

January 11, 2019

The Honorable Scott Gottlieb, M.D.  
Commissioner  
Food and Drug Administration  
Attention: Dockets Management Staff (HFA-305), FDA-2018-N-3272  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

Submitted electronically to: <http://www.regulations.gov>

**Re: FDA-2018-N-3272, Identifying the Root Causes of Drug Shortages and Finding Enduring Solutions; Public Meeting; Request for Comments**

Dear Commissioner Gottlieb,

The Premier healthcare alliance appreciates the opportunity to submit comments to the Food and Drug Administration (FDA) on the request for comments titled “*Identifying the Root Causes of Drug Shortages and Finding Enduring Solutions*” which was published in the September 10, 2018 *Federal Register*. In the request for comments, the FDA seeks input on the underlying systemic causes of drug shortages and recommendations for actions to prevent or mitigate drug shortages.

Premier is a leading healthcare improvement company, uniting an alliance of more than 4,000 U.S. hospitals and health systems and approximately 165,000 other providers and organizations to transform healthcare. With integrated data and analytics, collaboratives, supply chain solutions, consulting and other services, Premier enables better care and outcomes at a lower cost. A 2006 Malcolm Baldrige National Quality Award recipient, Premier plays a critical role in the rapidly evolving healthcare industry, collaborating with members to co-develop long-term innovations that reinvent and improve the way care is delivered to patients nationwide. A key component of our alliance is our Integrated Pharmacy Program, which combines essential clinical data with purchasing power to deliver reduced costs, improved quality and safety, and increased knowledge-sharing with other healthcare professionals.

***Premier has been a leader in addressing drug shortages for over twenty years and is committed to eliminating drug shortages.*** Premier believes that a holistic, multi-stakeholder, and inter-agency approach is necessary to truly address drug shortages. Premier applauds the FDA for its efforts to date to mitigate drug shortages, but drug shortages continue to persist and more needs to be done, including legislative and regulatory action, to eliminate drug shortages. ***Sustainable solutions to address drug shortages must decrease barriers to entry, namely the time and cost to enter the marketplace, while maintaining the quality and safety of the product.***

## I. Premier is a Leader in Eliminating Drug Shortages to Prevent Disruption to Patient Care

Over the past twenty years, Premier has been a leader in addressing drug shortages to minimize the downstream impact to health systems and patient care. Premier's multifaceted and ongoing initiatives to mitigate drug shortages include, but are not limited to:

- **Member Resources** – Premier maintains a drug shortage website for our members that is updated in real-time and is intended to serve as a “one stop shop” for our members by collating shortage information from both the FDA and American Society of Health System Pharmacists (ASHP). The website also provides information and educational materials about therapeutic alternatives, pertinent updates to clinical guidelines, and best practices for handling shortages. Premier also employs a dedicated team of pharmacists that serve as a resource for members during drug shortages, including assisting members with identifying alternative medication therapies. Finally, Premier has a weekly pharmacy newsletter for members that highlights information about shortages.
- **Failure to Supply Clauses** - Premier includes failure to supply (FTS) clauses in manufacturer contracts to help health systems recoup increased expenditures as a result of purchasing alternate medications at a higher cost during a drug shortage. Historically, FTS clauses have been difficult to enforce as the process to calculate increased expenditures and file claims with manufacturers was manual, complicated, and resource intensive. In 2009, Premier established an automated mechanism to help optimize recovery for drug shortage costs. Using Premier's extensive data capabilities, Premier can determine when an item is not shipped to a member due to a shortage and submits an FTS claim on behalf of the health system to the manufacturer. Premier's FTS program has helped members recoup over \$70 million of increased expenditures associated with drug shortages since its inception.
- **PremierProRx** – For the past eight years, Premier has invested in the PremierProRx program that focuses primarily on sterile injectable products and has 91 National Drug Codes (NDCs) that are currently on the drug shortage list. The PremierProRx program delivers additional value and savings to members by creating stability in the marketplace for both supply and pricing through long-term contracts. Manufacturers for the PremierProRx program are carefully selected based on their record of quality and history of compliance with all regulatory and FDA standards. The PremierProRx program has also contracted directly with active pharmaceutical ingredient (API) manufacturers, for example in the case of cephalosporin, to combat situations where a shortage of API resulted in a downstream drug shortage.
- **Data Mining** – In certain situations, Premier can utilize its robust data capabilities to predict future shortages and alert the FDA and ASHP, as well as proactively implement drug shortage mitigation strategies for its members. Premier also leverages its robust data capabilities to share data, for example most recently with the injectable opioid shortage, with agencies such as the FDA, Drug Enforcement Administration (DEA), Centers for Medicare and Medicaid Services (CMS), and others to underscore the duration and severity of shortages.
- **Interim Solutions** - To help temporarily combat drug shortages while a longer-term strategy is being developed, Premier maintains a network of 503B outsourcing facilities to compound products using current good manufacturing practices (cGMP). Given Premier's commitment to quality and safety, Premier personally inspects every 503B outsourcing facility using a 48-page

long assessment tool that goes above and beyond FDA and state board of pharmacy requirements.

- **Manufacturer Relationships** – A tenet of Premier's strategy to end drug shortages for our members is our positive and long-standing relationships with manufacturers. Premier is able to discuss shortages directly with manufacturers and understand the root cause behind the shortage as well as the manufacturer's remediation strategy. Manufacturers tend to be very transparent with Premier as a trusted partner and forthcoming about Title X reporting requirements, sometimes in advance of formally reporting to the FDA.
- **Allocation** – In shortage situations, Premier utilizes a dynamic allocation process to help ensure member access to an adequate supply of product based upon prior utilization. The allocation process helps to prevent hoarding and helps maintain a health supply chain for as long as possible while pursuing additional mitigation strategies.
- **ProvideGx** – To build upon Premier's eight-year track record of direct contracting for healthcare supplies and the PremierProRx program that is successfully providing uninterrupted access to more than 91 shortage NDCs, Premier has established a new subsidiary company to supply shortage drugs. The goal of the new company, ProvideGx, is to permanently address the drug shortage problem, ensuring continuous access to life-saving products at an affordable price. ProvideGx will also target and supply medications that lack market competition and are at risk for shortages and price spikes.

ProvideGx provides a vehicle for Premier to invest in innovative new business models and partnerships to address drug shortages, including partnering with quality generic drug manufacturers that can supply shortage products, co-funding the development of affordable products that address specific market needs, securing contracts for active pharmaceutical ingredients to ensure a continuous supply, as well as strategic sourcing agreements. ProvideGx has already partnered with five high-quality generic manufacturers to address a targeted pipeline of 60 crucial drugs, and expects to launch its first product next month, pending approval by the U.S. Food and Drug Administration.

ProvideGx is guided by an advisory council of 15 member health systems to help prioritize our efforts based on the need of providers on the front-lines of patient care that are most impacted by drug shortages.

- **Advocacy** - Premier has been, and will continue to be, an active voice in advocating for legislative and regulatory changes to help combat drug shortages. Recent examples of Premier's leadership in this area include:
  - Competitive Generic Therapy (CGT) Pathway – Premier was a major proponent of the CGT pathway and advocated for its inclusion in the Food and Drug Administration Reauthorization Act (FDARA)<sup>1</sup> legislation. Premier applauds the FDA for expeditiously implementing the pathway and approving the first product under the pathway in September of 2018.

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<sup>1</sup> Pub.L. 115-52

- Injectable Opioid Shortages – During the recent (and ongoing) injectable opioid shortage, Premier was able to proactively identify that a major shortage was about to occur and alert the FDA and ASHP. In addition, Premier worked tirelessly to identify alternate and able manufacturers of the products and provide monthly data to the DEA to demonstrate the severity of the shortage. However, communication with the DEA hit a roadblock as the DEA was unwilling to reallocate quota to able manufacturers. Premier was able to apply congressional pressure to the DEA that ultimately resulted in the DEA agreeing to reallocate quota to able manufacturers. To date, the severity of the shortage has eased, although it is still a major shortage impacting providers.
- FDASIA Title X – Premier was a major proponent of the drug shortage notification requirements and advocated for their inclusion in the Food and Drug Administration Safety and Innovation Act (FDASIA)<sup>2</sup> legislation. Premier believes these provisions have been impactful but can be strengthened to increase their impact in mitigating shortages.

While Premier has made significant progress in reducing the impact of drug shortages for our members, we have not been able to eliminate them. More needs to be done and ***Premier is continuing to grow and evolve our drug shortage strategy to eliminate drug shortages once and for all.***

## **II. Root Causes of Drug Shortages Are Multifactorial and Solutions Must be Attainable, Practical, and Sustainable**

Premier has worked extensively with its members to identify the root causes of drug shortages and develop sustainable solutions to address them. ***Given that there is no single cause of drug shortages and often multiple contributing factors lead to a drug shortage, there is also no single solution to address drug shortages.*** The FDA will need to implement multiple solutions targeting the various causes of drug shortages to truly address the situation and eliminate drug shortages. The following outlines several root causes of drug shortages that Premier has identified including examples of each as well as sustainable solutions to address each root cause. Many of the sustainable solutions can be implemented immediately under the FDA's current authority, while others may require legislative or regulatory action, as well as inter-agency collaboration, to implement.

- **Entry of a Low Cost Competitor** – In recent years, the entry of a low cost competitor to the marketplace has resulted in a ripple effect disrupting the supply chain ultimately resulting in a drug shortage. The following exhibits demonstrate two common examples of how the entry of a low cost competitor has resulted in a drug shortage.

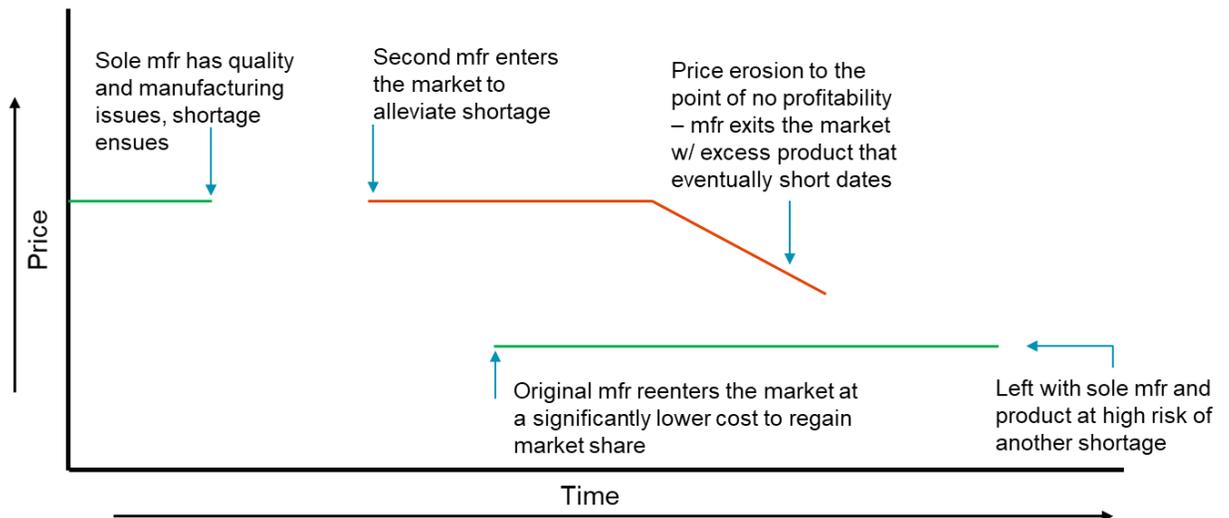
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<sup>2</sup> Pub.L. 112-144

*Exhibit A: Entry of a low cost competitor results in others exiting the market*



*Exhibit B - Reentry of a low cost competitor results in others exiting the market and hesitant to help mitigate future shortages*



Solutions to address the ripple effect caused by the entry of a low cost competitor hinge on the need to decrease barriers to entry, namely the time and cost to enter the marketplace, while maintaining the quality and safety of the product. Specifically:

- **Improve regulatory efficiency during drug shortages:** During a drug shortage, a key factor in determining the duration and severity of the shortage is how soon an alternate manufacturer can enter the marketplace to help alleviate the shortage. The FDA plays a key role in advancing abbreviated new drug applications (ANDAs) through the process, and there are opportunities for the FDA to improve regulatory efficiency during drug

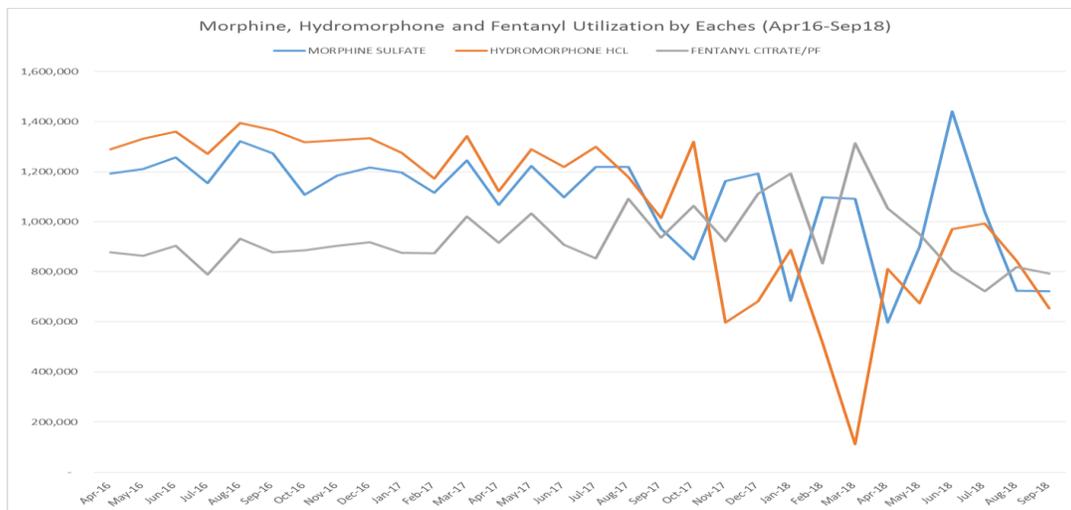
shortages to help decrease manufacturer burden and increase predictability. Specific examples include:

- ***Expedite review of newly submitted ANDAs*** by beginning review of the application while awaiting submission of the 6-month stability data. A parallel review process can decrease the amount of time needed to review an ANDA and therefore help bring a competitor to market sooner.
- ***Expedite facility inspections and review of manufacturing changes*** that would help mitigate or prevent a drug shortage.
- ***Appoint a senior-level drug shortage navigator*** to coordinate with each manufacturer who submits an ANDA for a drug shortage product. This position should reside within the Office of Generic Drugs (OGD) and responsibilities would include shepherding drug applications through the internal review and approval processes at FDA and maintaining communication with the manufacturer. The senior-level drug shortage navigator should also have the authority to request expedited review of ANDAs or inspections of facilities to help prevent or mitigate a drug shortage.
- ***Expedite new drug applications (NDAs) for shortage drugs in situations where a NDA is preferred over an ANDA*** to help improve the formulation, dosage form, delivery system, or safety of a shortage drug.
- **Create incentives for manufacturers to enter the market for low revenue products:**
  - ***Develop a mechanism for reimbursing generic drug user fee act (GDUFA) fees to manufacturers who submitted an ANDA for a shortage drug after a specified period of successfully entering the market.*** The increased GDUFA fees, and newly created program fees for generic manufacturers, are often a barrier to entry as the potential revenue on a shortage drug does not outweigh the cost of filing fees. A reimbursement mechanism, in lieu of waiving or reducing fees upfront, will help ensure market entry and provide incentive for manufacturers to ensure a quality manufacturing process. A reimbursement mechanism will also help deter manufacturers from purposely waiting until a drug is in shortage to file an ANDA in order to take advantage of a waived or reduced GDUFA fee.
  - ***Address the loophole in the Competitive Generics Therapy (CGT) pathway so that the first approved manufacturer is guaranteed exclusivity.*** Currently, the first manufacturer is only granted exclusivity if it begins marketing the product before the FDA approves a second manufacturer, something that can occur days after the first approval. A manufacturer needs affirmation that as the first manufacturer it will have a period of exclusivity and enough time to bring its product to market upon approval.

- **Create pathways for interim solutions to help address drug shortages:**
  - **Expand the FDA drug shortage list** to include regional shortages and shortages based upon dosage or administration form, similar to the criteria used for the ASHP drug shortage list. A more comprehensive list will allow the temporary use of 503B outsourcing facilities to mitigate shortages while a longer-term and more permanent strategy is being developed.
- **Quality and Manufacturing Issues** - In a market with few manufacturers, when one manufacturer encounters quality or manufacturing issues and exits the market for an extended period, downstream pressure is placed on the remaining manufacturers to ramp up supply and fill the market void. In certain scenarios, external factors prevent other manufacturers from ramping up such as capacity restrictions and DEA quota allocations, resulting in drug shortages.

As depicted in the following exhibit, a nationwide acute shortage of several injectable opioids that are critical for patient care occurred at the end of 2017 due to a single manufacturer encountering quality and manufacturing issues at several of their plants. The issue was further compounded by a lack of immediate coordination between the FDA and DEA to release additional quota to manufacturers who were able and willing to ramp up production to help mitigate the impact of the shortage.

*Exhibit C - The ongoing shortage of injectable narcotics has been a major patient safety concern for health systems*



Solutions to address quality and manufacturing issues include:

- **Improve the regulatory violation process for cGMP by shortening turnaround times** and improving and standardizing processes for FDA reviews to identify problems prior to shutting down facilities. More rapid review of corrective actions taken by manufacturers would help moderate fluctuations.

- **Improve coordination within various FDA offices** - such as ORA, ODS, OGD – to understand downstream impact of cGMP violations or manufacturer shutdowns on drug shortages and proactively develop mitigation strategies.
- **Develop a list of critical medications** that are needed for patient care in case of an emergency, natural disaster, or other urgent situation. Require manufacturers of critical medications to report where such medications are manufactured so the FDA can use mapping technology to account for potential impact of natural disasters, facility shutdowns, and other situations on drug shortages and appropriately mitigate.
- **Appoint an inter-agency, White House-level ‘Drug Shortage Point Person’** to improve cross-agency coordination on issues related to drug shortages, such as the ongoing shortage of generic injectable opioids. A Drug Shortage Point Person will streamline needed communication and cooperation among stakeholders such as the HHS, DEA, FEMA, VA, CMS, FDA, DOD and other stakeholders.
- **API or Raw Materials Shortages** - Over 80 percent of API and raw materials required for drug manufacturing are manufactured overseas.<sup>3</sup> The heavy reliance on foreign manufacturing of API and raw materials results in downstream drug shortages when a foreign manufacturer fails to meet cGMP or exits the market. In addition, the extent and duration of API or raw material shortages is unknown and results in downstream impact on hoarding and the gray market. Furthermore, the Chinese Blue Sky Initiative is resulting in API and raw material manufacturers being required to either halt production or shut down resulting in concerns that this may further exacerbate shortages, and may result in increased shortages for oral solid dosage forms. Finally, new tariffs are also putting pressure on foreign manufacturers of raw materials and may lead to entities exiting the market resulting in downstream drug shortages.

For example, the recent valsartan recall was due to an impurity with the API and almost all manufacturers relied on a single API manufacturer, resulting in a major shortage. In addition, the recent injectable opioid shortages were exacerbated by an inability of the manufacturer to acquire the raw materials necessary for the injector.

Solutions to address API or raw material shortages include:

- **Create incentives to encourage on-shore manufacturing** of API and raw materials.
- **Extend FDASIA Title X reporting requirements to API and raw material manufacturers**, including strengthening the reporting requirements to include disclosure of the problem resulting in the shortage, the extent of the shortage, and the expected duration of the shortage to help understand the downstream impact on drug shortages.
- **Prioritize FDA reinspection of facilities that are sole manufacturers of API or raw materials** when cGMP or other quality issues are identified. Develop action plans and work closely with manufacturers to prevent facility shutdown and downstream drug shortages.

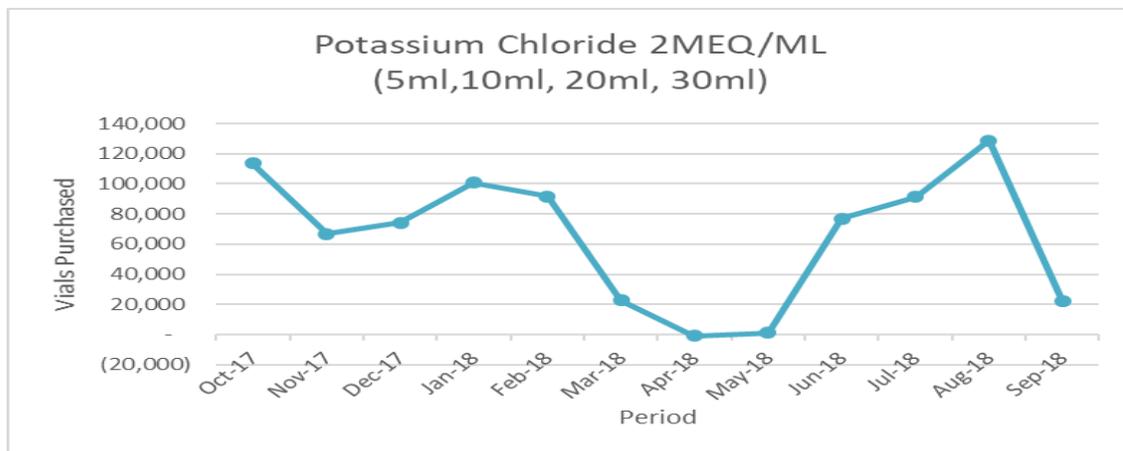
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<sup>3</sup> Source: <http://www.consumerreports.org/cro/news/2014/04/are-generic-drugs-made-in-india-safe/index.htm>

- **Maintain a directory of API sources** used by manufacturers to expedite downstream notification and recall procedures if there is an issue with an API manufacturer and implementation of drug shortage mitigation strategies.
- **Change in API Requirements** - Updates to United States Pharmacopeia (USP) monographs will often result in changes to API requirements. The changes to API requirements are typically effective immediately, resulting in shortages as manufacturers must suspend manufacturing using the old API and await new API, which can take several months, to resume manufacturing.

For example, as depicted in the following exhibit, changes to the USP monograph for potassium chloride resulted in an immediate shortage that lasted approximately six months until the new API was available and manufacturers could begin production of finished dosage forms again.

*Exhibit D - Changes to API requirements for potassium chloride resulted in a shortage*

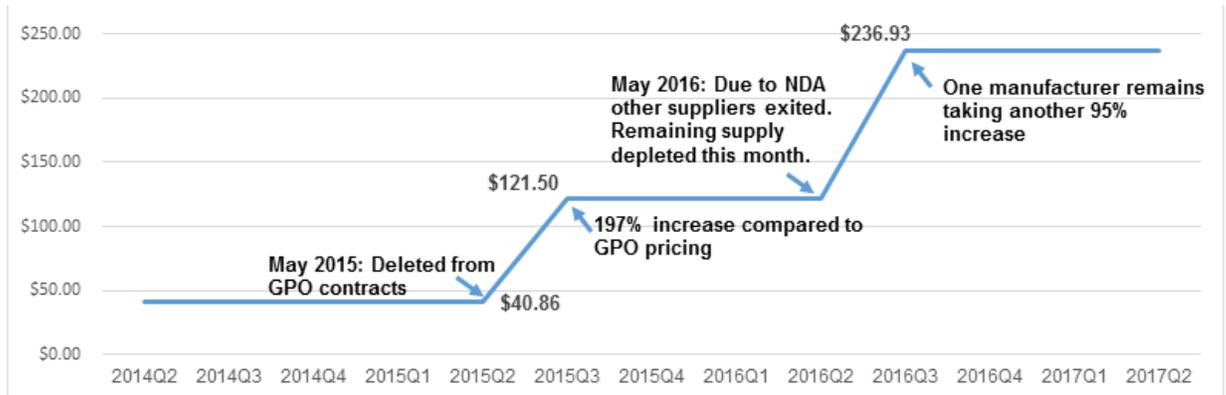


Solutions to address changes in API requirements include:

- **Permit a phase-in period** of at least 6-12 months for changes in API requirements where old API can continue to be used until new API is available. An exception should exist if the prior API was associated with harm or adverse events necessitating the need for a change in API requirements.
- **DESI Drugs** - Drug Efficacy Study Implementation (DESI) drugs are often at-risk for shortages as legacy manufacturers are required to exit the marketplace abruptly and typically only one or two manufacturers reenter the marketplace under the new requirements. During a DESI drug shortage, it is difficult for new manufacturers to enter the marketplace given the need to prove efficacy, an expensive and timely process for manufacturers, often resulting in significant price increases to offset the cost of entering the marketplace.

For example, as depicted in the following exhibit, potassium chloride experienced a significant increase in price due to the DESI drug pathway. In addition, it created a sole source situation that placed the drug at great risk for shortage.

*Exhibit E – Potassium chloride experienced price spikes as a result of the DESI drug pathway*



Solutions to address the DESI drug pathway include:

- Refine the “unapproved drugs” compliance policy initiative to ***permit the use of real-world evidence to demonstrate efficacy.***
- ***Announce in the Federal Register the first NDA submission for a DESI drug*** and solicit additional NDA submissions. Allow for 18 to 24 months after the Federal Register notice before requiring current manufacturers to exit the market. This would help provide stability in the market, mitigate threats of a shortage, and allow enough time for other manufacturers to consider submitting a competing NDA.
- ***Lower, or remove altogether, NDA filing fees for DESI drugs*** to encourage manufacturers to enter the market as high NDA fees are often a deterrent, or not feasible, for generic manufacturers.
- ***Streamline and simplify filing requirements for DESI drugs***, making the application more akin to an ANDA, or at most a 505(b)(2) paper NDA. Generic manufacturers are often not familiar with the NDA process and would be more inclined to submit applications if they resembled a traditional ANDA.
- ***Expedite review of competing NDAs to encourage competition*** in the marketplace and mitigate potential shortages due to reliance on a single manufacturer.
- **Gray Market** - During drug shortages, shortage drugs are often sold at exorbitant prices by unauthorized vendors. The gray market creates patient safety concerns as the products may not have been stored properly and therefore the integrity of the product cannot be confirmed. Recently, several PremierProRx products have been found in the gray market with significant price increases:
  - Ondansetron - 1642% price increase
  - Naropin – 291% price increase
  - Rocuronium – 691% price increase

Solutions to address the gray market include:

- **Timely implementation of the Drug Quality and Security Act (DQSA) track and trace requirements.**
- **Require distributors to implement checks and balances systems for shortage drugs,** similar to suspicious order monitoring requirements for controlled substances, to identify potential diversion of shortage drugs to the gray market.
- **Promote the reporting of gray market offers to the FDA Office of Criminal Investigations** and share reported incidents with the Federal Trade Commission (FTC).
- **Implementation of CMPs** for entities selling products to the gray market.
- **Hoarding** - During drug shortages, hoarding often occurs as providers are concerned about having adequate supply of products and do not know the duration and severity of the shortage. This further exacerbates shortages as product is not available in the supply chain for other entities and often results in product being returned as unused or expired in lieu of being used for patient care.

Solutions to address hoarding include:

- **Strengthen FDASIA Title X reporting requirements** to include disclosure of the problem resulting in the shortage, the extent of the shortage, and the expected duration of the shortage to help alleviate provider concerns and discourage hoarding.
- **Collate and make publicly available information about the severity of the shortage, expected duration, and mitigation strategies** (e.g. remediation efforts by manufacturer, entry of additional manufacturers, potential importation, etc.). This information should be provided in a uniform manner, be easily found on the FDA website, and updated in a timely and consistent manner (e.g. monthly).

### III. Robust Research Is Needed to Quantify the Clinical and Economic Impact of Drug Shortages

There is little research documenting the clinical and economic impact that drug shortages have on patient outcomes and healthcare expenditures. One of the only studies to date that looked at the total cost of care and patient impact of drug shortages utilized the Premier Healthcare Database (PHD) and found that the 2011 shortage of norepinephrine was significantly associated with increased mortality among patients with septic shock.<sup>4</sup> Understanding the clinical and economic impact of drug shortages is integral to understanding the true impact of shortages and also deciphering what appropriate incentives or offsets should be to help eliminate shortages. Therefore, **funding should be allocated to study the clinical and economic impact of drug shortages on patient outcomes and healthcare expenditures.** Research should be multi-faceted and encompass retrospective, prospective, quantitative, and qualitative studies.

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<sup>4</sup> Vail, Emily, Gershengorn, Hayley, Hua, May, Walkey, Allan, Rubinfeld, Gordon & Wunsch, Hannah. (2017). Association Between US Norepinephrine Shortage and Mortality Among Patients With Septic Shock. JAMA. 317.DOI: 10.1001/jama.2017.2841

The Premier Healthcare Database (PHD) is one of the most comprehensive electronic healthcare databases containing robust data on more than 108 million inpatient admissions and 765 million outpatient encounters for over 208 million unique patients. The PHD has been leveraged by hospitals, health systems, academia, pharmaceutical manufacturers, CDC, CMS, NIH, and others to use real-world data to conduct evidence-based and population-based analyses of drugs, devices, other treatments, disease states, epidemiology, resource utilization, healthcare economics and clinical outcomes. **Premier welcomes the opportunity to discuss how the Premier Healthcare Database and its dedicated staff of skilled professionals trained in medicine, pharmacy, epidemiology, public health, economics and statistics can partner with the FDA to support studying the clinical and economic impact of drug shortages.**

#### **IV. A List of Critical Drugs Should be Developed Through a Consensus Development Process Spearheaded by a Private Entity**

As previously discussed, **a list of critical medications should be developed** that are needed for patient care in case of an emergency, natural disaster, or other urgent situation. Medications on the critical drug list would be subject to additional reporting requirements by manufacturers regarding exactly where these medications are manufactured so the FDA can use mapping technology to account for potential impact of natural disasters, facility shutdowns, and other situations impacting drug shortages and appropriately mitigate.

In lieu of FDA creating the list of critical drugs, **Premier recommends FDA endorse a neutral third-party to work collaboratively with stakeholders representing pharmacy, providers, manufacturers, patients, and others to develop the list of critical drugs using a consensus-based process.** Having a broad spectrum of representation and a neutral third-party lead the consensus development process will allow those on the front lines of patient care to directly impact the list of critical medications. In addition, having a neutral third-party serve as the convener will also allow for frequent updates to the list of critical medications as needed and avoid differences between a FDA developed list and a privately developed list, such as the case with FDA vs ASHP drug shortage lists.

To help begin the process, Premier's National Pharmacy Committee and Pharmacy Affairs Subcommittee reviewed work to date on the development of a critical drug lists by comparing and cross-referencing work from the Healthcare and Public Health Sector Coordinating Council, World Health Organization List of Essential Medications, Advanced Cardiac Life Support (ACLS), Pediatric Advanced Life Support (PALS), CDC National Strategic Stockpile, and others. **The following exhibit is a preliminary list of critical drugs as recommended by Premier for further consideration and refinement.**

*Exhibit F – Draft List of Critical Medications*

| <b>Emergent Situation/Class</b> | <b>Critical Drugs</b>  |
|---------------------------------|--|
| Anesthetics                     | Local, Inhaled, Propofol   |
| Pre-operative/sedative          | Midazolam, lorazepam, emergency syringes, morphine, hydromorphone, fentanyl                    |
| Palliative care                 | Haloperidol, metoclopramide, ondansetron   |
| Anaphylaxis/allergy             | Diphenhydramine, methylprednisolone, hydrocortisone, inhaled bronchodilators                   |
| Antidotes                       | Expert Consensus Guidelines for Stocking of Antidotes in Hospitals That Provide Emergency Care |

|  |   |
|--|---|
|  | <ul style="list-style-type: none"> <li><a href="https://www.annemergmed.com/article/S0196-0644(17)30657-1/fulltext">https://www.annemergmed.com/article/S0196-0644(17)30657-1/fulltext</a></li> </ul>   |
| ACLS/PALS  | <a href="https://acls-algorithms.com/acls-drugs/">https://acls-algorithms.com/acls-drugs/</a>   |
| Anticonvulsants  | Midazolam, diazepam, lorazepam, phenytoin, VPA, phenobarb, mag sulfate  |
| Anti-infectives  | Vancomycin, zosyn, cefazolin, doxy, bactrim refer to critical care guidelines for drugs to be administered within an hour of sepsis   |
| Anti-tuberculosis  | Rifampin, INH   |
| Anti-fungal  | Fluconazole   |
| Anti-influenza   | Oseltamivir   |
| Oncology   | Sole therapy, single source generics  |
| Anti-anemia  | Multivitamin, folic acid  |
| Antithrombotic   | Enoxaparin, heparin, desmopressin   |
| Blood/blood components   | Immune globulins, albumin, FFP, KCentra   |
| Anti-arrhythmic  | Verapamil, nitroglycerin, diltiazem   |
| Anti-hypertensive  | Labetalol, hydralazine, furosemide, bumetanide  |
| Vasopressors   | Norepinephrine, epinephrine, dopamine, dobutamine   |
| Endocrine  | Insulin, Potassium iodide, Levothyroxine  |
| Neonate  | Caffeine citrate, ibuprofen lysine, surfactant  |
| Electrolytes   | Normal saline, 3% hypertonic saline, potassium chloride, calcium chloride, calcium gluconate, sodium bicarbonate, sterile water, sodium phosphate, potassium phosphate  |
| TPN  | Amino Acids   |
| <b>Guidelines that call for critical, time-sensitive medications</b> |   |
| Stroke   | Alteplase <a href="https://www.acc.org/latest-in-cardiology/ten-points-to-remember/2018/01/29/12/45/2018-guidelines-for-the-early-management-of-stroke">https://www.acc.org/latest-in-cardiology/ten-points-to-remember/2018/01/29/12/45/2018-guidelines-for-the-early-management-of-stroke</a> |
| Myocardial infarction  | Tenecteplase (+ others already mentioned above)<br><a href="https://academic.oup.com/eurheartj/article/39/2/119/4095042#107689883">https://academic.oup.com/eurheartj/article/39/2/119/4095042#107689883</a>  |
| Sepsis   | Antibiotic therapy<br><a href="https://academic.oup.com/cid/article/65/9/1565/3966709">https://academic.oup.com/cid/article/65/9/1565/3966709</a>   |
| Others?  |   |

Exhibit G – Sample Criteria to Determine List of Critical Medications<sup>5</sup>

**Drug Vulnerability Assessment Risk Tool : Theoretical**

| DRUG NAME | Population   |                     |             | Timing                                  | Raw Materials                     | Vendors  | Manufacturing                     | SCORE |
|-----------|--------------|---------------------|-------------|---|-----------------------------------|--|-----------------------------------|-------|
|           | Pre-Hospital | Acute Care Facility | OP Facility | 1 = 4-8 Hrs<br>2 = > 1 Hr<br>3 = < 1 Hr | 1 = Domestic<br>2 = International | 1 = > 2 Vendors<br>2 = 2 Vendors<br>3 = 1 Vendor | 1 = Domestic<br>2 = International |       |
|           |              |                     |             |   |                                   |  |                                   | 0     |
|           |              |                     |             |   |                                   |  |                                   | 0     |
|           |              |                     |             |   |                                   |  |                                   | 0     |
|           |              |                     |             |   |                                   |  |                                   | 0     |

<sup>5</sup> Work product of the Healthcare and Public Health Sector Coordinating Council

***Premier welcomes the opportunity to work with FDA and additional stakeholders to continue to refine the list of critical medications.***

## **V. Conclusion**

In closing, the Premier healthcare alliance appreciates the opportunity to submit comments on FDA-2018-N-3272. Premier looks forward to working with the FDA to eliminate drug shortages and the downstream impact to health systems and patient care.

If you have any questions regarding our comments or need more information, please contact Soumi Saha, Senior Director of Advocacy, at [soumi\\_saha@premierinc.com](mailto:soumi_saha@premierinc.com) or 202-879-8005.

Sincerely,

A handwritten signature in black ink, appearing to read "Blair Childs". The signature is fluid and cursive, with a large initial "B" and "C".

Blair Childs  
Senior Vice President, Public Affairs  
Premier Inc.