

Quality Metrics Public Meeting



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Generic Pharmaceutical Association

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- GPhA members manufacture more than 90% of all generic pharmaceuticals dispensed in the U.S., and their products are used in more than three billion prescriptions every year. Generics represent greater than 86% of all prescriptions dispensed in the U.S.
- The GPhA Quality Technical Group, formed in 2013, consists of Global Quality Leaders for approximately 77% of the U.S. drug supply.



GPhA Members

Regular Members

3M Drug Delivery Systems
Actavis Inc.
Alvogen Inc.
Amneal Pharmaceuticals LLC
ANI Pharmaceuticals
Apotex Corporation
Aurobindo Pharma USA Inc.
BD Rx, Inc.
Dr. Reddy's Laboratories, Inc.
Fresenius Kabi USA LLC
G & W Laboratories, Inc.
Glenmark Generics Inc., USA
Heritage Pharmaceuticals Inc.
Hospira Inc.
Impax Laboratories, Inc.
Kremers-Urban Pharmaceuticals Inc.
Lupin Pharmaceuticals Inc.
Mallinckrodt Pharmaceuticals
Momenta Pharmaceuticals Inc.
Mylan N.V.
Natco Pharma Limited
Novel Laboratories-Gavis Pharma
Par Pharmaceutical Companies, Inc.
Perrigo PLC
Sagent Pharmaceuticals, Inc.
Sandoz Inc.

Strides Pharma Inc.
Sun Pharmaceutical Industries, Inc.
Teva Pharmaceuticals USA
Therapeutic Proteins International, LLC
West-Ward Pharmaceuticals
Wockhardt USA Inc.
Zydus Pharmaceuticals USA

Associate Members

A.J. Renner & Associates
Aceto Corporation
ACIC
Amerisource Bergen Corp.
Baker, Donelson, Bearman, Caldwell & Berkowitz, P.C.
BioRasi LLC
Capsugel
Cardinal Health
Caremark Rx Inc.
ChemWerth Inc.
Clarkston Consulting
DAVA Pharmaceuticals, Inc.
Deloitte Consulting Services LLP
Econdisc Contracting Solutions, LLC (formerly Express Scripts)
Gedeon Richter USA
Greenblum & Bernstein

GYMA Laboratories
Haynes and Boone, LLP
Husch Blackwell LLP
InnoPharma Inc.
Interchem Corporation
Johnson Matthey Pharmaceutical Materials
Knobbe Martens Olson & Bear LLP
Lachman Consultant Services Inc.
McKesson Corporation
Midas Pharmaceuticals Inc.
Natoli Engineering Co. Inc.
New Chemic, Inc.
Novum Pharmaceutical Research Services
Polsinelli Shughart
Putney Inc.
Ren-Pharm International Ltd.
Rising Pharmaceuticals Inc.
Soverign Pharmaceuticals LLC
Spear Pharmaceuticals
Symbio LLC
TWi Pharmaceuticals USA
Vinchem Inc.
Walgreen Company

Vision Statement:

- The Quality Technical Group meets patient needs by assuring accessibility to affordable, quality medicines; ever mindful of the essential role the generic industry plays in healthcare and the healthcare system.

Mission Statement:

- **We** are a unified voice for quality in the generic drug industry.
- **We** champion and influence the continuous improvement of industry quality standards by actively leading their development, education, and communication.
- **We** work in partnership with global regulators and industry counterparts on quality initiatives that benefit patients.
- **We** are committed to providing dependable and sustainable value in healthcare and the healthcare system.

Patient Safety and Product Quality

- GPhA members produce high quality medicine, and we look forward to working closely with the FDA to develop drug quality initiatives that facilitate this goal.
- GPhA championed GDUFA in order to provide enhanced risk-based FDA inspectional oversight of the pharmaceutical industry.
- GPhA members strive to work closely with the Agency on quality initiatives that detect emerging manufacturing issues, which would allow for early discussions between FDA and manufacturers to proactively resolve potential issues.
- GPhA members commend FDA for continuing to work on ensuring that inspectional approaches focus on our shared goal of providing high quality drugs to patients.
- GPhA members believe that the Agency will need to look beyond regulatory compliance in order to be successful in elevating drug quality.

FDA's draft metrics guidance is based on good intentions, but may exceed FDA's statutory authority

FDA's mandatory inspection authority beyond the U.S.

- It is not clear; therefore, the authority to demand metrics would not extend outside of the U.S.

Requesting metrics in advance of inspections

- Inspections are of records companies already keep, not generating new records as FDA is requesting.
- There is no authority to require manufacturers to generate new records for investigators.
- Metrics are not necessarily kept in the way FDA prescribes. FDA has commented that there is no standardized approach to metrics in industry.
- Information about contractors and suppliers may not be available as specified.

Failure to supply metrics consequences

- Deemed by FDA as equivalent to refusing an inspection and may render products adulterated.
- Refusing metrics is not refusing an inspection.

Guidance imposes binding, rigid rules

- Provides no practical alternative to comply due to its prescriptive nature.
- Tracks performance vs. 30-day deadlines for APRs and for batch disposition that are not supported by rules.
- Imposes de-facto increased inspection penalties for failure to report voluntary information. There should be no penalties for not supplying voluntary information.

Metrics request not reasonable, as guidance defines

- FDASIA requires requests be provided within a reasonable timeframe, within reasonable limits and in a reasonable manner, but what the guidance specifies is not reasonable.

Risk Based Inspection System

FDA's risk-based model should:

- Hold all suppliers of drug products to the U.S. to the **same** quality standards regardless of whether they are located in the U.S. or abroad.
- Prioritize FDA's focus to those suppliers that FDA has never inspected, not inspected within the last four years, and those with a history of serious compliance problems.
- Strictly monitor those suppliers in industry who have not demonstrated a commitment to quality and/or lack a record for ensuring quality.

FDA's risk-based model should not:

- Over-inspect large manufacturing sites just by virtue of their size.
- Affect the cost of generic drugs by virtue of undue metrics burden.

Burden needs to be reasonable and realistic

- Paperwork Reduction Act estimates are grossly underestimated and need to include all the actual metrics processes required to assure realistic characterization of the burden.
- FDA should provide the means to report metrics on a site-basis, instead of product-aggregated.

Contractor reporting is heavily burdensome

- FDA should request metrics directly from contractors, in keeping with their direct regulatory relationship with them.
- FDA should not request application holders to gather and compile data from contractors, given that contract holders are not parties to contractor FDA inspections.

Internal use vs. reportable to an Agency

- Internal metrics collection processes and systems will need to be bolstered to provide 100% traceability as external reporting to FDA.
- Infrastructure and systems to support metrics reporting externally will require significant, added ongoing cost that must be factored into the burden.

Time to prepare

- At a minimum, provide the safe-harbor period FDA had communicated prior to the draft guidance in order for companies to prepare for accurate, meaningful metrics reporting. An incremental approach is recommended, as well as use of pilots(s) to determine effectiveness and allow FDA better understanding of how to utilize data.
- Although FDA has engaged with industry, there are many surprises in this guidance that have not been fully vetted (e.g., product-level reporting and the idea of covered/reporting establishments) and that create significant burden and complexity for industry.
- The process now seems unduly rushed, considering the significance of this initiative.

Unintended Consequences

Potential for drug shortages

- Companies that make low volume products in one campaign per year may require a different look at metrics than some other manufacturing models.
- Companies may be incentivized by FDA metrics to make choices on products and sites to the detriment of drug supply (for example, discontinue difficult to make products or U.S. production at certain sites).

Potential for gaming the metrics

- Putting products on hold rather than rejecting them among others.
- Avoiding re-training of personnel as a practice.
- The Agency should develop a process that could monitor these issues carefully.

Potential for increased inspection

- Production volumes, launches, and narrow therapeutic range products may flag manufacturers as inherent risks, regardless of good quality metrics performance.
- FDA should make metrics definitions clear using industry feedback and provide ability to have the metrics context included to prevent misinterpretation.

We share the Agency's goal of improved product quality and mitigation of drug shortages. As FDA moves forward with its quality initiatives, we look forward to an ongoing dialogue with the Agency.