CHPA

founded 1881

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Russell Wesdyk

Food and Drug Administration
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Dear Russ:

Thank you for contacting CHPA to assist FDA in identifying objective measures of product quality and plant operations performance for the purpose of supporting risk-based inspection approaches. We are supportive of risk-based inspection approaches and acknowledge that quality metrics should be investigated as one factor in assessing risk. We agree that certain metrics may be applicable as an indicator of a firm's overall quality system, quality culture, and compliance profile. Our member companies support the concept that well-designed metrics are critical in driving and measuring continuous improvement activities in both quality systems and improving processes. Indeed, most of our member companies already utilize a set of quality metrics to measure and monitor performance at the plant sites. These metrics are often selected based on overall goals, objectives and priorities within the individual companies and/or sites and are used to drive internal improvement efforts. The use of some of these same metrics to measure companies or sites from an external risk profile perspective would represent a significant change in the purpose of the use of these metrics and could potentially alter the selection and usefulness of the internal metrics.

CHPA member companies would like to emphasize that the specific definitions and calculation of the numerous metrics which are conceivable can vary between companies (and even sites within a company) based on process designs as well as the overall quality systems. Many of the common metrics being discussed have broad variability in the specific definitions which can cause challenges from a benchmarking or risk categorization perspective. Use of these metrics in a risk profiling exercise could lead to false or misleading conclusions and many corporate quality units therefore choose to focus on metric trends instead of an absolute value of the metric.

Using simple metrics appears straightforward but can be subject to misinterpretation. There is a risk that once a metric is collected for external review and risk profiling, unintended consequences could result. Consider the case of number of rejected batches. If rejected batches were to be reported to the

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agency and be used to establish a risk profile, it could encourage or incent the company to take a less conservative approach in disposition decisions for minor incident/events. Other time based metrics could drive a company to emphasize closure rather than timely completion of effective and robust CAPAs. A metric targeting a decrease in repeat deviations for example is more realistic than targeting a low number of deviations.

Plant metrics are a good indicator of how well manufacturing controls and the quality systems are executed within the plant. Metrics associated with individual products may be biased by several factors, including seasonality and volume of production. In the example where a product is manufactured on a frequent basis within a plant, isolated deviations or batch rejections may still allow the overall metric picture for that product to remain strong. Conversely, when a product is manufactured infrequently within the same plant, a single deviation or batch rejection would significantly impact the metrics for that product. It is cases like this latter example where individual product metrics become less meaningful and overall manufacturing plant metrics paint a more comprehensive picture of control. It is also common to manufacture a large number of products within a single OTC drug plant. The process of stratifying common plant metrics by individual product may be burdensome to industry and at the same time may paint an unclear picture for FDA.

While we recommend assessment of trending vs. absolute values of metrics, one must be aware of the fact that less developed continuous improvement cultures have much greater opportunity for improvement compared to more advanced companies in this area who may have been driving continuous improvement activities for many months or years.

We are aware that in some instances geographically separated facilities making identical or similar products have challenges in solely using metrics to draw conclusions on the quality performance or risk profile of the sites. This demonstrates the need for a holistic approach as no single metric or even combination of metrics is sufficient for risk profiling or benchmarking. Additional dialogue with the agency to come to agreement on these definitions and calculations are critical as we move through the process.

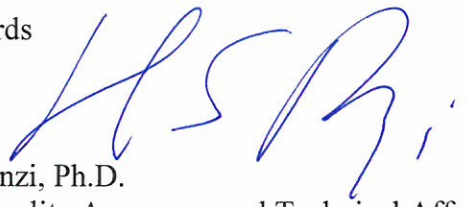
In general, there is less risk for shortages of OTC drug products as compared to prescription (Rx) drug products and less serious consequences in the event of a quality issue resulting in shortages. As an example, a higher level of regulatory oversight and scrutiny is appropriate for a lifesaving injectable product than a topical sunscreen. OTC products can be identified as lower risk (both dose limited and non dose limited) depending on indication, dose form, route of administration, prior use profile, safety profile, company profile, and product quality profile among others.

A risk-based approach to inspections has the potential of decreasing the regulatory burden on firms that have robust quality systems and allowing FDA to target areas that will benefit most from limited agency resources. Note that reduced inspections frequency for highly compliant firms may create a need for an alternative mechanism to substantiate a site's GMP status in the absence of an FDA

Establishment Inspection Report (EIR) which is often used to support registration activity outside the US and the issuance of a Certificate of Pharmaceutical Product (CPP).

We strongly believe that companies should continue to utilize a set of robust metrics to drive internal continuous improvement activities to enhance product quality and ensure consumer safety. The external collection of these metrics, reporting mechanisms and utilization by the agency to guide risk profile needs to be carefully reasoned and thorough understanding of the potential challenges and issues is required. We believe that product quality metrics, site and quality systems metrics and the statistical means for FDA to compare metrics do have unique OTC challenges and CHPA is willing to meet with our members and FDA to further discuss them.

Best Regards



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