can save the auditors from scrutiny. Individual companies will have the flexibility to use it based on their own processes, but the baseline will be the same."

Phipps added, "Collaboration among subject matter experts in the industry through BioPhorum was invaluable in creating the toolkit. Knowing we will soon be following an industry standard for EM feels fantastic! With current subjectivity in how to select samples and a lack of regulation or guidance surrounding the practice, there is also room for greater questioning from regulatory agencies during audits. But that subjectivity and potential pushback from regulators is removed when there is an industry standard that we can all follow."

Patel said, "There is no such thing as zero risk, we all know that. Therefore, we need to decide what is an acceptable risk. This must be qualified by using an ideal risk assessment. The tool that we are developing intends to define the risk of product contamination so that it is covered by other risk management tools focused specially on product risk."

Publication

A final version will be published towards the end of 2018. "Our vision is that, we will know we have been successful when an inspector visits a site and says that they have seen the model before and that they trust it," said Wery. "We hope to increase objectivity in the definition of our sampling locations and have the right number of tests at the right location. Use of this tool should also support discussions with auditors when explaining EM strategy."

The workstream will take a proactive approach by engaging with regulatory authorities before the final guidance is published. "Our primary goal is to get a final draft of the toolkit exposed to as many regulatory agencies as possible to start the process of its acceptance and adoption as the standard practice across the industry," said Phipps.