



November 25, 2015

Division of Dockets Management (HFA-305)
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Comments from Cross-Industry Quality Metrics Collaboration Group regarding Docket FDA-2015-D-2537: Request for Quality Metrics.

The undersigned trade and technical organizations, representing a broad informal group across the pharmaceutical industry, stand together collectively as the Cross Industry Quality Metrics Collaboration Group (the “Collaboration Group”) to provide consolidated feedback on FDA’s Draft Guidance on Quality Metrics. These comments should be considered in addition to comments submitted by each individual organization.

Our organizations all value patient safety and understand the Agency’s goals behind the proposed quality metrics program. We have comments on the approach, including the request that FDA adopt a phased-in approach in an effort to maximize learning, minimize burden on both industry and FDA, and enhance the chances of a successful implementation. It is our hope to obtain additional clarity and continue our dialogue with the Agency.

The Collaboration Group has agreed that the intentions behind FDA’s quality metrics program have potential benefits for industry, for patients, and for FDA. There is general agreement that FDA has taken action on industry’s request to differentiate and reward those manufacturing sites that have strong quality systems and routinely produce high quality products and that, if successfully implemented including incentives for reduced inspection or reduced post approval change reporting, the metrics program could result in benefits appropriately segmented within the industry. The benefits of less frequent inspections and potentially reduced post approval

change reporting would allow those sites that qualify to transition some of the resources supporting inspections and change reporting to further continuous improvement of product quality.

There is also agreement that once the quality metrics are established with clear and consistent definitions, and as long as the confidentiality of confidential commercial information is adequately safe guarded, FDA's quality metrics program could be used to drive quality improvements across industry.¹ Also, we ask that FDA provide an explicit acknowledgement that any information concerning a specific establishment or product that is obtained through the quality metrics program is confidential commercial information and protected from disclosure. However, questions remain regarding the benefit vs. risk balance, such as whether the program would place an undue burden on industry or whether a focus on the metrics themselves could lead to unintended consequences. To better understand these risks, these organizations request that FDA take a phased-in approach.

Phased Approach

The undersigned groups all concur that FDA should commence its quality metrics program with a phased introduction, structured to maximize the learnings for industry and FDA, while managing burden and working towards realization of potential benefits.

There are several options for implementing a phased-in approach. These will be discussed in each individual organization's comments to the docket. However we all concur on a number of aspects as outlined here:

1. Regardless of which phased approach ultimately prevails, we all agree that there should be an evaluation / phased-in learning period of two years, after which FDA, industry and an objective third party should conduct a formal collaborative evaluation of the benefits and risks of the Quality Metrics program, and present the results at a public meeting. The suggested criteria for assessment should be defined at the start of the metrics program and should at a minimum include the actual and projected:

- burden experienced by industry;
- applicability of metrics within and across sectors;
- discriminatory and predictive power of the selected metrics and their associated analytics;
- unintended consequences;
- impact on drug quality;
- impact on drug shortages; and
- impact on FDA surveillance inspections, preapproval inspections, and post-approval change programs.

The outcome of this assessment would then inform further evolution of the metrics program.

¹ NB: To be clear, the Collaboration Group is not weighing-in on the issue of using quality metrics data to publicly rank manufacturing establishments.

2. The Collaboration Group recommends that, for at least the two-year evaluation period, data submitted under the FDA Quality Metrics program and/or failure to submit data under the program should not be the basis for an adulteration finding. We ask that FDA make this point explicitly clear. Quality metrics should be a means for incentivizing and improving quality, not a punitive measure.

3. This group also requests 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. 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 posed by companies, so that industry can reach a collective understanding of what FDA is requesting. Companies should have the ability to update and correct data post-submission to ensure accurate reporting.

There are a number of reasons we request a phased-in approach:

Firstly, our collective experience with deploying metrics programs indicates that there is a large variation of understanding and interpretation of definitions which can be a function of factors such as the technology, size, supply chain complexity and maturity of the operations. Such variability of interpretation can confound analytics and their resultant interpretations, limiting the ability for the metrics to provide incisive insight into the site and/or product performance. In addition, the operability of a Quality Metrics program on such a scale across all sectors of the pharmaceutical industry simultaneously is undemonstrated. Consequently, commencing with a phased approach will allow for learnings that would be associated with the inevitable evolution of the metrics program as the predictive and discriminatory power of the selected metrics within and across sectors is better understood.

Secondly, establishment of a standardized quality metrics program across almost all sectors of the pharmaceutical industry simultaneously is complex for firms and may require considerable support from both industry and FDA. In order to submit data to the FDA under this program (as opposed to using it for internal purposes), manufacturers may be required to make changes to the types of data they collect, as well as reporting structures, electronic systems, review processes, confidentiality and quality agreements, impacting the business practices of the entire supply chain. FDA states in its guidance that most companies currently use quality metrics. We believe that is correct. However, as FDA has recognized, there is not one set of metrics used across industry and different companies can define the same metric in many different ways.

A phased-in approach is analogous to engineering runs or sandbox testing where studies are typically conducted to ensure errors are uncovered before going "live." These studies are consequently very deliberately designed to maximize the targeted learnings in advance of formal validation or launch. FDA's metrics program will likely draw on existing Quality Unit and Manufacturing/Operations resources, and use of a phased approach should maximize learning and minimize the impact on existing operations. It is our belief that substantial learning can be achieved through a carefully designed phased implementation approach.

Points to Consider/Clarify

The Collaboration Group requests that the first twelve months reporting period not commence until at least six months after the Agency issues its final guidance, in order to allow industry to activate data compilation, analysis, governance and reporting processes on the final identified set of requested data. Companies may not currently be collecting the data requested by FDA, at least not in a readily retrievable way, and they will need time to adjust their processes and systems.

We believe reporting should be done annually with specific submissions dates to be determined by each firm to balance workload or align with existing quality system processes. For example, firms may decide to submit data in alignment with their Annual Product Review schedules (which will vary by product). This will significantly reduce the burden on companies, as well as decrease the likelihood of data inconsistencies between APRs and FDA metrics.

The Collaboration Group believes that trending is an important component of the analysis of metrics within and across sites, companies, and products. Trending should be incorporated into the analysis model and may be better than direct comparison of metrics.

The group believes it is important to recognize the complexity of contractual relationships and the diversity of contract manufacturing arrangements within the industry. It will require time and effort to ensure that there is clarity about who is responsible for reporting which metrics, and for adjusting quality agreements accordingly. The group asks that FDA provide time for those adjustments to be made and provide clear guidance about who is accountable for reporting which metrics.

Due to the complexity of the industry, we also request that FDA clarify if and under what circumstances API manufacturers should report their own data and how that data should be reported. In many cases an API manufacturer does not know the drug product that their API is used in, and thus cannot report data by drug product without significant input from the license holder/drug product manufacturer. The group recommends that API manufacturers report their own data and by API/drug substance within sites, including lot acceptance rate. However, we feel that the invalidated OOS data is a better metric of overall lab quality and thus should be reported solely by site across all products.

There is also agreement that a positive quality culture is an important underlying factor in manufacturing high quality products but that it is difficult to define and collect any metrics on culture at this point in time. This group values the current dialogue on the topic between FDA and industry and hopes to continue as the program evolves.

Transparency

We believe transparency in this proposal is critical, therefore we ask that FDA provide further clarification into how it calculated the burden of its metrics program. Based on our collective experience we believe FDA's calculation is significantly underestimated both in terms of upfront investment and ongoing costs. Without further detail, it is difficult to ensure that FDA's

calculations for the OMB Information Collection Request related to its current request for quality metrics have included all relevant factors. We have mentioned some of these factors above, including that manufacturers may be required to make changes to the types of data they collect, as well as reporting structures, electronic systems, processes, and quality agreements, impacting the business practices of the entire supply chain. In addition, our experience in the industry and internal estimates lead us to conclude that FDA's hourly per product estimate is too low. Additionally, any changes to the metrics would lead to additional costs.

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. We hope FDA will be able to provide industry and the public with the roadmap it will follow to determine what the metrics program will ultimately look like. This is especially necessary because, as the draft guidance stands now, the FDA has given itself the authority to alter the program at any time. In fact, at the public meeting held on the draft guidance on August 24, 2015, the FDA indicated it will issue changes to the requested metrics as soon as six months after the first metrics submission. This is of concern to industry, and we request 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. New metrics will require a revision to some current industry practices including revisions to IT systems and other internal systems.

A phased implementation is an opportunity to evaluate the impact of the collection and reporting activities on resources, while establishing the program and long term reporting requirements. Additionally, a public review and comment process will allow the public and industry to continue a transparent dialogue with the FDA.

Conclusion

In closing, this group supports a phased approach for quality metric collection in order to maximize learning, minimize burden on both industry and FDA and enhance the chances of successful implementation. While specific comments will be submitted by individual organizations, including technical questions and requests for clarification, there is consensus that definitions outlined in the Agency's proposal need to be clarified. While questions remain concerning the full benefits and risks of FDA's approach, we request transparency in order to meet the collective goals of FDA and industry. We appreciate the opportunity to provide our input on this program and aspire to continue the dialogue with the Agency.

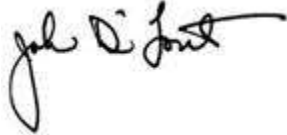
Sincerely,

A handwritten signature in black ink, appearing to read 'Luisa Paulo', with a long horizontal flourish extending to the right.

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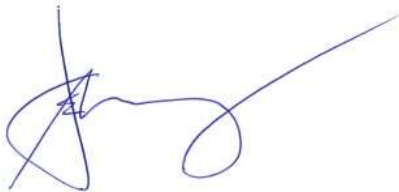
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