CHPA

founded 1881

November 24, 2015

Food and Drug Administration
Division of Dockets Management (HFA-305),
Food and Drug Administration, 5630 Fishers Lane, rm. 1061
Rockville, MD 20852
Docket Number FDA-2015-D-2537

Dear Madam or Sir:

On behalf of the Consumer Healthcare Products Association (CHPA), a 134 year-old trade association representing the nation's leading over-the-counter (OTC) medicine and nutritional supplement manufacturers, I'd like to thank you for the opportunity to comment on FDA's request for Quality Metrics Guidance for Industry.

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 manufacturing processes. Indeed, most of our member companies already utilize a set of quality metrics to measure and monitor performance at the manufacturing sites. 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 and compliance profile.

CHPA members have participated not only in numerous public meetings with FDA, industry, and other trade associations, but also with ISPE in a quality metrics pilot program and appreciate that the agency has used the input to develop this draft guidance. However, since the agency is expected to receive comments from numerous pharmaceutical companies, several trade associations along with professional societies and the general public each with a different set of observations, we would ask the agency to republish the guidance as a draft document for a second round of review after considering the public comments.

Consumer Healthcare Products Association
900 19th Street, NW, Suite 700
Washington, DC 20006
T 202.429.9260 F 202.223.6835
www.chpa.org • OTCsafety.org

We believe this quality metrics initiative, once the guidance is finalized, should commence with an initial, voluntary pilot phase, excluding products where there is little risk of product shortage and quality issues. 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. We would also request a Safe Harbor Period of two years, whereby there would not be direct consequence for pilot data submitted, during an inspection at participating manufacturers. As an example, a higher level of regulatory oversight and scrutiny is appropriate for a lifesaving injectable product than a topical antipruritic. 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. We do not support excluding compounding pharmacies, vaccine producers, processors of various blood products and cell and gene therapy products and all drug products intended to be administered by intravenous (IV) injections including saline and dextrose containing IV solutions as proposed in the draft guidance when developing the pilot phase.

CHPA has more than 80 members manufacturing OTC pharmaceuticals and would be willing to work with the agency to recruit companies to volunteer to participate in the pilot phase. We also request that there be a mechanism for dialogue between companies and FDA during the evaluation period. There will be a need to ask questions and seek clarification on how to collect the metrics requested by FDA (this was an important lesson from the ISPE pilot). There are many nuances associated with FDA's definitions that have not yet been addressed. We ask that FDA publicly post the answers to questions asked by companies and provide further clarity to the proposed guidance so that industry can reach a collective understanding of what FDA is requesting.

The collection, management, and use of these data represent an entirely new area for the FDA and industry. This effort represents a considerable amount of data for the agency to receive and process. The FDA and companies need to standardize the definitions required to capture and report data and learn how to appropriately assess the results. This pilot approach would allow the agency to develop and validate the internal procedures for collections and processing the data and develop experience with calculations and evaluation of the metrics. FDA should then determine which metrics provide the most meaningful information about risks to product quality, reduced frequency of inspections and potential for streamlined and faster post approval changes, before relying upon this information when making regulatory decisions. Data that are of interest, but are not as valuable in assessing risk to product quality or are duplicative of information already being collected by FDA should not be requested.

CHPA believes the agency has underestimated the unintended consequences of this program both in the diversion of quality resources to simply meet the requirements of providing the data and the potential benefit of reduced inspection frequency. Key quality personnel will be diverted from their normal activities of ensuring high quality pharmaceuticals through compliance oversight and towards producing and reviewing data reports for submission. Although establishments do use quality metrics currently, they most likely do not collect the data the in the manner the FDA requests in the draft guidance. The FDA metric definitions do not align with those used by establishments for internal management decisions needed to measure to run their operations nor are they the metrics currently provided during current FDA inspections. It is likely the data gathering will remain duplicative and separate; meaning the burden will be on-going. Information systems need to be retooled to support the standard definitions and will add considerable burden compared to internal metrics currently in use. Consider the effect on specifications. If manufacturers have tighter internal specifications than those established in an application or for release would this data be required also? If so would this prevent companies from establishing tighter specifications?

It is unlikely that reduced inspection frequencies will be experienced for larger or smaller establishments, regardless of quality metrics profile for the OTC industry. In fact, large establishments are more likely to experience an increase in FDA inspection frequency, simply by virtue of the size and volume of metrics, posing an inherent risk. Many OTC companies are required by their retail partners to have an annual GMP inspection either by FDA or a third party.

Finally, we believe transparency in the metrics program is critical and encourage FDA to inform companies of the agency's risk ranking relative to the overall risk scale calculated. Our companies could get the benefit of FDA's perspective on the data that the agency is collecting. We request that FDA be transparent as to what it plans to do with the data it collects and how this will translate into proven value to the public health. If the agency can alter the request for metrics program at any time we strongly suggest that any changes to the metrics program be made through the normal public review and comment process so that all parties are well informed and metrics requests are equally applied to all sites.

Comments on Metrics

Manufacturing plant metrics are a good indicator of how well manufacturing controls and the quality systems are executed within the plant. In cases where several sites produce the same product,

individual product metrics are less meaningful and overall manufacturing plant metrics paint a more comprehensive picture of quality control. Metrics associated with individual products should be excluded from the initial pilot.

A metric targeting a decrease in repeat deviations for example is more realistic than targeting a low number of deviations. 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 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 incidents/events. Other time-based metrics could drive a company to emphasize closure rather than timely completion of effective and robust CAPAs.

Comments on Reported Data

Reporting on the Plant Site Segmented by Product consistent with FDA's current inspections

It is 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. Focusing on the site by product data will also ensure consistency with how data is gathered during inspections. This process reduces complexity, aligns with current metrics for annual product reviews and assures visibility at the site and product level.

The proposed Text Field Commentary is important to the OTC industry

The proposed text field commentary is important to provide context and insight to a potential metric. OTC products may receive a disproportionate number of consumer communications about the product and this field provides an opportunity to better interpret the data. For example consumers often comment on an unrealistic expectation of an OTC product performance and this field can be used to clarify quality complaints from dented packages to performance expectations which might be seen in an acne product or laxative. This field could include other critical information in helping the agency understand the data and resulting metric.

API data should be reported by the API producer

Because API's may be supplied to multiple customers and multiple API suppliers might be used at each plant, the agency would be getting redundant and complicated data from the finished dosage form manufacturer. We suggest the API data should be reported by the API producer.

Clarify Reporting Establishment

We request clarity about the request for reporting requirements for contract manufacturers. If one of our companies purchases finished goods from a supplier why would each site have to report the same metrics? Manufacturers have numerous suppliers and complex manufacturing networks. It would be challenging for suppliers and contractors to split out data for manufactures in industry given the proposed reporting requirements. We suggest CMO data come directly from the contract manufacturer, as is the current practice during site inspections.

NDC numbers may not be specific to a manufacturer

The use of the National Drug Code (NDC) number for quality metrics product reporting is problematic for the OTC industry. NDC numbers are often not assigned until the later processing stages or even the final stage of packaging for OTC products. Bulk manufacturing has the potential to be allocated to multiple packaging lots and therefore multiple NDC numbers. Product reporting, identified by NDC, would impose a significant burden for our members. CHPA proposes the use of internal bulk formula numbers for a product or family of products (or alternative Annual Product Review grouping) supported by the current Annual Product Review reporting process for a site. Even these alternatives may present their own set of challenges depending on the scope of the product level detail required. The internal bulk formula number is not a perfect solution as it brings with it the challenge and burden of tracing the internal bulk formula code across the product lifecycle.

Corrections to submitted data

We believe it is critical to have a system in place to document corrected/resubmitted data and recalculate changes in risk scores accordingly.

Submission of data within 60 days consistent with the current APR cycle

ISPE found no correlation with APR on time rate (submission within 60 days) and other metrics or risk. Therefore, we suggest the agency consider this an optional metric or if required allow flexibility consistent with the current APR cycle.

A number of definitions of the reported data need refinement and clarification

1. Number of lots attempted
2. Specification related rejected lot
3. Product quality complaint rate
4. Number of products produced at the establishment
5. Number of lots attempted
6. Right first time
7. Lot acceptance rate
8. Invalidated out of specification rate.

CHPA would like to emphasize that the specific definitions, data format and calculation of the metrics which are proposed can vary between companies (and even sites within a company) based on process designs as well as the overall quality management systems. The common metrics proposed have variability in the specific definitions which can cause challenges from a benchmarking or risk categorization perspective. The FDA should work with trade associations and their member companies to refine these definitions by seeking the advice of current industry professionals, in order to understand all the nuances and questions that will arise before implementing this program. The means to provide comments, data inclusions, exclusions and definition clarifications is vital to the industry and FDA correctly interpreting the metrics.

Optional Metrics

Senior management engagement: It is appropriate for the subject matter experts to review the APR's rather than a senior management review and we do not support senior management engagement as a useful metric.

Corrective Action and Preventative Action (CAPA) effectiveness is potentially a useful metric if the agency and industry could conceive of a standard definition.

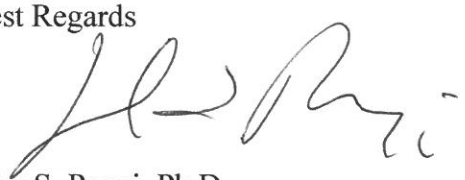
Process capability and process performance (Cpk or Ppk). These indices are not considered annual assessments but are used as tools to evaluate the capability of a process to consistently meet specifications. This requires a minimum set of observations to be statistically significant, useful and cannot be used on all critical quality attributes. Our preference is to have the agency review these metrics during inspections.

We suggest that the optional metrics be deferred to a future phase of this program.

We strongly believe that companies should continue to utilize a set of robust metrics to drive internal continuous improvement activities which 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 a 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 challenges. CHPA is willing to meet with our members and FDA to further discuss them.

We look forward to working together with FDA to determine objective measures of product quality and manufacturing plant operations performance for the purpose of supporting risk based inspection approaches, including improving the effectiveness and efficiency of inspections and potentially streamlining and accelerating post approval changes.

Best Regards



John S. Punzi, Ph.D.
Director Quality Assurance and Technical Affairs