Automating and Accelerating the Environmental Monitoring Process in Pharmaceutical Manufacturing

PEER REVIEWED

As part of a highly regulated industry, pharmaceutical companies must perform various levels of product monitoring in the manufacturing process. In addition to product testing, the manufacturing environment must also be tested. This includes testing of the room, surfaces, air, and personnel throughout the manufacturing cycle. In large environments, this can involve a significant number of samples that must be captured, tracked and reviewed after incubation. Automating even a portion of this process can provide tangible benefits, and accelerating the process as part of a rapid testing programme can bring product to market faster.

The current test used in microbial quality control, the culture-based test, has been the staple for over 100 years. It has many advantages that have made it the gold standard for quality control testing in pharmaceutical manufacturing. Unfortunately, the test has drawbacks, specifically in the area of time. In the traditional test, the micro-colonies need to grow to a size for the human eye to see. For the traditional environmental test that can take 3-5 days.

The traditional environmental monitoring test is manual and leverages a contact plate and growth over time to get results. What makes environmental monitoring uniquely challenging is the large number of samples that need to be managed, handled and tracked. In a manual process, the larger number of samples that need to be managed increases the chance for error, leading to time-consuming and costly investigations.

The attached image illustrates the various steps associated with an environmental monitoring process. This represents one example of the activities that have to be performed when executing environmental monitoring. The analyst starts his day by gathering test materials, and he moves through the process collecting samples in an area, gowning in and out, collecting samples in the next area, and finally returning to the incubator, filling out forms and monitoring cassettes. This sample process includes up to 23 unique steps. Because environmental monitoring testing involves a large number of tests, certain steps in this process, like recording counts, or entering data into a LIMS system, become more time-consuming. It is in these areas where automation can have an impact.

Automation could eliminate steps following sample capture, such as retrieving or moving plates, and counting plates. Technologies coming in 2013 can eliminate nearly all the steps after the sample is captured, potentially including a few of the administrative tasks like organising paperwork and sample labelling. Automation could take the 23 steps down to seven, or perhaps less.

In addition, technologies coming in 2013 will also provide the results in about half the time. Microbial quality control professionals

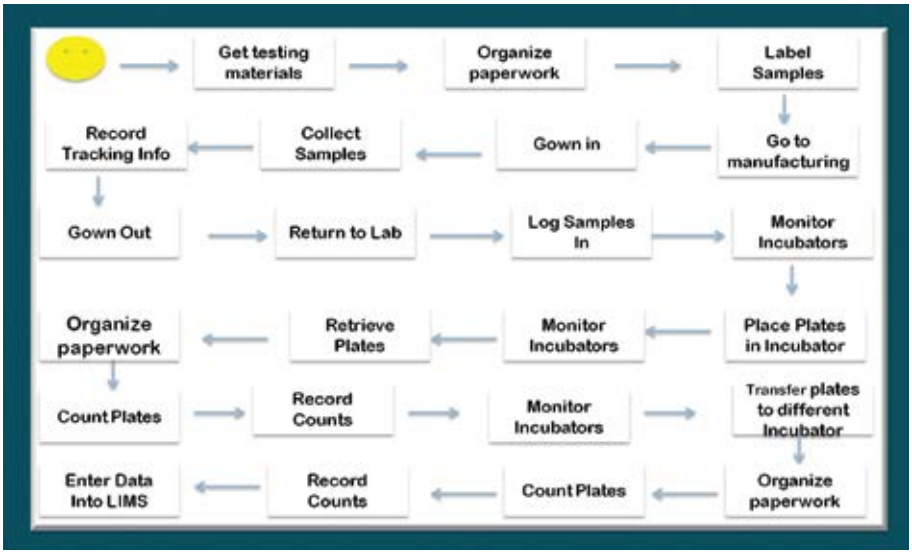
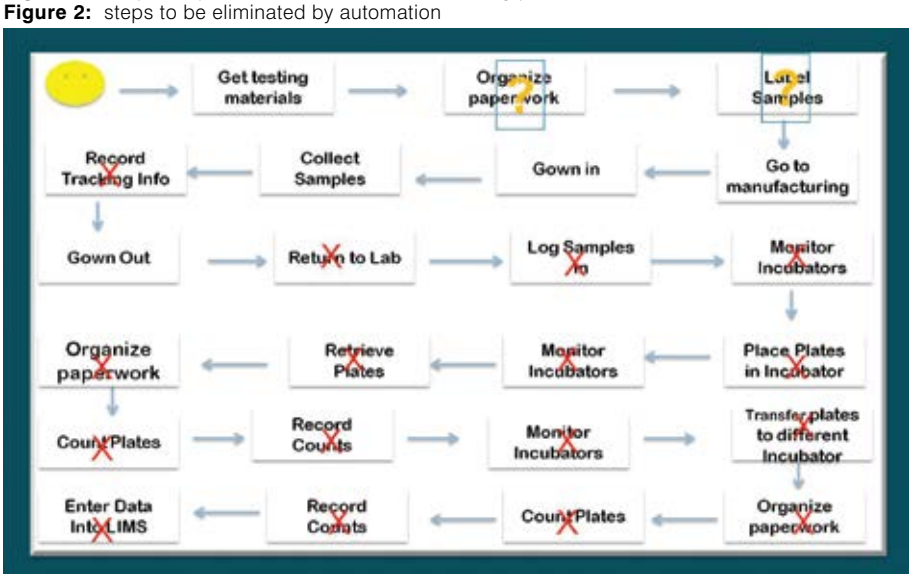


Figure 1: sample steps in the environmental monitoring process

Figure 2: steps to be eliminated by automation



are overburdened with other responsibilities. This approach saves time and eliminates steps.

When technology is discussed, it can mean many things to many different businesses. Every company is at a different stage in their use of technology in the labs. Some are highly automated, with a laboratory information management system (LIMS), and others are still using paper forms and spreadsheets. Automated rapid detection technology needs to fit into either environment. Even if the business does not have a LIMS system, automation can still provide the value of detection, enumeration and reporting in half the time. In the LIMS environment, the process is simplified to include more automated steps in sample tracking and routine updates to the LIMS system. This allows all stakeholders to operate from the same information.

While the process may be automated, there are several other criteria that must be met to facilitate the shift to automation. These include sample preparation, breadth of application and availability of the sample. The sample preparation must mimic as closely as possible the traditional method. The application must handle air, surface and personnel testing. The technology should function in a way that provides rapid results and it should be non-destructive.

Benefits beyond automation and use of standard growth media include reduced time to results, comparable sample preparation, and support for high volumes. As an example, feasibility studies have shown that a typical three-day test can provide results in around 1.5 days, and a typical five-day test at one or two temperatures provides results in about 2.5 days. An area where automated detection can also have a value is interim results. Because the automation is regularly analysing the sample for changes at pre-set intervals, positive results can be attained within hours, and final results in the timeframes previously discussed. This allows the QC team to be pro-active in response to positive events.

The use of automation simplifies a user's workflow. The user gathers her cassettes and takes her work order out to perform sampling. She captures her samples as she moves through the manufacturing area, perhaps labelling as she goes. When she returns, she loads the cassettes into the automated technology and the instrument takes over. From here the instrument images the samples every few hours, and based on defined parameters will alert users to any variations or positives, or in the event of a sample that has no issues, simply dispose of that sample and provide reporting either through an internal report engine or through integration to a LIMS system. This frees the analyst to work on more pressing projects, and react only if she receives an alert.

One area of concern for businesses is the validation of these types of technologies. It is important that the right performance verification tests are done and the information is available to any company that is interested in evaluating the technology. Using the Growth Direct™ as an example, the types of organisms being testing to ensure the technology performs as expected include the typical USP organisms, as well as difficult, finicky organisms. We are testing disinfectants, surfaces and various air monitors to simplify the validation process for businesses.

Continuing to use the Growth Direct™ as an example, the sample capture is exactly the same as the traditional method using contact plates. The validation entails a two-pronged approach. The first part is validation of the automated incubation and counting, and the second part is validation of the growth-based media. For environmental monitoring, this means proof of equivalence of micro-organism capture through microbial spike and recovery experiments with suitable replicate numbers to allow estimates of accuracy with suitable precision for statistical analysis.

In conclusion, opportunities exist to improve the efficiency and reduce the time to results of environmental monitoring through the use of automated detection and enumeration. Reduction of time and effort allows analysts to focus on higher-value activities. Automated rapid detection addresses the needs by not only providing results in half the time, but significantly reducing the steps associated with the traditional method. Validation of this type of technology can be straightforward.

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