

**CASE AND COMMENTARY: PEER-REVIEWED ARTICLE**

**Which Drugs Should Be on the Essential Medicines List?**

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**Abstract**

The World Health Organization (WHO) published its first Essential Medicines List (EML) in 1977, and it is updated biennially. One might reasonably think drugs on the EML are there because they are critical to effective, evidence-based patient care and intervention. One might not reasonably guess, however, that a particular drug's supply chain vulnerabilities that make it a shortage risk would contribute to a drug's listing on the EML. This commentary on a case first describes why the WHO makes the EML and suggests reasons why it might be important to consider a drug's shortage risk when revising and updating it. This commentary also suggests how distinguishing "essential" drugs from "vulnerable" drugs could bolster supply chain resiliency and mitigate drug shortages' disruptions to patient care.

**Case**

Dr C is an oncologist at an academic health center who has practiced for 15 years. Dr C's patient is JJ, a child newly diagnosed with cancer. Dr C has now received a second notice from the hospital pharmacy that a standard chemotherapeutic intervention drug, cisplatin, for the treatment of JJ's cancer is in short supply. Dr C starts planning ahead and wonders whether and how to adapt JJ's—and possibly her other patients'—care plan, perhaps by omitting at least one of JJ's chemotherapy cycles or by limiting other patients' access to the drug by modifying their treatment plan so that JJ's care plan is not altered.<sup>1,2</sup>

**Commentary**

Suppose Dr C has faced this issue several times before, as shortages of several oncology medications have persisted for decades,<sup>3</sup> and remembers the impacts on patients—and the impacts on *her* of not being able to provide the best care for her patients—of the shortages of various oncology drugs. She therefore decided to look into the reasons why medicines critical to her patients' treatment regimens are often unavailable. The exact reasons were difficult to find, but she learned that a major reason for shortages in the past was supply chain issues, including problems with manufacturing processes, increased demand, and shortages of the necessary active pharmaceutical ingredients. In the end, though, all that she knows is that the supply chains for numerous cancer drugs need strengthening. They should not be bending or breaking this frequently, to the detriment of her patients, who are among the sickest in

her hospital and for whom timely treatment with the most effective therapies is absolutely essential.

Dr C's analysis of data revealed that pediatric oncology drugs have a 90% higher likelihood of a shortage event than the average drug and have few or no therapeutic alternatives.<sup>4</sup> These treatment shortages lead to delays in chemotherapy, changes in treatment regimens, missed treatments, complicated clinical research, increased risk of medication errors, adverse outcomes, and even patient death.<sup>5</sup> Dr C has also read news articles about the federal government and Congress taking action on drug shortages. A lot of what she has read has been about ensuring the availability of drugs deemed essential in times of crisis and medical countermeasures to ensure reliable and resilient supply chains. The focus of efforts to date seems to be on identifying and preventing shortages of critical medicines during public health emergencies, natural disasters, or geopolitical threats, rather than on what she and her patients experience every day. One article linked to essential and critical products lists recently developed by federal agencies, but Dr C found that many of the drugs used in the treatment of her patients were not included on the lists. She struggles with this focus and approach, as it sends a message that the cancer drugs that she relies on to treat her patients, many of whom are children, are not essential or as high of a priority as other drugs or have supply chains that are not worth investing in and strengthening. Dr C understands the need for the nation to be able to have critical medicines during public health emergencies but believes her patients should not be left behind in these efforts to prevent or mitigate drug shortages and ensure medicine supply chain resiliency.

While current research is evaluating strategies to [manage these drug shortages](#),<sup>6</sup> better, more enduring solutions are required to ensure that all patients have access to the medicines they need. In what follows, we examine differing policies and explore better ways to balance public health needs in times of uncertainty or crisis and to ensure an appropriate supply of critical medicines, as well as medicines with vulnerable supply chains, that are crucial to the everyday lives and well-being of patients.

### **What's "Essential"?**

The World Health Organization (WHO) published its first Essential Medicines List (EML) in 1977, and the first Essential Medicines List for Children was published in 2007.<sup>7</sup> These lists are updated every 2 years and "aim to address global health priorities, identifying the medicines that provide the greatest benefits, and which should be available and affordable for all"<sup>8</sup> and are "intended to be available in functioning health systems at all times, in appropriate dosage forms, of assured quality and at prices individuals and health systems can afford."<sup>9</sup> WHO EMLs guide the development of country-level EMLs, which influence national formularies, prescribing and practice guidelines, and price negotiation and procurement mechanisms,<sup>8</sup> although considerable variation exists in the medicines included on country-level EMLs.<sup>10</sup> The creation of EMLs was historically considered a public policy intervention to prevent and mitigate drug shortages by identifying those drugs that are vital to addressing the health care needs of populations and by guiding governments' and purchasers' prioritization of medicines and interventions necessary to support public health and encourage favorable health outcomes.

How "essential medicines" are defined, what drugs are included on EMLs, and the stated purpose of EMLs are critical questions, as they are directly linked to and serve as the impetus for numerous policy efforts and initiatives to improve medicine supply chain

resiliency, including investments in innovation, stockpiling considerations, and trade decisions, which may ultimately affect the availability or accessibility of these medicines to clinicians and patients.<sup>11,12,13,14,15,16,17</sup> While the WHO EMLs were referenced as a starting point for such lists, country-level EMLs have evolved to include critical drugs needed for emergency response and for saving and preserving life.<sup>11,18</sup> The onset of the SARS-CoV-2 public health emergency and its impact on pharmaceutical supply chains brought the concept of essential medicines into sharp focus.

### **Policies Related to Essential Medicines**

Two recent supply chain executive orders issued in the United States each had different aims, which affected the focus and content of critical product lists that the US Food and Drug Administration (FDA) and the US Department of Commerce (Commerce) put forward. The first, Executive Order on Ensuring Essential Medicines, Medical Countermeasures, and Critical Inputs Are Made in the United States (EO 13944), “directed the ... FDA to identify a list of essential medicines, medical countermeasures and critical inputs that are medically necessary to have available at all times in an amount adequate to serve patient needs and in the appropriate dosage forms.”<sup>19</sup> The stated goal of the list was “to ensure the American public is protected against outbreaks of emerging infectious diseases, such as COVID-19, as well as chemical, biological, radiological, and nuclear threats.”<sup>19</sup> Previously, the FDA did not maintain this type of EML. As a result of EO 13944, the FDA published a list of 227 drug and biological product essential medicines and medical countermeasures, as well as 96 device medical countermeasures.<sup>20</sup> The second, Executive Order on America’s Supply Chains (EO 14017), focused and expanded on the potential and real impacts of pandemics and other biological threats, cyberattacks, climate shocks and extreme weather events, terrorist attacks, geopolitical and economic competition, and other conditions bearing on manufacturing capacity and supply chain resiliency in multiple industry sectors.<sup>21</sup>

Subsequent to EO 14017, the US Department of Health and Human Services (HHS) directed a review of the FDA EML and recommended that 50 to 100 most critical drugs from the FDA list be available at all times for US patients because of their clinical necessity and lack of therapeutic redundancy (Critical Drug List). The resulting list was narrowed down to 86 critical medicines for acute patient care.<sup>12</sup> Also fulfilling the intent of EO 14017, Commerce developed a list of critical goods, including medicines, intended to “serve as a tool to facilitate ongoing targeted analysis of trade data and the evaluation of policies to strengthen these supply chains.”<sup>22</sup> Because of the different objective of the Commerce list, the drugs on this list differ from those included on the FDA list or the HHS Critical Drug List. For example, only one chemotherapeutic drug, cyclophosphamide, is included on both the FDA list and the Critical Drug List, but it does not appear on the Commerce list.

Therefore, what are considered essential medicines—and the purposes of EMLs—if not properly defined, can leave countries, regions, or the world unprepared or underprepared or cause initiatives and finite resources to be potentially misdirected. For example, if EMLs only focus on medicines critical to responding to public health **emergencies or national disasters**, then countries may not be adequately prepared to prevent or mitigate drug shortages of more commonly used drugs that are life-supporting, life-sustaining, or intended for use in the treatment of a debilitating disease or condition, including pediatric oncology drugs. Medicines with the most vulnerable supply chains that have the highest likelihood of breaking in the event of an unexpected shock—vulnerable medicines—should be considered an integral part of the exercise to

establish EMLs. If the evaluation of essential medicines is based not only on clinical importance and demand indicators, but also on their supply chain vulnerabilities, then domestic, regional, and global supply chain resiliency efforts can be better informed, designed, and implemented—resulting in better outcomes for patients.

### **Incorporating Supply Chain Risk**

There is no common definition of or approach to EMLs within the United States, across countries and regions, and globally. However, there is a common shortcoming of EMLs generally: a medicine's risk of shortage, or supply chain vulnerability, is not adequately factored into whether a medicine is included on the list. A disconnect between medicines identified as being "essential" and medicines in short supply has been reported: of the 276 drugs that were in short supply in 2021 in the United States,<sup>20,23,24</sup> only 86 were on the FDA Essential Medicines, Medical Countermeasures, and Critical Inputs List.<sup>20</sup>

Medicines with vulnerable supply chains can also be among those already included on an EML, but there must be a broader recognition that medicines with vulnerable supply chains can cause patient harm and should be factored into how products are considered for inclusion on essential or critical medicines lists. Both demand-side analysis and supply-side analysis are needed to prioritize medicines and target policy interventions to prevent and mitigate drug shortages and improve medicine supply chain resiliency, including for essential medicines and vulnerable medicines. Factoring vulnerable medicines into the conversation can potentially help bolster the visibility and supply of those medicines, which have been notoriously present on drug shortage lists and are needed to support patient care—and without which public health crises may emerge.

### **Conclusion**

When drugs are in short supply, clinicians must often make **difficult decisions** about how to treat their patients, given limited or inconsistently available options, and these decisions can potentially result in suboptimal outcomes. Clinicians are not expected to understand the nuances of the supply chains that provide the resources they require to treat their patients, but it can be useful to understand EMLs, how they are developed, and their implications for the availability and accessibility of medicines. Considering both essential medicines and vulnerable medicines will enable a more comprehensive strategy for preparedness initiatives, minimizing drug shortages, and bolstering supply chain resiliency—and will ultimately ensure that more patients' medicine needs are met.

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