The Security of America's Medical Product Supply Chain: Considerations for Critical Drugs and Devices: Proceedings of a Workshop in Brief (2021)

DETAILS

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Proceedings of a Workshop

IN BRIEF

April 2021

The Security of America's Medical Product Supply Chain

Considerations for Critical Drugs and Devices

Proceedings of a Workshop—in Brief

Recent disasters and health emergencies, including the COVID-19 pandemic, have increased recognition of the fragility of the U.S. medical supply chain and underscored the need to explore potential policy, regulatory, and systems solutions to prevent and mitigate the impacts of shortages on public health, national security, and patient care. Section 3101 of the Coronavirus Aid, Relief, and Economic Security (CARES) Act, signed into law on March 27, 2020, directed the Secretary of the U.S. Department of Health and Human Services (HHS) to enter into an agreement with the National Academies of Sciences, Engineering, and Medicine (the National Academies) to establish an ad hoc committee to examine the security and resilience of the U.S. medical product supply chain.[1] Specifically, the committee was asked to assess and evaluate the impact of U.S. dependence on critical drugs and devices sourced or manufactured outside of the United States and provide recommendations to improve the resilience and address the vulnerabilities of the medical supply chain.

On December 1 and 2, 2020, the Committee on Security of America's Medical Product Supply Chain held a 2-day virtual public workshop focused on assessing lists of critical and essential medical products.[2] The committee sought to conceptually explore how critical and essential medical product lists are developed and used in practice.

This Proceedings of a Workshop—in Brief highlights key points made by workshop participants during the presentations and discussions. It is not intended to provide a comprehensive summary of information shared during the workshop. The statements in this proceedings reflect the knowledge and opinions of individual workshop participants and have not been endorsed or verified by the National Academies or the committee; they should not be construed as reflecting the consensus of the workshop participants, the committee, or the National Academies. The committee's consensus study report will be available in 2022.

KEY CONSIDERATIONS FOR ESTABLISHING A RESILIENCY FRAMEWORK FOR CRITICAL MEDICAL PRODUCTS

The workshop began with an exploration of broad considerations around establishing a resiliency framework for critical medical products and how these considerations relate to demand surge and supply shocks, the severity of impacts on an individual affected by a shortage versus the number of people potentially impacted by a shortage, outcome measures that matter to end users, and products that are most at risk. Panelists included Stephen Schondelmeyer,

[1] More information on H.R. 748—CARES Act is available at https://www.congress.gov/bill/116th-congress/house-bill/748/text?q=%7B%22search%22%3A%5B%22coronavirus+aid+relief+and+economic%22%5D%7D&r=2&s=1 (accessed February 12, 2021).

[2] The web page for the second meeting and public workshop of the National Academies of Sciences, Engineering, and Medicine's Committee on Security of America's Medical Product Supply Chain is available at https://www.nationalacademies.org/event/12-01-2020/security-of-americas-medical-product-supply-chain-committee-meeting-2-and-public-workshop (accessed February 12, 2021).

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professor in the Department of Pharmaceutical Care & Health Systems, College of Pharmacy, University of Minnesota; James Lawler, associate professor, Department of Internal Medicine; director, International Programs and Innovation, Global Center for Health Security; and director, Clinical and Biodefense Research, National Strategic Research Institute, University of Nebraska Medical Center; Khatereh Calleja, president and chief executive officer (CEO), Healthcare Supply Chain Association; Nathaniel Hupert, associate professor of population health sciences and medicine, Cornell University, and co-director, Cornell Institute for Disease and Disaster Preparedness; and Christopher Liu, director, Department of Enterprise Services, Washington State. The panelists discussed how a product can be considered "critical" by virtue of being medically essential or logistically vulnerable. Box 1 details key takeaways from this session.

Schondelmeyer, co-principal investigator of the Resilient Drug Supply Project at the Center for Infectious Disease Research and Policy (CIDRAP), University of Minnesota, stated that this project aims to establish a drug supply, shortage, and tracking framework and build a real-time platform to monitor, predict, and prevent critical supply failures.[3] Since 2018, CIDRAP has been compiling lists of critical acute and chronic drugs (described in the next section). Each drug's supply chain is being mapped from active pharmaceutical ingredient (API) to patient—including countries of origin at each link—to assess the root causes of shortages and conduct risk assessment. He stated that, according to limited data available, much of the precursor materials to produce critical drugs (e.g., antibiotics, analgesics, anti-epileptics, insulin, heparin) come from China. India, which provides a large proportion of finished products to the U.S. market,

BOX 1
KEY POINTS FROM SESSION ONE DISCUSSION[a]

- **Highlighting issues from the COVID-19 pandemic**
  - Vulnerabilities to shortages and disruption in the current just-in-time medical supply chain (Schondelmeyer)
  - The need for strong national leadership (Schondelmeyer)
  - The potential value of multi-institutional resource management and distribution systems across the local, state, and federal levels (Hupert)
- **Identifying and addressing critical systems needs**
  - Preemptively modeling product criticality in different scenarios (Hupert)
  - Diversifying supply chains for active pharmaceutical ingredient and raw materials (Calleja)
  - Developing a critical list for health security scenarios (Lawler)
  - Forecasting supply disruptions (Schondelmeyer)
- **Improving market resiliency and robustness**
  - Incentivizing manufacturers to expand capacity across multiple geographic locations (Calleja)
  - Addressing the asymmetry of information between buyers and sellers (Schondelmeyer)
  - Shifting from a "fail-and-fix" model to a "predict-and-prevent" model of market failure using supply chain maps that should be developed by federal agencies (Schondelmeyer)
- **Addressing the rate-limiting step of obtaining raw materials**
  - Collecting better data on the supply chain for starting materials (Schondelmeyer)
  - Addressing supply chain dependencies in precursor components (Lawler)
  - Encouraging pre-competitive collaboration between industry and government, with economic incentives to expand access to low-cost material/ingredients needed by manufacturers (Lawler)
- **Mitigating vulnerability to potential shortages of inert/inactive ingredients (e.g., talc) and dosage forms (e.g., inhalers, sterile injectables) due to overreliance**
  - Building in redundancy through greater geographic diversity in production both nationally and globally (Calleja, Schondelmeyer)

[a] This list is the rapporteurs' summary of points made by the individual speakers identified, and the statements have not been endorsed or verified by the National Academies of Sciences, Engineering, and Medicine. They are not intended to reflect a consensus among workshop participants.

[3] More information on CIDRAP's Resilient Drug Supply Project is available at https://www.cidrap.umn.edu/rds (accessed February 12, 2021).

is also heavily dependent on China as its API source. He noted that the COVID-19 pandemic has highlighted both the impact of shortages and the extent of the U.S. drug supply's foreign dependence (Schondelmeyer et al., 2020). Per 2019 data, 19 of 21 critical antibiotics are >75 percent dependent on foreign sources and 14 of 21 critical antibiotics are >50 percent dependent on Asian (Bangladesh, China, India, South Korea, Taiwan, and other Asian countries) sources.[4]

In thinking about critical medical supply chains, Lawler suggested framing vulnerabilities as threats to both national security and day-to-day care provision. For example, geographic concentration of supply chain links (e.g., reliance on China for the majority of certain APIs) could lead to undue foreign influence in navigating bilateral and multilateral agreements from a national security perspective, while the increasing frequency of antibiotic shortages impinges on the ability to treat patients effectively from the providers' perspective. He noted that wider recognition is needed among policy makers about the breadth of the impacts of supply chain vulnerabilities.

Calleja underscored the need to understand the health care supply chain's vulnerabilities before emergencies occur, so systemic steps can be taken to bolster its resilience through visibility, redundancy, and diversification. Better planning to predict and prevent shortages involves enhanced visibility across the supply chain into manufacturers' sources, locations, and volumes of raw materials, API, and finished products. However, many manufacturers are reluctant to provide that information, said Calleja. Redundancy can be advanced by encouraging competition to ensure that multiple manufacturers are available, while diversification can be fostered by leveraging the supply chain's global nature to avoid overreliance on certain geographic regions. She suggested that essential products lists should consider site of care, effective populations, clinical circumstances, available alternatives, and shortage vulnerability.

A recurring discussion throughout the workshop focused on "last-mile" supply chain considerations, including distribution. Within the disaster preparedness architecture, the distribution system for critical medical products spans five complex, interdependent systems,[5] Hupert said. This process depends on tightly coupled decision support systems and parallel flows of information within and across organizations: from the point of dispensing back up to regional or state distribution managers and suppliers and from business processes that track product demand, supply, and use. He added that in contexts of uncertain demand and potential oversupply (e.g., COVID-19 vaccine), risk pooling and reverse logistics for reallocation are essential. Furthermore, rigorous modeling can help gain buy-in from policy makers.

Liu outlined lessons learned during the COVID-19 response, during which his department served as principal purchasing agent for the state's emergency operations: (1) support enterprise-wide organization with a layered infrastructure for information, decision making, operations, and communications; (2) develop a common language and communicate frequently with all stakeholders; and (3) build and apply a model to purchasing, logistics, and the supply chain to prioritize goals and improve organizational agility.

CURRENT CRITICAL OR ESSENTIAL MEDICAL PRODUCT LISTS

Session two focused on critical or essential medical product lists that are currently available or under development. The committee was interested in gathering information regarding how these lists were developed and are currently being used to inform decisions. Panelists included Doug Throckmorton, deputy director for Regulatory Programs, Center for Drug Evaluation and Research, U.S. Food and Drug Administration (FDA); Linda Ricci, director, Division of All Hazard Response, Science and Strategic Partnerships, Office of Strategic Partnerships and Technology Innovation, Center for Devices and Radiological Health, FDA; Schondelmeyer; Lisa Hedman, group lead, Supply and Access to Medicines, World Health Organization (WHO); and Pernette Bourdillion Esteve, team lead, Incidents and Substandard/Falsified Medical Products, WHO. The lists presented by the panelists prioritized critical and essential medical products and involved identifying the acute and chronic drugs that would have the most severe impact on patients if unavailable. Box 2 details key takeaways from this session.

Presenting on the development of FDA's Essential Medicines List, Throckmorton and Ricci pointed to the August 2020 Executive Order on Ensuring Essential Medicines, Medical Countermeasures, and Critical Inputs Are Made in the United States, which directs FDA to identify—within 90 days—a list of essential medicines, medical countermeasures (MCMs), and their 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.[6] Criteria for each of the categories were developed in consul-

[4] Schondelmeyer noted that the 21 critical antibiotics are identified in Metlay et al. (2019). The geographic origin of the drug products at the National Drug Code level were identified by extracting data from the U.S. Food and Drug Administration (FDA) Drug Label Files as of February 2, 2020, and found at https://dailymed.nlm.nih.gov/dailymed/spl-resources-all-drug-labels.cfm (accessed February 12, 2021).

[5] The systems include (1) system and process design; (2) justification, funding, and promotion; (3) fixed infrastructure management; (4) logistics systems; and (5) management systems.

[6] Language on Executive Order 13944 List of Essential Medicines, Medical Countermeasures, and Critical Inputs can be found at https://www.fda.gov/about-fda/reports/executive-order-13944-list-essential-medicines-medical-countermeasures-and-critical-inputs (accessed February 12, 2021).

BOX 2
KEY POINTS FROM SESSION TWO DISCUSSION[a]

- **Defining alternatives to one definitive essential drugs list**
  - Multiple overlapping/complementary lists may be needed depending on the purpose, setting, and population being targeted, with additional considerations regarding the timing of potential supply chain disruptions, time needed to start up and increase production, and the impact of active pharmaceutical ingredient versus finished product shortages (Schondelmeyer)
- **Preparing for unpredictable supply disruptions**
  - Identifying single-source drugs that are not on essential lists but at risk of global shortage (Schondelmeyer)
  - Building manufacturing capacity and resilience to respond to unanticipated impacts (Throckmorton)
  - Prepositioning products (e.g., stockpiles) and processes (e.g., regulatory flexibility) (Hedman)
  - Adopting a process-focused rather than product-focused approach to map unknown risks (Bourdillion Esteve)
- **Understanding how medical device shortages differ from drug shortages**
  - Device shortages differ in terms of product type, supply chains, product life cycles, and regulatory flexibility during a disruption, which can weaken monitoring systems for counterfeit products (Ricci)
  - The less stringent global regulatory environment for medical devices compared to drugs increases the potential for substandard and falsified products, particularly those purchased directly online by consumers, which calls for extending greater regulatory reliance into the postmarket end of the supply chain as well as the premarket (Bourdillion Esteve)

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tation with subject-matter experts and multiple federal agencies and partners; the list is being refined based on further consultations and public comments, Throckmorton noted. The initial essential medicines list,[7] published in October 2020, had 96 medical device codes and 227 drug and biologic products: 174 essential medicines and 53 MCM products. The essential medicines list focuses on products necessary to address immediately life-threatening medical conditions encountered in U.S. acute medical centers and that are used to stabilize patients with those medical conditions rather than to manage longer-term chronic conditions. Throckmorton added that the essential medicines list is focused on those medical needs that are most likely to occur in a public health emergency. Specific criteria were used to select drug and biologic MCMs, drug and biologic critical inputs, and device MCMs. For example, Ricci noted that a device MCM had to meet the following criteria:

- "Fits within the definition of one of four elements of the medical countermeasure definition provided in the executive order,
- Is always medically necessary to have available in adequate supply,
- Is not able to be substituted by another device on the list, and
- Meets one or more of the following:
  - Diagnostic testing and supplies generally applicable to polymerase chain reaction (PCR) testing to enable rapid test development and processing;
  - Personal protective equipment needed to protect health care workers from airborne, blood-borne, waterborne, chemical, biological, radiological or nuclear events;
  - Devices that are not permanently implanted that are intended to provide acute mechanical support in treating an acute event or condition in a health care setting for vital physiologic functions and are not intended solely for the treatment of chronic conditions;

[7] FDA's Essential Medicines List is available at https://www.fda.gov/media/143406/download (accessed January 26, 2021).

- Devices that provide adequate vital signs monitoring in a health care setting to enable the use of the mechanical support MCM devices;
- Devices used for the delivery of a vaccine that are intended to prevent or mitigate the spread of an epidemic or pandemic; or
- Devices used for the acute management of injury or illness caused by chemical, biological, radiological or nuclear events."[8]

Since 2018, a panel of intersectoral experts convened by CIDRAP's Resilient Drug Supply Project has been compiling lists of critical and life-saving drugs, said Schondelmeyer. These drugs are defined as those with no reasonable alternatives whose absence would excessively or substantially increase mortality, cause serious health outcomes, or preclude the ability to provide humane care. CIDRAP's Critical Acute Drug List—of "drugs that when medically needed in acute care, must be available and used within hours or days of the need or the patient will suffer serious outcomes which may include disability or death"—includes 156 drug molecules.[9] Prior to the COVID-19 pandemic, a substantial number of those molecules were already in shortage. As the pandemic unfolded, the panel defined a subset of Critical COVID-19 Drugs within the Critical Acute Drug List that includes 40 drug molecules, many of which were also in shortage as of December 2020. Given that most medical conditions are chronic, the project is now developing a Critical Chronic Drug List, which is expected to include around 500 molecules that "when medically needed in chronic care, must be available and used within a few days or weeks of the need, and on a regular basis, or the patient will suffer serious outcomes which may include debilitating disease progression and worsening health status resulting in emergency care, hospitalization, or death."[10] For example, insulin would qualify.

Hedman explained that WHO's Interagency Emergency Health Kit[11] is a product list and packed-ready inventory, shared across United Nations agencies and implementing partners, that contains supplies to treat 10,000 people for 3 months during large-scale emergencies. It is modular, adaptable, deployable within 72 hours, and updated regularly by disease program and emergency experts. Hedman said that the list for the kit must be linked to published treatment guidelines and/or WHO's Model List of Essential Medicines[12] that should be available at every health center to ensure basic functionality of a health system. During the COVID-19 pandemic, WHO has been developing and monitoring a list of medicines—specifically those that are anticipated to have demand increases or other threats to supply—using a dynamic, multilevel, risk-based approach. She noted that the highest-risk products are those with multiple, changeable risk factors. Hedman explained that this COVID-19 list is intended to support negotiations with governments and manufacturers to prioritize medicines, determine realistic demand, sustain manufacturing operations, and protect workers.

Building on Hedman's presentation on WHO's Model List of Essential Medicines, Bourdillion Esteve spoke to the lack of oversight to prevent the manufacture of unregistered/unlicensed, substandard, and falsified (SF) medicines as a result of the globalized nature of the supply chain. She said that this lack of oversight can undermine global health investments in myriad ways (e.g., treatment failure, increased morbidity and mortality, antimicrobial resistance, eroded public trust, increased costs) and may disproportionately affect countries lacking the resources to rapidly replace falsified inventory. WHO's Global Surveillance and Monitoring System for SF medical products is a case-reporting database but cannot extrapolate to country-specific prevalence, because regulatory authorities are not necessarily willing, able, or incentivized to report incidents, Bourdillion Esteve said.[13] She noted that the primary drivers of SF medical products are poor governance, weak technical capacity, and constrained access that undermines affordability, acceptability, and availability. During the COVID-19 pandemic, WHO is monitoring links between perceived efficacy, demand, and SF versions of certain COVID-19 products. Bourdillion Esteve said that as of December 2020, SF versions of diagnostics, hydroxychloroquine, antiretrovirals, and vaccines had all been reported. SF products have not traditionally been as high a regulatory priority in

[8] Throckmorton's presentation to the committee, titled *Essential Medicines Executive Order—FDA List*, is available at https://www.nationalacademies.org/event/12-01-2020/security-of-americas-medical-product-supply-chain-committee-meeting-2-and-public-workshop (accessed January 26, 2021).

[9] CIDRAP's Critical Acute Drug List is available at https://www.cidrap.umn.edu/sites/default/files/public/critical_access_covid-19_drugs_shortages_156-40_2021-1-18_002.pdf (accessed January 26, 2021).

[10] Schondelmeyer's presentation to the committee, titled *Resilient Drug Supply Project: Examining Current Lists,* is available at https://www.nationalacademies.org/event/12-01-2020/security-of-americas-medical-product-supply-chain-committee-meeting-2-and-public-workshop (accessed January 26, 2021).

[11] More information about WHO's Interagency Emergency Health Kit is available at https://www.who.int/emergencies/emergency-health-kits (accessed January 26, 2021).

[12] WHO's Model List of Essential Medicines is available at https://www.who.int/groups/expert-committee-on-selection-and-use-of-essential-medicines/essential-medicines-lists (accessed January 26, 2021).

[13] WHO Global Surveillance and Monitoring System is available at https://www.who.int/medicines/regulation/ssffc/surveillance/en (accessed February 12, 2021).

higher-income countries as in lower-income countries, but the development and production of COVID-19 vaccines and therapeutics in higher-income countries may shift the burden of risk related to SF products, Bourdillion Esteve noted.

PRACTICAL AND TACTICAL APPROACHES FOR EXECUTING A RESILIENCY FRAMEWORK FOR CRITICAL MEDICAL PRODUCTS

During the third session, panelists described practical and tactical approaches for executing and implementing a resiliency framework for critical medical products from the perspectives of generic drug suppliers, group purchasing organizations, pharmaceutical companies, device suppliers, and policy makers. Panelists included Heather Wall, chief commercial officer, Civica; Dan Kistner, group senior vice president of pharmacy service, Vizient; Craig Kennedy, senior vice president, Global Supply Chain Management, Merck; Bill Murray, medical device specialist executive, Deloitte Consulting; and Nicole Lurie, strategic advisor to the CEO and response lead, Coalition for Epidemic Preparedness Innovations; senior lecturer, Harvard Medical School; and former Assistant Secretary for Preparedness and Response, HHS. The panelists noted that the concept of resiliency can be defined and operationalized in different ways (e.g., manufacturing redundancy; product quality; ability to make up for shortages whenever some part of a supply chain is disrupted while continuing to provide safe, quality care even under crisis standards). Wall said that resilience can also be segmented into the ability to respond to either acute shortages or infrequent but unprecedented increases in demand. Box 3 details key takeaways from this session.

BOX 3
KEY POINTS FROM SESSION THREE DISCUSSION[a]

- **Barriers to increasing transparency in manufacturers' supply chains**
  - Competition among manufacturers (Lurie)
  - Concerns about privacy and confidentiality (Lurie)
  - Concerns about counterfeiting (Kennedy)
  - Lack of incentive structures (Kistner)
  - Potential risk to shareholders (Kistner)
  - Interest in maintaining security of sources (Kennedy)
  - Complexity and multiplicity of components (Kennedy)
- **Strategies to increase transparency in manufacturers' supply chains**
  - Maintaining stakeholder privacy (Lurie)
  - Using regulatory authority to compel visibility (Kistner)
  - Linking with Medicare conditions or federal contracting requirements (Lurie)
  - Encouraging manufacturer-developed standards as components of patient safety (e.g., active pharmaceutical ingredient source on product labels) (Wall)
  - Focusing on resiliency (e.g., stockpiles), not manufacturing locations (Kennedy)
- **Resolving tension between risk management and public health goals**
  - Conducting long-term risk management as a responsible approach to long-term profit-making (Kennedy)
  - Coupling quality management systems with risk mitigation strategies to focus on patient outcomes and potentially reduce costs (Wall)
- **Benefits of a digital dashboard for transparency**
  - Facilitating situational awareness to achieve public health goals (Lurie)
  - Guiding decision making with near-real-time data transmission (Wall)
  - Enabling public and private sector forecasting using diagnostic data (Murray)
- **Barriers to capturing quality metrics**
  - Interoperability and connectivity challenges for device manufacturers (Murray)
  - Lack of bidirectional transparency with manufacturers regarding data use (Kennedy)
  - Use of homogenous quality metrics for diverse processes (Kennedy)
  - Quality metrics do not address shortages due to other causes (Kennedy)

continued

BOX 3 CONTINUED

- **Applying an equity lens to supply chain challenges**
  - Seeking input from a range of populations, settings, therapeutic areas (Wall)
  - Equitably allocating drugs disproportionately used by at-risk populations (Lurie)
  - Leveraging regulatory tools to ensure supply continuity around market exits that would disproportionately impact vulnerable populations (Lurie)
  - Mitigating risk rather than waiting for and reacting to disruptions (Lurie)
- **Barriers to increasing production intermittently**
  - Maintaining standing capacity to ramp up production rapidly is not logistically or financially feasible (Kennedy)
  - Redundant/surge capacity does not address shortages caused by demand surges or quality issues (Kennedy)
  - Activating surge capacity has costs eventually passed on to payers (Kennedy)
- **Developing a multipronged strategy to maximize resiliency**
  - Stockpiling as a response to immediate need differs from building resilience to ensure long-term sustainability (Murray)
  - Redundancy and stockpiling are appropriate for essential products susceptible to acute shortages; other essential products need sourcing from multiple sites (Wall)
  - A smaller number of committed, high-quality manufacturing partners, appropriately incentivized to stay in the market, would be preferable to a larger number of manufacturers producing at a lower quality (Kennedy, Kistner)
  - A multipronged, multistakeholder strategy requires commitment and transparency for suppliers (Kistner) and public–private partnerships to ensure that the market meets national interests (Lurie)
  - Systems and partnerships developed in response to the COVID-19 pandemic could be repurposed for other shortage scenarios (Kistner)

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Civica is a not-for-profit generic drug supplier collaborating with health systems nationwide to address shortages and lower the costs of generics.[14] To support supply chain resiliency, Civica works directly with frontline clinicians and pharmacists, which allows for quick pivoting to meet evolving needs related to changes in demand and evolving clinical protocols, said Wall. Medications are only manufactured if prioritized by their hospital drug selection committees and medical trends advisors. The organization currently focuses on manufacturing chronic shortage medications (those that cause the most harm to patients when unavailable) and maintains a several-month safety stock of essential medications for use by their partners if demand or supply fluctuates, with a high degree of transparency around its manufacturing supply chain.

Kistner explained how Vizient, a health care performance improvement company supporting more than half of the nation's hospitals, responded to the unprecedented demand for certain products—and potential embargos on pharmaceuticals or starting products—during the COVID-19 pandemic. Vizient developed a publicly available essential medication list[15] of 219 critical and life-saving drugs that warrant heightened focus from FDA, manufacturing partners, and Vizient members. Novaplus, Vizient's private-label program, offers enhanced supply and redundancy by holding a supply of up to 6 months of more than 151 essential medications, with manufacturers required to disclose API manufacture location. Vizient analysts monitor fill rates across the United States to identify supply and demand trends and enable rapid response to disruptions.

[14] More information on Civica is available at https://civicarx.org (accessed February 12, 2021).

[15] The medication list is available at https://www.vizientinc.com/-/media/documents/sitecorepublishingdocuments/public/essential_meds.pdf (accessed March 23, 2021).

As a pharmaceutical company serving a population of patients worldwide, Merck has a supply chain that is global by design to ensure resiliency and efficiency, Kennedy said. He continued that its strategies to strengthen supply chain resiliency include a rigorous risk management assessment and mitigation program, diversified and redundant global supply routes, dynamic inventory positioning, and flexible manufacturing capabilities to avoid disruption. In recent years, the resiliency of its supply chain has been tested by cybersecurity attacks, hurricanes, and the COVID-19 pandemic but, by preparing for and mitigating supply chain stressors, Merck's service to patients worldwide has increased, rather than decreased, during the pandemic, noted Kennedy.

Murray explained that medical devices face unique challenges compared to biologics and pharmaceuticals, because they are reliant on complex, interconnected global networks of supply chains driven by specialization, global competition, and efficient capacity use. Although these networks support competition, they are susceptible to global disruption. Specialization helps to scale and economize technological developments but can create logistical bottlenecks, and efficient capacity use supports resource allocation but minimizes available surge capacity, said Murray. At the outset of the COVID-19 pandemic, the finished goods supply chain for critical medical products faced major challenges in handling demand surges, minimizing supply disruption, and sustaining operations while preserving workforce safety. He highlighted several strategies to mitigate disruptions and promote resilience in the medical device supply chain: avoiding single sourcing, managing supply risk, ensuring end-to-end transparency, segmenting inventory by critical need, and using a patient-centric approach to assess need and demand.

Concluding the session, Lurie framed supply chain resiliency as a day-to-day issue that can be defined operationally as the ability to make up for shortages whenever some part of a supply chain is disrupted, while continuing to provide safe, quality care even under crisis standards. She emphasized that a good response depends on strong day-to-day systems that can address bottlenecks and spot shortages but also has baked-in mechanisms to trigger "on-ramps" and ramp up production during emergencies. The ability to anticipate and mitigate shortages would benefit from enhanced supply chain visibility through digital dashboards and regular reporting, as well as policies and authorities to require more transparency from manufacturers. Collaboration across government and industry should encourage flexibility and innovation that is sustained after a crisis. Furthermore, she noted that planning for how products will be allocated and administered to end users is often neglected in supply chain considerations.

END-USER PERSPECTIVES: WHAT MAKES A MEDICAL PRODUCT CRITICAL?

The final session of the workshop focused on what makes a medical product critical from the perspective of end users, including the patient, pediatric care providers, intensive care unit (ICU) providers, frontline providers, pharmacists, and health care systems. The committee sought to understand what outcome measures mattered to end users when it comes to supply chain resiliency and success. Panelists included Suzanne Schrandt, founder and CEO of ExPPect; Christopher Newton, director, Trauma Care, and co-director, Neuroscience Center, University of California, San Francisco, Benioff Children's Hospital, Oakland; Ryan Maves, faculty physician, Naval Medical Center, San Diego; Sally Watkins, executive director, Washington State Nurses Association; Michael Ganio, director, Pharmacy Practice and Quality, American Society of Health-System Pharmacists (ASHP); and Michael Schiller, senior director, Association for Health Care Resource & Materials Management, American Hospital Association. The panelists discussed how non-emergency drug shortages, as well as pandemics or other major emergencies that can cause supply disruptions and demand surges—the two major threats to a supply chain—can have devastating consequences. Box 4 details key takeaways from this session.

BOX 4
KEY POINTS FROM SESSION FOUR DISCUSSION[a]

- **Transferring specialized knowledge from frontline providers/institutions back to systems-level decision makers**
  - Increasing visibility and transparency into the supply chain (Schiller)
  - Identifying the most effective "McGyvering" techniques and operational processes (Schiller)
  - Engaging the full range of stakeholders in different care settings through communication forums (Watkins)
  - Engaging patients and patient advocacy organizations to help develop front-end (e.g., predicting, identifying, and mitigating the shortage) and back-end (e.g., reacting to the shortage once it occurs) solutions (Schrandt)

continued

BOX 4 CONTINUED

- Creating mechanisms to share operational lessons learned by end users upstream (Newton)
- Encouraging leadership and administrators to spend time on the front lines to understand the impact of shortages on the ground (Maves)

- **Strengthening the fragile supply chain for single-source medical devices**
  - Accounting for device quality and functionality when diversifying manufacturing (Newton)
  - Considering lack of cross-compatibility in consumables for durable goods (Maves)
  - Expanding use of reusable equipment when possible (Maves)
  - Providing education on reuse and decontamination of reusable goods (Schiller)
- **Discouraging hoarding during shortages**
  - Consider the implications of providing health systems with comprehensive lists of first- and second-line essential items (Newton)
  - Providing context-specific lists of minimum requirements for at-risk items (Ganio)
- **Incentivizing resource sharing and risk pooling**
  - Framing risk pooling as a means to alleviate pressure to select certain products due to costs, budget constraints, and reimbursement issues (Ganio, Newton)
  - Developing shared economies (Schiller)
  - Leveraging technology to "fatten" supply chains (Schiller)
  - Creating regional coalitions for surge inventory management (Schiller)

[a] This list is the rapporteurs' summary of points made by the individual speakers identified, and the statements have not been endorsed or verified by the National Academies of Sciences, Engineering, and Medicine. They are not intended to reflect a consensus among workshop participants.

Schrandt offered a patient's perspective on the criticality of medical products, noting that patients are typically unaware of the risks and realities of shortages. She emphasized that in addition to treating people in acute care settings with life-or-limb emergencies, an equally important goal is to keep chronically ill patients maintained at home to minimize the number of people in acute care settings. For this second layer of "pre-emergent" high-risk patients living with chronic conditions, sudden treatment interruptions can quickly escalate into acute emergency situations that could have been averted by reliable access to necessary therapies. Furthermore, Schrandt explained, because some drugs on essential lists have multiple indications, patients with chronic conditions may be disadvantaged—albeit unintentionally— if lists create hierarchies that privilege certain categories of patients in prioritizing those therapies for emergency use, thus limiting the supply available for non-critical mainstay therapy.

Newton is the principal investigator for the Western Regional Alliance for Pediatric Emergency Management (WRAP-EM), which works on supply chain issues related to pediatric care. Identifying critical medical products for pediatric care is complex, he said. It is challenging to define "child" for emergency management purposes, and lists of critical products for pediatric needs are context dependent across emergency scenarios and settings. WRAP-EM's approach is to compile an exhaustive master list of critical pediatric items that can be tailored for different scenarios.[16] Newton said that pediatric supply chain planning should consider rare versus common needs—some medications are rarely used but critical for populations that rely on them, and some rarely used pediatric specialty equipment is only produced by a single vendor. Although many critical items for adults can be adapted for children, it is important that items that cannot are identified and accessible when needed. Furthermore, many practical items needed for children's care are not on essential supply lists (e.g., pediatric personal protective equipment).

Maves discussed critical care limitations in adults in emergencies, noting that loss of ICU capacity is a rate-limiting step for most major hospital functions. A hospital surge response typically focuses on finding innovative ways to address imbalances between supply—"stuff, staff, and space"—and demand (patient care), with coping measures based on levels of care (Hick et al., 2014). However, the COVID-19 pandemic is a chronic contingency with an ongoing need to surge, de-surge, and resurge, rather than a time-limited event, said Maves. In a crisis situation, Maves noted

[16] More information on WRAP-EM is available at https://wrap-em.org (accessed February 17, 2020).

that "stuff" on its own is not often considered critical. Rather, it is a necessary but insufficient means to provide capabilities (e.g., many drugs[17] can be substituted, but a ventilator is useless unless it provides the needed capability and has experts to operate it based on available staff). He noted that most ventilators produced to meet initial pandemic shortages were not "full function" in providing adequate levels of respiratory support, which was an unintended consequence of mass production of specialized medical devices by companies new to the industry (Branson et al., 2020).

Watkins offered a frontline provider's perspective on supply shortages. The primary focus of those who deliver direct care, including nurses and other frontline providers, extends beyond safety to quality of patient care. However, frontline providers are reliant on others to provide them with the supplies and equipment they were trained to practice with; shortages of those necessary products can lead to moral distress, frustration, and burnout among providers. She emphasized that essential lists should include critical preventive medications to prevent acute medical emergencies that vary in different care settings (e.g., hospital versus home care) to help keep patients at home when critical care beds are scarce. Furthermore, transparency in communication between frontline health care workers and leadership teams can contribute to a culture of trust and honesty about resource limitations and challenges faced on the ground.

Ganio framed his comments about essential medical lists from a pharmacist's perspective, with the caveats that every medication is essential to a patient taking it and lists would not be necessary if the underlying causes of drug shortages were sufficiently addressed. ASHP[18] co-convened summits in 2017[19] and 2020[20] to examine, from a national security perspective, the impact of drug shortages and the availability of safe, effective, and accessible high-quality medications.[21] Both summits recommended developing an essential medicines list, the contents of which depend on its intended purpose, such as incentivizing domestic manufacturing, stockpiling, or creating a buffer inventory. He noted that stockpiling materials for essential medicines is only effective if manufacturing capacity can be rapidly increased when necessary. Furthermore, multiple lists may be needed for various types of immediate patient needs—from routine functions to critical care—during various emergency scenarios, with appropriate consideration of package or vial sizes and dosage forms.

Schiller remarked that the COVID-19 pandemic has spurred many hospitals and health systems to rethink and transform their supply chain models to address their fragility. Strategies include expanding partnerships, ensuring redundancy, diversifying vendor and manufacturer portfolios, and leveraging digital technologies to understand product utilization and anticipate needs. Many are transitioning from a singular focus on product pricing toward a more evidence-based approach to improve patient outcomes while lowering overall costs of care. He suggested that health systems might consider whether to develop separate operational and surge inventories or have a singular managed inventory extending upstream through the entire supply chain. Furthermore, developing a list of clinically acceptable substitutes at the industry level could contribute to consistent product availability in a time of increased demand.

CLOSING REMARKS

In closing the workshop, Wallace Hopp, chair of the Committee on Security of America's Medical Product Supply Chain, thanked all of the speakers, noting that the presentations and discussions on critical drugs and devices generated a great deal of thought and dialogue and will be invaluable as the committee works to develop recommendations to enhance the resiliency of the medical supply chain going forward. He concluded that to develop a more resilient medical supply chain for times of crisis and beyond, lessons learned from the COVID-19 pandemic should be woven into the fabric of health care supply chains—from manufacturing and distribution to clinical and operational practice—because future events could create even more profound shortages of medical products. ◆◆◆

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[17] Maves also noted that the FDA List of Essential Medicines includes a single antiretroviral drug that has relatively little clinical utility, while prednisone is excluded despite its common use in a range of scenarios.

[18] ASHP represents pharmacists serving as care providers in acute and ambulatory settings.

[19] Additional information on the 2017 summit can be found at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6382262 (accessed February 23, 2021).

[20] Additional information on the 2020 summit can be found at https://academic.oup.com/ajhp/advance-article/doi/10.1093/ajhp/zxaa392/6009025 (accessed February 23, 2021).

[21] The 2017 summit was convened in response to the effects of Hurricane Maria. The 2020 summit was convened after the COVID-19 pandemic exposed the vulnerability of the drug supply chain based on not only geographic concentration but also quality issues.

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