CIVICA
Serving Patients is Our Privilege

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

Re: Docket No. FDA-2018-N-3272: Identifying the Root Causes of Drug Shortages and Finding Enduring Solutions; Public Meeting; Request for Comments

Dear Sir or Madam:

Civica Rx (Civica) wishes to thank FDA, FDA Drug Shortage Office, FDA Drug Shortage Task Force, and FDA Commissioner Scott Gottlieb for their efforts to reduce shortages in the United States, an ongoing challenge for patients and their families, nurses, physicians and hospitals.

Civica is a pro-competitive, not-for-profit generic drug company founded by leading health care systems that know first-hand about the impact of inconsistent, unpredictable, and often unstable market dynamics leading to drug shortages. Civica has met with FDA in October 2018 to discuss our solutions to reduce drug shortages and will continue to seek partnership with FDA in addressing drug shortages in the United States. The mission of Civica is to improve accessibility, consistency, and affordability of products in the generic drug market. Civica's foundational values of safety, efficacy, quality, adequacy, affordability, and fairness drive the company's efforts.

We also request your review of our plans to curtail drug shortages and how we think you can help.

Many medicines that have been on and off the drug shortage lists are generic sterile injectable drugs and are essential medications used within hospitals every day. These shortages not only cause significant disruptions with hospitals, but also have the potential to harm patients or require drug substitutes that provide sub-optimal therapies. We appreciate the work of the dedicated, hard-working professionals throughout the FDA in responding to the required notification from manufacturers of potential shortages and the FDA's response to prevent or minimize the patient impact of such drug shortages. We at Civica are encouraged by the recent formation of the Drug Shortages Task Force to support FDA's efforts to alleviate and prevent shortages and look forward to working with this task force.

As of October 2018, and as you well know, there are currently 91 medically necessary drugs on the FDA's shortage list[1]. Approximately 200 drugs have been on and off the FDA's drug shortage list during the past several years. Economics and market dynamics are a primary

driver of this problem. When a drug's patent expires, the initial competition among generics can yield a stable supply and lower prices. As more generic manufacturers enter the market, however, prices can be driven unsustainably low, which leads some manufacturers to exit the market to use their resources for other endeavors. These departures create a fragile pharmaceutical supply chain or outright shortages and leave one or two remaining generic producers with monopolistic power to dominate the market, dictating price and often shorting supply.

For example, Lidocaine, an injectable, local anesthetic used for countless surgical and interventional procedures for pain management, has been on the shortage list for many months. When a dominant sole source manufacturer fails to supply, it immediately creates a surge demand and capacity from other manufacturers, who may not be prepared to fill the void, leading to drug shortages. With few manufacturers, a single delay at one facility caused an almost immediate shortage, forcing health systems to devote significant time and money to try to secure necessary supplies. Even with this effort, more than 57% of health systems report that the Lidocaine shortage is negatively impacting patient care, through delay or cancellation of surgeries.[2]

Civica Solutions: Promote Competition and Create a Reliable Supply of Quality Generic Drugs at Fair, Sustainable and Transparent Prices that are Essential for Hospitals to Serve Patients

Civica has been specifically designed to do what is in the best interest of patients.

Civica intends to stabilize the supply of essential medicines and promote market competition by challenging the economics and market conditions that lead to drug shortages. Partnering closely with health systems and manufacturers, Civica will develop a fair and sustainable and transparent price to address the "race-to-the-bottom" paradigm that leads to shortages and skyrocketing prices during shortages.

Civica will enter into up-front long-term guaranteed contracts with hospitals and hospital systems for supplied drugs, which Civica aims to price at fair and sustainable prices. Civica, in turn, will make long- term guaranteed commitments with trusted manufacturing partners. This ability to guarantee volumes will prevent Civica from being 'pushed out' of the market through traditional "race-to-the-bottom" competition and thus stops the typical cycle that ultimately leads to monopolistic realities of a few manufacturers. Also, for a manufacturer, the guarantee of long-term volumes, revenues and margins eliminates economic uncertainty and allows manufacturers to invest in capacity, facility improvements, process improvement and quality suppliers.

Civica will have a disruptive distribution model that will not pay fees or rebates to "middlemen" in the pharmaceutical supply chain, breaking the grip of sole source providers and closed distribution systems.

Civica will offer one transparent, single price to all customers, whether they are the smallest hospital in a rural community or the largest health system in the United States, thus preventing the typical inequities between customers. This will allow hospitals and patients to get their fair quantities of a drug and not be disadvantaged based on the price a hospital pays or the quantity a hospital purchases.

Civica will require redundant manufacturing capabilities for finished drug products, APIs (active pharmaceutical ingredients) and critical materials, therefore reducing the risk of a shortage due to a potential issue at one manufacturing facility. Additionally, safety stocks of finished drug product, APIs and critical materials will be maintained at strategic locations.

Furthermore, as a not-for-profit company, Civica is not burdened by the same profit pressures of typical drug manufacturers. This will allow Civica to invest excess revenue to improve our ability to meet patient needs by supplying additional critical drug products to the market at affordable prices, while continuing to reduce overall costs.

To start, Civica will target production of generic drugs that meet specific criteria including:

- Drugs present on shortage lists or "top concern" lists for health system partners.
- Drugs that are essential to day to day operations of health systems.
- Drugs that experienced a price increase of 50% or more over a three-year time period.
- Drugs for which a few vendors make up the majority of the market share.

Using the above criteria, Civica will target production of 30 plus drugs and associated SKUs by 2020. Civica will pursue its efforts via a combination of approaches, including:

- Using manufacturers who originally held the ANDA and have exited the market.
- Acquiring or developing ANDAs and working with contract manufacturers.
- Purchasing or building Civica manufacturing facilities.

The manufacturing, distribution, inventory and pricing strategy will ensure a stable supply and reduce the risk of shortages, ultimately supporting Civica's ability to act in the event of a market failure. Although this approach will not solve shortages universally, it will make an appreciable difference with high priority generic drugs. Civica may also drive subsequent market dynamics that beneficially reshape the generic drug market as other manufacturers reevaluate their production decisions and approaches.

Success Metrics: Increased Availability and Affordability of Generic Drugs

Civica aims to be a model generic drug manufacturer by providing a reliable supply of FDA-approved products at affordable prices. Through strategic partnerships, Civica's non-profit status will strengthen the generic drug manufacturing structure to alleviate shortages, decrease market price manipulations, and serve as a check against natural monopolies.

Civica aims to succeed by:

- Establishing fair and sustainable prices to address the economics and market forces that have resulted in drug shortages.
- Securing long-term guaranteed contracts with our members.
- Providing long-term guaranteed contracts with our trusted manufacturing partners.
- Refusing to pay fees and rebates to "middlemen" in the pharmaceutical supply chain.
- Offering one price, whether to the smallest hospital in a rural community or to the largest health system in the United States.
- Ensuring transparent pricing throughout the supply chain.
- Ensuring redundant manufacturing capabilities for finished drug products, APIs (active pharmaceutical ingredients) and critical materials.
- Maintaining safety stocks of finished drug product, APIs and critical materials in strategic locations.

Civica is implementing our strategies and will contribute to significantly reducing drug shortages. However, more actions are necessary than any one company can implement to solve the drug shortage crisis in the United States. Therefore, Civica is encouraging the FDA to continue to advance their efforts and respectfully provide the following suggestions.

Additional Things That Policy Makers and Regulators Can Do To Reduce Drug Shortages:

Quality Metrics: FDA should continue to pursue their Quality Metrics initiative. Civica believes that payors, health care provides, and patients should be able to determine, and rely upon, a drug's quality level, country of origin and consistent availability of drugs. In every industry, when transparency and a scoring system is implemented, good suppliers increase their business at the expense of poor suppliers. Furthermore, as the saying goes: "you don't improve what you don't measure." The Quality Metrics initiative will help lead to a market driven reaction whereby all suppliers improve their products and services.

Qualified Manufacturing Program: The use of a qualified manufacturing partner program, like the one used under the Biomedical Advanced Research and Development Authority (BARDA), has been suggested as a potentially useful approach to expanding manufacturing capacity and preventing shortages. FDA recognizes that there are important potential differences between the BARDA program and the use of a parallel program to address shortages. For example, the BARDA program covers a relatively stable and limited number of products, but drugs at risk of shortage are many, may change rapidly over time, and are difficult to predict in advance. In addition, FDA does not have funding to pay manufacturers to participate in a drug shortages qualified manufacturing partner program or to guarantee purchase of the finished drug product. These barriers could be overcome by FDA creating a list of essential medications that

have limited alternatives and are life sustaining or saving. Also, legislative changes could be enacted to fund and allow the FDA to pay for manufacturers to participate.

Government Incentives: There are incentives that FDA can provide to encourage manufacturers to establish and maintain high-quality manufacturing practices, to develop redundancy in manufacturing operations, to expand capacity, and /or to create other conditions to prevent or mitigate shortages. Examples include:

- Faster and more streamlined approval of 1) new technologies (such as isolator technology for parenteral filling operations), 2) redundant manufacturing facilities, or 3) raw material suppliers, all of which have a positive impact on reducing potential and real drug shortages. This would also include both faster review of filings and expedited cGMP inspections where deemed necessary.

- Faster and streamlined approval of new products for companies that the Agency has determined are compliant and have adequate risk mitigation plans to prevent drug shortages.

- For companies with a good compliance status and adequate risk mitigation plans to prevent drug shortages, FDA could reduce regulatory oversight / requirements including: 1) downgrading filing categories for other filings such as site transfers and assay improvements, 2) increased use of extended comparability protocols, and 3) reduced validation requirements.

- Extend the interval between routine GMP inspections for those companies with excellent compliance status, and who have established and implemented a risk management program to protect against potential drug shortages for the products they manufacture.

FDA can collaborate with other government agencies in the best interests of patients by offering additional incentives, including:

- Financial incentives, such as tax credits and/or federal grants, provided to companies that develop a robust risk management program that includes establishing and maintaining redundant manufacturing capacity or extra manufacturing capacity that is dedicated to preventing and mitigate drug shortages.

- For generic drugs where there is minimal competition and the economics are such that firms will not invest in developing or manufacturing a product, the Agency should waive certain fees, i.e., associated with filing and maintaining the ANDA.

- In addition, for generic drugs where there is minimal competition and the economics are such that firms will not invest in developing or manufacturing a product, the Agency should work with other agencies to waive fees, i.e., the 13% rebate required for 304B products.

The other benefit would reduce the regulatory burden and associated overhead to offset the develop of a 304B monitoring and compliance program.

- Under terms of an agreement like BARDA agreements, the FDA could mandate inventory levels of essential critical drugs.

Information Sharing: FDA's drug shortage web page and email notifications to interested stakeholders are excellent and timely. We strongly encourage FDA to continue in this manner. Civica also encourages the FDA to continue their collaboration with organizations such as Rx-360 and The American Society of Health System Pharmacists.

Inventory Monitoring: FDA can create an internal database to mitigate or prevent drug shortages by:

- Identifying and publishing a list of "essential critical drugs".
- Determining national inventory levels required for essential critical drugs based on currently available data, for example the IMS IQVIA database.
- Requiring manufacturers of essential critical drugs to report their monthly inventories to the FDA by entering the data directly into the FDA's database. This information would give FDA transparency to the supply levels with an overall picture of drug supply capability across manufacturers. This would be particularly relevant for ANDA approved drugs where the drug is available from more than one manufacturer.
- Monitoring when inventory levels fall below a safe level, giving the Office of Drug Shortages an early warning. Then the Office of Drug Shortage can follow their protocol to prevent the drug shortage. First, they can ask for increased production from all licensed manufacturers.

Civica knows that serving patients is a privilege, and that privilege comes with responsibilities that require delivering quality medications in a robust and reliable manner that is affordable. Civica wants to thank the FDA for giving us the opportunity to provide our most recent thinking on how to prevent drug shortages. Civica is supportive and appreciative of the FDA and their dedicated hard-working professionals in their efforts to prevent drug shortages. Our suggestions provided are in the sprit of continuous improvement and what is in the best interest of patients.

Sincerely,

Martin VanTrieste
President & CEO

1 U.S. Food & Drug Administration, “FDA Drug Shortages,” accessed March 28, 2018. https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm.

2 Modern Healthcare, “Injectable Opioid Shortage Compromises Care,” March 21, 2018. http://www.modernhealthcare.com/article/20180321/TRANSFORMATION03/180329986