Drug Shortages in the United States – Core Underlying Issues and Potential Solutions

At the time of writing, there are approximately 200 drug products listed as in shortage on the US FDA drug shortage database. Many of these medicines are critical, lifesaving medications such as albuterol, the treatment for an acute asthma attack. Several chemotherapeutic drugs for cancer are in shortage. The rates of morbidity and mortality for pediatric cancers in the US have gone up in recent years as the medications necessary to treat them are increasingly unavailable. The majority of these medications are relatively simple to make and have been available for many decades. How is it that they are unavailable in the United States, the wealthiest country in the history of human civilization?

The root underlying causes are complex and multifactorial. However, the essential underlying dynamic in my view are dysfunctional markets for pharmaceutical distribution.

For the majority of retail generic drug products, there are effectively only three purchasers, the source programs of the three major pharmaceutical wholesalers. Together, these entities make up approximately 90% of the generic pharmaceutical purchases from pharmaceutical companies. The overall result of this consolidation of purchasers is that without a contract with one of these entities, it is generally not viable for a generic pharmaceutical company to keep a manufacturing line for a product functioning. These entities generally contract with a single primary provider for any given product, which artificially limits the number of manufacturers who can maintain a viable manufacturing line for a product.

Generic pharmaceuticals are also mostly viewed as commodity products and contracts typically go to the lowest cost manufacturer of any given product. This incentivizes a “race to

the bottom" development strategy wherein any action that reduces manufacturing cost must be taken, including offshoring manufacturing and potentially cutting corners on redundancy.

The net result is a brittle supply chain, which few (at most) offshore manufacturers for any given product. Inevitably, where unexpected events arise, a single supply line going down can cripple supply for an essential, life-saving medication throughout the United States. It can take a year or more for new manufacturing lines to be become established to address drug shortages.

Mark Cuban Cost Plus Drug Company (MCCPDC) is attempting to assist in addressing drug shortages through a combination of both business model and technologic innovation.

Mark Cuban Cost Plus Drug Company Advanced Manufacturing Technologies Strategy

The Mark Cuban Cost Plus Drug Company has constructed an advanced pharmaceutical manufacturing plant in Dallas, Texas. The facility utilizes robotic fill-finish technology optimized by AI machine vision systems that is designed to incorporate single-use disposable components. The robotic manufacturing systems installed at our manufacturing facility can transition between making batches of different types of medication within hours rather than months with full cGMP (current good manufacturing principles) compliance. This allows us to very rapidly pivot from making one drug type to another in order to address pharmaceutical drug shortages as they arrive. In principle, we can have a new manufacturing line up in four hours. In combination with a regulatory strategy as a 503(b) compounding site, we are very rapidly able to pivot from make a shortage drug product with full compliance with FDA regulations.

Images of MCCPDC Robotic Fill-Finish System

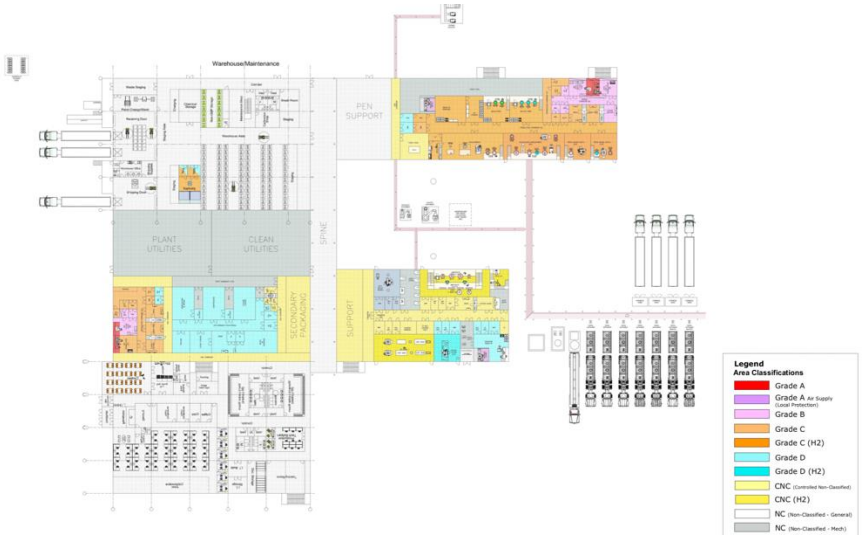
Image of MCCPDC Water for Sterile Injection Generation Skid

Image of MCCPDC Manufacturing Facility Exterior

Our pilot facility is currently completing its validation process and is expected to begin commercial sales in the next few months. It has an estimated capacity of between 1-2M sterile

doses of medication a year, either pre-filled vials or syringes. We estimate that this will be effective in assisting to alleviate drug shortages for between 4-5 large health systems.

MCCPDC has also drafted preliminary plans for a significantly larger facility based on similar technologies that would be able to produce over 100M units of sterile injectable medication and hopefully be able to alleviate the majority of acute drug shortage issues in the United States. We believe such a facility would likely cost approximately $300M to construct based on current estimates.



A diagram of the proposed MCCPDC "facility to end drug shortages"

Mark Cuban Cost Plus Drug Company Business Model Innovation Strategy

Simultaneous to our efforts in advanced manufacturing technologies, MCCPDC is also developing alternative pharmaceutical distribution strategies based on bedrock principles of transparency and honest dealing in order to make US based pharmaceutical manufacturing and distribution cost effective.

The MCCPDC strategy revolves around the construction of a parallel supply chain to ensure that our products or any products we acquire can reach the end patient with minimal

markup and no price distortions. The MCCPDC strategy revolves around four verticals: 1) Manufacturing, 2) Wholesale, 3) Pharmacy, 4) Employee Benefit Solutions.

At present, pharmaceutical pricing revolves around discounts from artificially inflated list prices. The most commonly utilized metrics are Average Wholesale Price (AWP) and Wholesale Acquisition Cost (WAC).

A pharmaceutical benefit manager will typically negotiate rebates off AWP, generally ranging between 85-88%. Conventionally, they will keep a percentage of the rebate negotiated. This practice regularly nearly doubles the cost of a generic drug product. For example, let's assume product X has an AWP of $100. After an AWP discount, the cost of the drug is $15. Let's assume that a PBM keeps 10% of an AWP rebate. The price of the drug is now $23.50, of which the PBM keeps $8.50.

In addition, the large PBMs create large webs of subsidiary companies which capture additional revenue off of rebate dollars. For example, "rebate aggregators" or "group purchasing organizations" which take a percentage of rebate dollars. These entities are often domiciled internationally preventing transparency or audits, so the exact amount of rebate dollars captured at this level is unclear. However, we have heard it estimated that another 8% of rebates may be captured here. That would raise the price of hypothetical drug X to $30.30.

In addition, the big PBMs charge large fees to pharmaceutical companies that work with them. As of 2021, 29% of PBM revenue is estimated to arise from fees up from 15% in 2015 according to research firm Nephron. Some examples of fees we have seen charges include: Promotional Allowances, Implementation Allowances, Rebate Submission Fees, Formulary Placement Fees, Administrative Fees, Data Fees, Health Management Fees, Educational Fees.

The big PBMs also are permitted to mandate that certain prescriptions be filled through internal, self-owned “specialty pharmacies” which can charge hundreds of dollars to dispense a medication.

The net result of this web of affiliated entities, including many others not listed here such as copayment maximizer programs, can be to radically inflate drug costs. One edge case is the chemotherapy drug imatinib. It is currently available for $35.10 for a one-month supply at costplusdrugs.com. The actual adjudicated price, the price patients with a high deductible plan or payers are asked to pay for the same product, has been reported between $2000-3200 for the same product.

In additional, wholesalers are often paid a percentage of the inflated WAC price for a pharmaceutical. An additional 8-12% of the WAC price of a drug may be reimbursed to a wholesaler for services rendered. This is often in addition to fees charged be the sourcing programs previously described.

Multiple independent studies from academic groups and consultancies have found that the MCCPDC pricing model, based on flat transparent costs saves on average ~60% on generic drug spend.

To accomplish this, we build or partner with entities that allow us to dispense or distribute medications on a cost-plus basis with transparent pricing. At the moment, we operate a direct-to-consumer, cash pay mail order pharmacy in partnership with a fulfilment vendor which allows us to sell at a low cost directly to patients.

In the next few months, we will launch Cost Plus Wholesale, a web platform that will allow pharmacies, hospitals, and others to order products at our prices. This will operate in

direct partnership with pharmaceutical companies and will enable multiple pharmaceutical companies to drop-ship direct to buyers or through a cost-plus wholesale partner.

We are also in the process of launching a host of employee benefit solutions that will allow employers to have access to our cost-plus pricing as well. This will be in partnership with smaller, transparent PBMs, large self-insured employers, and regional health insurers.

Our underlying hypothesis is that by eliminating the costs associated with middlemen in the pharmaceutical supply chain, there will be enough savings to repatriate pharmaceutical manufacturing with more redundancy in the United States.

Mark Cuban Cost Plus Drug Company API Strategy

At the moment, MCCPDC does not have plans to establish active pharmaceutical ingredient (API) manufacturing facilities. For the shortage drug products we aim to manufacture, API supplies are available without significant issues at this time. This can of course change and is product specific, however the major bottleneck we see at the moment is at the level of sterile finished dose product manufacturing.

However, we do see it as a potential geo-strategic vulnerability that on overwhelming large percentage of our pharmaceutical APIs are generally sourced internationally and specifically from China, potentially creating risk for our national security due to reliability on foreign nations for these API. We at MCCPDC source a disproportionate amount of our APIs from strong regulatory jurisdictions, approximately 40% compared to an estimated industry average of 10%. However, a large number of drugs APIs are simply not manufactured in strong regulatory jurisdictions.

Given the market dynamics described above, our hope is that by redistributing pharmaceutical revenue towards generic manufacturers from supply chain intermediaries, there will be enough resources available to incentivize domestic API manufacturing while still maintaining a net savings to patients and payers.