Testimony of

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Summary of Testimony:

- Civica is a non-profit generic drug company created by US health systems and philanthropies to address drug shortages.
- Civica currently delivers 80+ drugs, all chosen by US hospitals because they are at risk of shortage, with more than 140 million containers delivered over five years.
- The "Civica model" is designed to ensure a resilient supply and relies on:
    - Long-term purchase and supply contracts that add stability to the market. Civica contracts directly with hospitals, rather than through middlemen that may contribute to price and supply instability.
    - Maintaining approximately 6-month buffer inventory of every drug
    - US sourcing whenever possible, with the EU and Canda as a second choice. We don't source finished drugs or API from China unless there is no other source.
    - Intensive quality oversight of suppliers.
    - A single cost-plus price, available to every purchaser.
- The Civica model works, as demonstrated by the fact that 20 of our top 25 drugs are currently in national shortage. We are able to supply hospitals at or above committed volumes.
- Policy responses to shortages, discussed in greater detail below, should include:
    - Measures to ensure adequate buffer inventory.
    - Measures to ensure that generic sterile injectable drugs are priced sustainably.
    - Measures to create market demand from manufacturers that are less likely to have quality failures; and
    - Direct investments in U.S. manufacturing to ensure adequate capacity and redundancy to ensure a resilient supply of these essential medicines.

Full Testimony

Chairman Guthrie, Ranking Member Eshoo, and Members of the Health Sub Committee,

Thank you for the opportunity to speak with you today on the pressing issue of drug shortages, and on policies to prevent and mitigate future shortages.

My name is Allan Coukell. I am a pharmacist by training, and I lead public policy for Civica – also known as Civica Rx.

The problem of drug shortages

Drug shortages have been a chronic and ongoing problem in the U.S. for well over a decade. At any given time, hundreds of drugs appear on the FDA drug shortages list. Currently, we are seeing an acute exacerbation of shortages as a number of manufacturers have experienced quality problems, causing them to permanently or temporarily leave the market. Cancer drugs and penicillin and cephalosporin antibiotics are among those products of highest current concern, but shortages cut across therapeutic categories of generic drugs. Sterile injectable drugs are predominantly affected, though not exclusively, due to the complexity of manufacturing and the low profit margins associated with these products.

Drug shortages disrupt patient care, causing procedures to be canceled or delayed. They require treatment regimens to be adjusted to alternate products, potentially increasing the risk of medication error or resulting in suboptimal care. They require commitment of enormous pharmacy and hospital staff time attempting to source drugs that are in shortage. And, while the low cost of drugs is the ultimate driver of supply failures, once in shortage, prices spike, adding to costs.

About Civica

Civica is the only pharmaceutical company established specifically to address generic sterile injectable drug shortages.

We were founded as a non-profit, non-stock organization by a group of U.S. health systems and philanthropies who, after more than a decade of chronic shortages, recognized that the market was not self-correcting and that a different approach is required.

They created Civica with the mission if delivering a safe, stable and affordable supply of essential medicines to U.S. patients.

Civica marked its 5th anniversary last week. In that time, our hospital membership has grown to 55 health systems, accounting for one-third of licensed beds in the United States, and we have supplied more than 140 million containers of generic sterile injectable drugs – more than 80 different drug products.

With substantial support from the U.S. government, we recently completed construction of our own state-of-the-art sterile injectable manufacturing facility in Petersburg, Virginia.

The model

The drugs that Civica delivers are those that are in shortage or at high-risk of being in shortage.

They are chosen by a committee of physicians and pharmacists from Civica member hospitals.

They are typically old, low-cost, but essential medicines. They are not the products with the highest return on investment; they are the products required to deliver care every day in hospitals across the country.

Because our mission is to prevent shortages, several features of the "Civica model" are different from the traditional generic drug supply chain and may suggest potential improvements to the larger US system. In particular:

- Civica enters long-term purchase and supply contracts that add stability to the market.
- We target a 6-month buffer inventory of every drug to ensure continuity of supply.
- We emphasize US sourcing whenever possible, with the EU and Canda as a second choice. We don't source finished drugs or API from China unless there is no other source.
- Civica performs an intensive quality audit of potential suppliers, supplemented by ongoing review of key metrics, to reduce the risk of a failure to supply.
- Every drug is sold on a cost-plus basis, with the same price available to any purchaser. Our prices remain stable even when the drug is in short supply.

Success of the model

The Civica model has demonstrated benefits. In fact, of our top 25 drugs, 20 are currently in shortage,[1] but we are able to supply without interruption.

When a tornado recently hit a generic drug manufacturing facility in Rocky Mount, North Carolina, the Civica portfolio included 21 products that overlapped with products produced in

[1] ASHP Drug Shortage list as of latest update (15 Aug 2023)

that plant. We immediately let member hospitals know that we could supply double their committed volume for all 21 drugs.

Forthcoming data also show net cost savings to the health system associated with sourcing through Civica.

Policy responses

When considering policy responses to drug shortages, it is important to recognize that chronic drug shortages have now become a built-in outcome of the current system. Market trends and the resumption of FDA inspections after COVID mean shortages are more likely to increase than to abate in the years ahead.

Therefore, policy responses must strike a balance between *responding* to shortages and changing incentives in order to *prevent* them.

The immediate cause of most shortages of sterile injectable drugs is quality problems in the manufacture of the finished dosage form.

But it is widely acknowledged that the root cause is the low cost of these products, which reduces the incentive or ability for manufacturers to invest in quality or in newer manufacturing facilities and pushes production offshore to low-wage markets where quality problems proliferate, and the FDA presence is less consistent.[2]

[2] For example, see FDA "Drug Shortages: Root Causes and Potential Solutions," 2019; Brookings "Federal Policies to Address Persistent Generic Drug Shortages," 2023; Duke Margolis, "Advancing Federal Coordination to Address Drug Shortages" 2023.

Pharmaceutical production is relatively inelastic: when a manufacturer with a substantial market share stops producing, a shortage is likely, even if there are other companies producing versions of the same drug.

Therefore, policy responses to reduce shortages should include:

- Measures to ensure adequate buffer inventory,
- Measures to ensure that generic sterile injectable drugs are priced sustainably,
- Measures to create market demand from manufacturers that are less likely to have quality failures; and
- Support for domestic manufacturing.

Buffer inventory

As noted above, production of injectable medicines is relatively inelastic. If a particular facility stops producing, others take many months to ramp up production (assuming other companies already have approval to produce the drug). Therefore, a system that operates on just-in-time inventory will always be at high risk of shortages.

However, the resources required to establish and maintain access to a buffer stock of essential medicines will generally be greater than the resources required to establish and maintain access to these medicines without such a buffer stock.

Congress should incentivize supply chain stakeholders to maintain buffer inventory. Civica's experience is that a 6-month reserve is the appropriate quantity to create added resiliency, as it allows suppliers to deliver additional batches in the event of a supply interruption.

The cost of a holding a buffer inventory can be calculated on a straightforward basis, by taking into account the weighted cost of capital[3] for the inventory held, along with the cost of the storage facility itself.

Congress could incentivize manufacturers, wholesalers, or providers to hold extra inventory. The most practical approach would be to provide incentives for providers to contract with manufacturers or wholesalers who actually hold the buffer stock. This maximizes the effectiveness of inventory allocation in a shortage situation and does not require providers to directly maintain or operate storage facilities, with the attendant cost, complexity and risk of outdated inventory.

Sustainable pricing

As noted above, the root cause of ongoing shortages of generic sterile injectable drugs is low prices that reduce investments in quality and push manufacturing to less-regulated markets.

While the overall "race to the bottom" on generic drug pricing is driven by commercial market forces, there is no doubt that mandatory rebates further erode manufacturer margins. Eliminating Medicaid and 340B rebates for generic sterile injectable drugs would restore meaningful margin and remove a source of overhead costs for generic companies.

Civica supports the rebate provisions in the STOP Drug Shortages Act; however, the definition of "serious disease or condition," referenced in §312.300, may inadvertently exclude important products that are frequently on the drug shortage list established under 506E. For example,

[3] Weighted cost of capital is a measure of the cost companies pay to finance their operations.

lidocaine and bupivacaine are local anesthetics that are essential products but may not meet the definition in §312.

A preferable alternative approach would be to exempt all generic sterile injectable drugs, or all injectables with a cost under $5 per unit of sale (e.g. per vial or syringe). This would specifically help to address the challenging economics of the lowest cost drugs, while leaving rebates untouched for high-cost products.

Eliminating rebates for drugs priced at this level would have an inconsequential impact on provider revenues (a tiny fraction of 1%) but may ensure the viability of a product for a manufacturer, encouraging them to stay in the market and therefore helping to ensure supply. If accumulated by a non-profit manufacturer such as Civica, the savings could be reinvested in shortage mitigation (e.g. increased inventory or product development).

<u>Measures to create market demand from reliable manufacturers</u>

Currently in generic drug procurement, purchasers have little basis to distinguish between manufacturers of apparently identical FDA-approved products. While FDA's Quality Management Maturity program remains under development, there is a source of quality information that could be made more readily available.

FDA's inspection reports – Form 483's or 483's – are a source of existing information that, if it were more readily available, could be used in multiple salutary ways, including:

- Knowledge that a 483 would quickly become publicly available with little or no redaction would spur manufacturers to proactively improve quality rather than face increased public scrutiny associated with adverse findings.

- Timely access to 483s would provide a near-real-time quality signal that could help the market anticipate or mitigate potential shortages. For example, knowledge of quality problems at a facility could allow Civica to increase orders with alternate manufacturers and could allow health systems to reduce use of a drug by using an alternate product, where possible.
- Improved access to 483 information would provide purchasers of drugs, such as health systems and group purchasing organizations, with a quality signal that could inform procurement decisions and vendor selection.

Unfortunately, not all 483's for drugs are posted on FDA's website and those that are posted often take up to a year to appear. Moreover, in many of the documents posted, FDA redacts information that is critical to predicting drug shortages, including the name of the drug(s) that are the subject of adverse findings, even though disclosure of that information is not restricted by law.[4]

There is precedent for automatically posting a specific category of 483's where the use of FDA resources is justified by important public health concerns. After a serious incident related to compounding pharmacies, FDA started to post all 483's issued to compounding pharmacies.

[4] According to FDA's regulations, a trade secret consists of "commercially valuable plan, formula, process, or device that is used for the making, preparing, compounding, or processing of trade commodities and that can be said to be the end product of either innovation or substantial effort. There must be a direct relationship between the trade secret and the productive process." 21 C.F.R. § 20.61(a). Commercial or financial information includes "valuable data or information which is used in one's business and is of a type customarily held in strict confidence or regarded as privileged and not disclosed to any member of the public by the person to whom it belongs." Id. at § 20.61(b). (Wiliam B. Schulz, Partner, Zuckerman Spaeder. Letter to Commissioner Califf, 17 July 2023)

Congress should require FDA to adopt a similar approach with respect to 483's that are issued to drug/biologics manufacturers, and to post all drug-related 483's within 30 days of issuance.[5] Eliminating or reducing the extent of redactions would allow more detailed information about quality risks into the public domain. Less redaction would presumably also facilitate speedier release of information.

Support for Domestic Manufacturing

Drug shortages are relatively predictable. A variety of risk factors can be considered, but the strongest prediction of a future shortage is whether the drug has been in shortage previously.

Shortages occur across therapeutic classes, but predominantly affect generic sterile injectable drugs, with the proximal cause of shortages generally being problems with manufacturing quality. When manufacturing moves offshore for economic reasons, much manufacturing occurs in older physical plants where the risk of contamination is high.

"ANDAs at the Ready"

When a shortage occurs there is generally not a facility with the capacity or approved process to rapidly increase production. In addition, there are no new entrants due to the inability to recover the cost of development and approval.

As noted, some drugs are at high and predictable risk for shortage but cannot be manufactured competitively in the United States at current market prices. Development of a new ANDA is time consuming -- typically 29 to 32 months from initiation of development to availability in the

[5] This could be accomplished by dedicating a single employee to the task. Even in a year with a high number of drug-related 483's there were 500. A single employee dedicated to this effort would only have to redact and post on average two 483's per day.

market.[6] Therefore, development of a new ANDA once a drug is unavailable is not an effective response to a shortage. It is critical to complete the ANDA development and approval process and be ready to manufacture well in advance of a shortage.

Congress could direct the Administration for Strategic Preparedness and Response (ASPR) to invest in resiliency by supporting domestic manufacturers to develop ANDAs for high-risk, essential drugs in order to be able to begin manufacturing quickly in a shortage situation. With such "ANDAs at the ready," it would be possible to address shortages in a timely manner.

At a cost of approximately $3 million per ANDA, plus the relatively modest cost of maintaining a reserve of active pharmaceutical ingredient, the "ANDAs at the ready" approach is an efficient and targeted way to create a safety net for essential medicines.

Early FDA Inspections for New Manufacturing Facilities

Sec. 506 of the STOP Drug Shortages Act establishes a pilot program under which FDA would conduct preapproval inspections for a new domestic pharmaceutical manufacturing facility for the purposes of expediting the licensure and distribution of domestically manufactured generic drugs.

Civica sees significant value in the proposed program: at no added cost to the government, earlier FDA inspection of new pharmaceutical manufacturing facilities would reduce time to market and lower the cost of establishing new domestic production capacity.

[6] For example, typically 6 to 9 months for drug development, 6 months for tech transfer and initial qualification batch production, 6 months for stability, one month to file with FDA and 10 months for FDA review.

Establishing a new pharmaceutical manufacturing facility involves a series of time-consuming stages, which generally run sequentially. In a sterile injectable drug facility, these include construction, equipment installation and validation, initial vial/syringe filling, product stability testing, regulatory submission, and FDA approval. These steps might typically take 36 months from start to finish, with an FDA pre-approval inspection (PAI) potentially occurring within the last month or two.

However, to distribute drugs, the facility must obtain up to 40 individual state licenses. Obtaining these entails a timeline of 12 to 18 months and about a dozen states require evidence of an FDA inspection before they will issue a state license.

If the FDA inspection is the step that dictates state licensing, a facility could lose several months after FDA approval before it is able to sell and distribute drugs, with significant financial implications and delays for patients.

Therefore, if the facility were able to undergo FDA inspection when it is determined to be inspection ready by facility management and the quality unit (e.g. at the time of initial vial filling operations), it could have relevant state licenses in place by the time of FDA approval.

Under the pilot program established in this section, FDA would be undertaking the same pre-approval inspection of the physical plant as in the current system, except several months sooner. Stability data and lot-specific information would be submitted with the regulatory filing, as usual. The cost of such inspections is covered through GDUFA fees, which would still be paid for the product, and likely within the same fiscal year.

In addition, as very few new domestic pharmaceutical facilities are established each year, the practical impact of the program on FDA inspectional resources would be small.

Conclusion

Thank you again for your attention to this important topic and for the opportunity to be with you today. I welcome your questions.