# Understanding How the Public Perceives and Values Pharmaceutical Quality

Private Workshop Summary
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## Introduction

Ensuring the quality of pharmaceutical products is essential and part of the mission of the U.S. Food and Drug Administration (FDA). When pharmaceutical products do not meet quality standards, patients can be harmed or drug shortages can arise.

Stakeholders, including patients, providers, pharmacists, drug purchasers, and payers, may each consider quality when making decisions about pharmaceuticals; however, very little research explores the role of quality in stakeholder decision making. To this end, the Robert J. Margolis, MD, Center for Health Policy at Duke University, under a cooperative agreement with the FDA, convened a private workshop to better understand how stakeholders perceive and value the quality of pharmaceutical products, and how quality impacts decision making. **This summary provides a high-level overview of the discussions that occurred and synthesizes key takeaways for the entire stakeholder community.**

### What is Pharmaceutical Quality?

Within FDA's Center for Drug Evaluation and Research (CDER), the Office of Pharmaceutical Quality (OPQ) is responsible for overseeing the quality of drugs. The OPQ report on the State of Pharmaceutical Quality states that "A quality drug is consistently safe and effective, free of contamination and defects."[1]

Throughout the day, stakeholders used the term "pharmaceutical quality" to refer to two distinct concepts. First, they used it to describe the quality of the manufacturing process, and its ability to produce a reliable supply of drugs that is resilient against supply disruptions and shortages. Second, stakeholders used the term to describe a product that is free of contamination and defects that might affect its safety or effectiveness. These different uses of the term "pharmaceutical quality" highlight one of the key takeaways of the workshop: there is a need for a better shared understanding of what pharmaceutical quality means, how it affects stakeholders, and how it can be measured.

### The Private Workshop

The workshop consisted of two breakout groups representing patient and provider perspectives as well as buyer and payer perspectives. The groups explored stakeholder understandings of pharmaceutical quality and the ways that quality impacts decision making. In the final portion of the day, the breakout groups joined together to share lessons learned and discuss ways forward.

Key areas for future action included assessing perceptions of pharmaceutical quality; continuing communications about quality with patients and providers; facilitating transparency between manufacturers, regulators, and purchasers; and developing quality ratings and scores.

## Breakout Group A: Patients and Provider Perspectives

Breakout Group A first considered how patients and providers define pharmaceutical quality, differentiate between pharmaceutical quality issues and drug side effects, and perceive FDA's role in regulating pharmaceutical quality. The group then considered the decisions healthcare providers make surrounding pharmaceutical quality and how those decisions impact patient care, as well as how patient preferences around quality influence medical decision making. Group A consisted of fifteen providers, patient advocates, professional society representatives, and pharmacists, as well as additional FDA

participants and observers. Key topics from the Group A breakout discussion included the importance of transparency, ways in which stakeholders currently assess pharmaceutical quality, quality systems, quality ratings, opportunities for patient and provider education, and patient willingness to pay for higher quality.

The Importance of Transparency

Stakeholders called for access to more comprehensive information about pharmaceutical quality, FDA's role regulating quality including details about the inspection of manufacturers, drug distribution, drug recalls, and data about drug quality over time.

Many in the breakout group called for more information to be shared about drug manufacturers. Specifically, stakeholders were interested in knowing if manufacturers are subject to unannounced inspections, if companies follow Current Good Manufacturing Practices (cGMP), and if companies' manufacturing practices conform to International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) standards. Information about inspections (including FDA Form 483[1]) was also of interest to stakeholders, who noted that while Form 483s are posted on the FDA website, 483s are not well-publicized, posted on a delay, difficult to aggregate or search, and missing data that stakeholders deem relevant.

Beyond the manufacturing of drugs, stakeholders noted that it can be difficult to trace drug products and determine whether a patient who experienced an adverse event received a particular batch of drugs. This is due to longstanding challenges with following the distribution and dispensing of drugs. As such, some called for increased regulation of drug distribution, including the use of lot numbers to trace drugs and quality problems from manufacturer to patient.

When a drug recall is issued, stakeholders reported that both physicians and patients may not always have access to necessary information to act on the recalls. Specifically, many drugs are recalled by lot number. These lot numbers are not always present on patient medication bottles, and patients may struggle to find out if their medication is subject to the recall.

Finally, stakeholders emphasized that data, as opposed to patient anecdotes about drug quality, should guide patient and provider decision making. Relying on anecdotes is concerning because, scientifically, it is difficult to isolate problems of drug quality from problems of treatment safety and efficacy for individual patients.

Stakeholder-Designed Systems to Assess Pharmaceutical Quality

Some stakeholders (including those at large academic medical centers and hospital systems) have implemented their own procedures and systems to assess pharmaceutical quality. One stakeholder at the discussion, for example, developed a dashboard that contains information about the quality of pharmaceutical products collected from publicly available information on the FDA website, including recall summaries, inspection reports, citations, and warning letters.[2] One purpose of this dashboard is to be responsive to drug shortages. Additionally, in coordination with the Pharmacy and Therapeutics

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[1] According to FDA, a "Form 483 is issued to firm management at the conclusion of an inspection when an investigator(s) has observed any conditions that in their judgment may constitute violations of the Food Drug and Cosmetic (FD&C) Act and related Acts." (https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-references/fda-form-483-frequently-asked-questions)

(P&T) committee, the Cleveland Clinic identifies their preferred generic manufacture for certain narrow therapeutic index drugs.

While the creation of dashboards may help some organizations address quality concerns, some pharmacists and prescribers stated that they do not have time to research the quality of particular drugs. Nor do some pharmacists feel that it is within their job responsibilities to collect and analyze quality data before purchasing or dispensing a drug. Rather, one stakeholder representing pharmacists felt that pharmacists currently spend too much time trying to determine if drugs available for purchase meet quality standards (i.e., that the drug be free of contaminants and, if generic, have the same potency as the brand name drug).

FDA noted that they do not always know the additional actions stakeholders are taking to assess quality. FDA is interested in learning about the existence and content of existing pharmaceutical quality dashboards in order to better coordinate with stakeholders.

Quality Metrics and Quality Systems

Discussion covered the creation of some form of quality rating or metric for pharmaceuticals. In this session, stakeholders more often used the term quality to describe a product that is free of contamination and defects that might affect its safety or effectiveness. A variety of factors were suggested as relevant to a quality rating including the quality of APIs and other ingredients, the procedures used to transport the ingredients and finished drug products, and the existence of quality manufacturing systems.

Stakeholders were also interested in quality ratings as a way to quantify and therefore incentivize companies to improve quality. Tying quality ratings to financial incentives, for example, was discussed as a way to motivate companies to improve the quality of pharmaceuticals.

Many stakeholders noted that the best approach to quality is one that emphasizes the prevention of quality problems. Rather than relying solely on testing of products or inspections, stakeholders advocated for the implementation of systems to drive better quality manufacturing. Analogies were made to different industries (e.g., semiconductors) and how other industries have used methodologies such as six sigma to improve quality.

Supporting Patient and Provider Education

Stakeholders agreed that consumers and patients should have some understanding of pharmaceutical quality, but that many currently do not. The discussion covered current gaps in patient and provider knowledge of pharmaceutical quality, and steps to address those gaps.

Patient and provider education should appropriately contextualize risk. Stakeholders noted that humans are generally not well-equipped to interpret or compare very small levels of risk (e.g., people are more afraid of plane crashes than automobile accidents, even though car crashes are far more prevalent). This phenomenon is important because as quality testing tools become more specific, very low levels of contaminants may be identified. There are outstanding scientific questions in some areas regarding what levels of some of these contaminants are of concern to patients. Therefore, there may be a role for regulators to interpret standards for such aspects of quality. Effective educational strategies could also contextualize the risk and communicate actions that consumers should take if contamination is discovered.

When discussing generic drug quality, stakeholders noted that it is important to contextualize concerns. Several recent popular books and articles have painted a picture of generics as of lower quality than brand name drugs; however, despite the real concerns raised about particular generic drug factories, many Americans use generic drugs safely every year. Furthermore, generic drugs play an important role in reducing patient costs and may also be a tool to help avert drug shortages. It is therefore important to avoid fearmongering when discussing quality.

To that end, stakeholders agreed that there is a need to further identify what patients and providers ought to know about quality and how this information should be shared with patients and providers in a rapidly changing and social media-oriented communication environment. Although there are many areas where more education would be beneficial, one frequently raised was the need to address common misconceptions about quality. For example, some stakeholders believe that a drug's quality can be assessed based on the country in which the drug was made. However, a, a single drug may include components from multiple countries, and different steps of the manufacturing process may occur in different countries. Furthermore, a label attesting that the drug was, for example, "made in America," is not a reliable indicator of the drug's quality.

Patient Willingness to Pay for Higher Quality Products

During the discussion, stakeholders often stated that they believed patients would pay higher prices for drugs that have evidence of being high-quality. There is a need for data to determine if, and how much more, patients might pay for quality because creating reliable manufacturing systems that are resistant to drug shortages costs money and the current paradigm in which generics are competing for the lowest price does not incentivize such spending.

Additionally, stakeholders noted that consumers may have a role in advocating for quality. While patients do not negotiate drug pricing contracts, consumer pressure to have a safe and reliable source of drugs may be one important force in advocating for quality.

## Breakout Group B: Buyer and Payer Perspectives

Group B consisted of eleven representatives from group purchasing organizations (GPOs), distributors, health system pharmacy departments, trade organizations, and other related groups, as well as FDA participants and observers. Stakeholders first discussed how buyers and payers define pharmaceutical quality, how stakeholders perceive FDA's role in regulating pharmaceutical quality, and what data stakeholders use to inform understanding of quality among other topics. Group B then considered how healthcare organizations, institutions, and GPOs factor pharmaceutical quality into drug purchasing decisions, what barriers stakeholders face in obtaining information about quality, and how drug shortages related to pharmaceutical quality. Key topics in the Group B breakout discussion included strategies used by GPOs to promote quality, the need to improve transparency, quality ratings or metrics, and the importance of common quality standards.

Strategies Used by Group Purchasing Organizations to Promote Quality

Discussion in the buyer and payer breakout group focused on the ways that GPOs acquire and use data about the quality of drugs. Unlike FDA, GPOs can leverage longer term contracts or committed volumes to incentivize manufacturers to obtain confidential information about supply chains or even modify some aspects of them. One way that GPOs use this information is to select quality products with reliable supplies. GPOs shared that they create lists of medicines that they consider to be essential for their

members to have in reliable supply. For these essential medicines, GPOs spend additional time considering the quality and availability of the medicines. Some of these lists are publicly available.

Much of the discussion that followed focused on ensuring a reliable supply of essential medicines and assuming that such efforts would also improve pharmaceutical quality. GPOs shared that, for some medications, they ask manufacturers to share information about their supply chains. One GPO noted that they prefer manufacturers with vertical integration in supply chains, or redundancy.[2] Only once this particular GPO has identified the manufacturer with the supply chain that they prefer do they negotiate with the manufacturer regarding pricing. This practice is different from the usual GPO bidding process, where the price of the product is the central deciding factor.

Throughout the session, stakeholders made connections between quality and shortages. The 2019 shortage of vincristine, which was not related to a quality issue, was frequently referenced as a type of drug shortage to prevent in the future. The vincristine shortage occurred after Teva Pharmaceuticals exited the market and the remaining manufacturers could not meet demand. While problems with quality are not the only cause of drug shortages, they are an important factor. GPOs believe that their efforts to mitigate shortages of essential medicines will also improve the quality of those medicines, although the current lack of quality ratings makes this difficult to empirically demonstrate. Stakeholders suggested that trade organizations may play an important role in sharing GPO best practices to promote quality.

GPOs noted that contracting strategies may not be effective in every case. The products must be frequently used. If the product is used only by a small number of patients it is difficult to commit to purchasing large volumes from the manufacturer. Additionally, for products that have only a single source, GPOs may lack the leverage to negotiate. Finally, smaller health systems lack the contracting leverage that large GPOs may have. Additionally, while some suggested that there is a role for purchasers to buy from different suppliers and thus diversify the market, preventing shortages, GPOs noted that this may be difficult for some products, particularly for opioids or other controlled substances where the U.S. Drug Enforcement Agency implements annual production quotas.

Non-Contracting Quality Improvement Strategies

Buyer and payer efforts to improve quality were not limited to contracting-related strategies. GPOs mentioned that they promoted the supply and quality of drugs through auditing manufacturers, creating private drug labels, and working with non-profit drug manufacturers such as Civica Rx. Some GPOs also shared that they have advocated for the proposed Mitigating Emergency Drug Shortages (MEDS) Act.

Looking forward, stakeholders also considered ways to ensure quality as the drug moves through the supply chain, including employing product tracking technologies such as RFID, DNA tags, quantum tracking dots, barcodes, and blockchain tracking. Buyers and payers also discussed additional legislative advocacy, including bills that would allow FDA to issue mandatory recalls, and laws to speed up the process of recalls.

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[2] In vertically integrated supply chains, the manufacturer of the finished product also manufacturers the API. When there is a shortage of an API,  manufacturers with vertically integrated supply chains are better able to ensure that their products are not affected. Geographic redundancy of supply minimizes the impact of natural disasters or other events on the drug supply.

The Need to Improve Transparency

Stakeholders highlighted the need to improve the transparency around pharmaceutical quality. This discussion is particularly important because concerns about the quality of pharmaceuticals have become more prevalent in the media in recent years. Such concerns may lead to a lack of patient trust in their medicines, which is concerning, particularly if it leads to nonadherence.

Stakeholders noted that while the concept of transparency is important, there is not a common understanding of what appropriate transparency surrounding quality might look like. One important aspect of transparency is understanding how poor quality is identified and remediated. For example, GPOs noted it would be helpful to know how manufacturing lines are remediated after quality concerns are identified.

Additionally, others advocated for more information to be shared when recalls occur, beyond warning letters and Form 483s. GPOs noted that they were aware of the existence of some "bad actor" companies but wanted more data about manufacturers that consistently have quality problems. Stakeholders wanted to make decisions based on aggregate data, rather than anecdotal patient reports about quality. Organizations like GovZilla were referenced as examples of groups that are currently collating public data, albeit providing it to clients for a fee. Several stakeholders also suggested new techniques that might be used to improve transparency, including independent chemical testing of drugs.

Stakeholders discussed wanting to be able to view 483s more rapidly. FDA noted that releasing them more rapidly may be challenging. A Form 483 is an inspection report, not a final decision. Organizations have a chance to make changes to address quality concerns. Additionally, 483s must be redacted before being posted publicly, which is a time-consuming, and expensive process.

Despite the suggestions raised by stakeholders, challenges remain to improving transparency. Many emphasized that transparency, particularly when considering the global sourcing of active product ingredients (APIs), is complex. It may not be easy to label a product, or an API as "made in America." Different steps in the drug production process may take place in different locations, even if a final product is packaged in the United States.

Another important challenge raised was that FDA may not always have access to all of the information stakeholders would like to receive. For example, stakeholders were interested in learning the volume of a product being made at a particular manufacturing location. FDA shared that they receive yearly reports of manufacturing volume, but not real-time data.[3] Increasing transparency is an important goal, but will require creative solutions, flexibility, and varying approaches.

Quality Ratings, Metrics, and the Need for Common Quality Standards

Many stakeholders felt that a common understanding of what factors matter to quality would help the industry be more consistent when discussing quality. Some GPOs and buyers at the workshop shared that they have developed their own quality ratings or scores for products and manufacturers. Other organizations are thinking about ways to produce quality scores based on chemical testing and

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[3] In the 2020 CARES Act, as part of their annual registration and listing requirements, all drug companies will be required to submit a report of the amount of drug product they manufacture for commercial distribution. The Secretary may also require this information at the time a public health emergency is declared.

regulatory data. Stakeholders worried that competing determinations of quality may be confusing to the industry, as well as patients and providers. Even within the stakeholder groups present at the workshop, terms like "quality scores" were used to refer to both the quality of the manufacturing process as concerns its ability to produce a reliable supply of drugs and the quality of the product that is free of contamination and defects.

A shared understanding of quality is particularly important when considering the "cost of quality." Stakeholders noted that once a product is FDA approved, there is no additional official delineation of high or low quality of the product. It is therefore difficult to quantify quality (e.g., a 5% increase in quality) and difficult to determine how much more patients will pay for a higher quality product. In this discussion, there was some overlap between the discussion of a higher quality product as one that is more resistant to shortages, and a higher quality product that has fewer impurities or contaminants. This terminological confusion should be clarified going forward, so that different stakeholders understand the proposals that others are putting forth.

To come to a shared understanding of what factors matter to quality, stakeholders suggested leveraging existing data sources. GPOs shared that it would be helpful to know what data FDA currently has regarding quality and what data FDA does not have access to. GPOs noted they might then be able to advocate for legislative changes that would allow FDA to have access to such data, or acquire the data through their own contracts and share it with FDA, if legally permitted.

One way to combine data on factors that matter to quality is to create quality scores. Stakeholders felt that quality scores might be one a way to "heal" the system. Specifically, low quality scores might incentivize competition in certain markets, and push companies to fix quality concerns. Scores might be generated by industry partners, or by FDA. Stakeholders suggested that even if FDA is not issuing its own quality scores, FDA may be able to generate a standard list of elements that should be considered when organizations design scores.

Although stakeholders generally were interested in the idea of quality scores, some raised concerns that patients may confuse quality scores with efficacy or that, rather than taking steps to improve quality, lower scoring companies would drop out of the market, thus reducing competition. Others wanted to reiterate that the location of manufacturing is not a surrogate for quality. To that point, FDA stressed that quality scores must be backed by data.

### Synthesis Discussion

After the breakout sessions, Group A and B combined to share lessons learned and develop strategies for promoting pharmaceutical quality. Buyers, payers, patients, providers, and FDA representatives considered ways in which the industry can collaborate to address issues of quality. Building on earlier discussions, stakeholders identified three key areas to focus future work and collaboration across the stakeholder community: assessing perceptions surrounding quality to improve communication, improving transparency, and developing quality ratings.

Continue to Assess Perceptions of Quality and Improve Communications

Stakeholders discussed the importance of continuing to assess patient and provider perceptions of pharmaceutical quality. Understanding perceptions of quality can improve and shape communications directed at patients and providers about quality. When communication occurs, stakeholders should

account for patient perspectives. Online surveys and social media can be tools in assessing and conveying messaging about quality.

Improving Transparency

Stakeholders largely wanted access to more information about pharmaceutical quality. Discussion covered questions of which stakeholders need to be involved in the transparency process, how information should be shared, and what steps might be taken in the future.

No single stakeholder group can address issues of transparency. While GPOs receive information about quality through contracting, they noted that contracting cannot be the only tool used to improve drug quality, and it can only be leveraged with manufacturers if there are multiple sources for a product. Confidentiality agreements may also limit how widely they can share information acquired through contracts. The Drug Supply Chain Security Act (DSCSA) was discussed as an important step to transparency, but, the DSCSA does not provide all the information stakeholders want about quality. Finally, while access to information is important, some providers noted that they wanted assurances that products were of high quality, but did not want to be making comparative quality decisions on a day-to-day basis.

Discussions also covered considerations about how to share information. FDA noted that one worry about discussing pharmaceutical quality is that sometimes information is presented without context. Sharing information without context or actionable recommendations might make patients unnecessarily worried, or make patients stop using a product when the benefits of the product outweigh the risks.

Finally, stakeholders talked about steps to advance transparency. Some wondered if information about the location of manufacturing should no longer be considered proprietary—particularly given recent examples of natural disasters and pandemics impacting drug shortages.[4] Additional strategies to improve transparency around pharmaceutical quality include legislation and sharing of information across and between industries. There is also a need for global regulatory alignment, particularly given that the original systems for regulation and quality were not designed with a global supply chain in mind. The ICH was presented as one opportunity for such regulatory alignment.

Developing Quality Metrics and Quality Scores

Stakeholders largely agreed that there is a need to develop and implement quality metrics or scores within the industry. One reason to develop quality ratings that they might help differentiate products at a level beyond price. When price is the differentiator between generics, companies are incentivized to purchase the cheapest product. To incentivize producing higher-quality products, stakeholders discussed included tying quality scores to determinations of therapeutic equivalence for generic drugs, or using contracting mechanisms to require manufactures to have independent third parties chemically test drugs.

Stakeholders proposed various forms that quality scores might take. Some advocated for a single quality score. Others noted that many industries rely on multiple consumer scores and that the public can choose between those scores. FDA noted that good quality scores would be clear, rigorous, and applicable across a range of products. Despite some differences in opinion, stakeholders largely agreed

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[4] This meeting was convened on February 3, 2020 before broad quarantines went into effect in March 2020 due to the COVID-19 pandemic.

that it is important not to legislate bad metrics, that are then difficult to change at a later time. One idea suggested was that FDA could help create a list of information that is helpful to know when assessing quality. Additionally, FDA suggested that knowing more about the existing quality ratings used by industry might help FDA identify possible inspection targets—an important prospect because FDA has limited resources to conduct inspections and must prioritize based on risk.

Some stakeholders expressed concerns that manufacturers may disapprove of quality ratings, particularly if they are perceived to be an unreliable indicator of quality or if a poor quality score would affect their stock price. This concern was countered by one stakeholder who stated that workplace safety complaints are public knowledge and often motivate companies to rapidly address the cause of the complaint. Similarly, within other aspects of the medical industry, stakeholders cited examples of areas where people have protested the use of transparency and metrics, but now there is growing acceptance and recognition of their role to improve understanding of pharmaceutical quality. These examples include Medicare quality ratings, state reports on cardiac surgery outcomes, and the Physician Payments Sunshine Act.

Stakeholders agreed that quality ratings are only the first step to improving pharmaceutical quality. Stakeholders noted that as the system improves, the standard for acceptable quality could be raised. Similarly, quality ratings should not be a replacement for quality systems, which should also be developed and implemented. The discussion concluded on the idea that that quality ratings may be a place for GPOs and FDA to work together to have a stronger industry voice.

References
1. US Food and Drug Administration. Report on the State of Pharmaceutical Quality. fda.gov/media/125001/download. Published 2019.
2. Cox B. Cleveland Clinic Drug Quality Dashboard Helps Guide Product Choices. *Pink Sheet.* 2/20/2020, 2020.