Drug product shortages are a significant and increasing concern for critical care practitioners. While the true impact of these shortages is not completely understood, they can lead to substantial problems related to patient care. The American Society of Health-System Pharmacists (ASHP) has developed resources for both tracking and handling drug shortages.1 These resources include a continually updated list of drugs and drug products that are on shortage, listed by generic name and date of addition or revision to the list.2 As of June 2013, 239 products were listed as having an unresolved shortage, a major increase from only 70 products reported in 2006.3 Many of the products on the list are used in the care of critically ill patients, including fentanyl, propofol, vecuronium, atropine, sodium bicarbonate, and famotidine, to name a few.

The impact of drug shortages has been described in several specific patient populations, including solid-organ transplantation and oncology. Drug shortages in these patient populations have led to consequences such as alterations in patient care and the use of alternative agents, which increase the number of medication errors and adverse events; shortages can disrupt clinical research as well.4,5 In a survey of pharmacy directors at 327 acute care institutions, 95% responded that drug shortages had led to a change in practice, and 61% felt that shortages had compromised patient care.6 Furthermore, drug shortages led to reported delays or cancellations of procedures (65%), increased hospital length of stays (31%), and serious medication errors (10%). In a more recent survey of 353 pharmacists, drug shortages were associated with an increased burden on staff (97% of respondents), increases in medication costs (93%), alterations in clinical practice (80%), and compromises to patient care (55%).7
Numerous factors may contribute to the development of drug shortages. These include, but are not limited to, (1) the availability of the raw and bulk materials needed for production, (2) issues related to drug manufacturing, (3) federal regulatory issues or concerns, (4) voluntary (or forced) drug recalls, (5) changes to drug product formulation, (6) changes in drug product manufacturers, (7) economic decisions of manufacturers that affect the drug supply chain, (8) industry mergers and consolidations, (9) restricted distribution and allocation of some medications, (10) wholesaler and institutional inventory decisions, (11) unexpected changes in demand, (12) changes in clinical practice, (13) nontraditional distributors, and (14) natural disasters.

Due to the complexities of managing these events, several strategies have been proposed for handling drug shortages. ASHP recommends a 3-phase approach, beginning with an identification and assessment phase. During this phase the institution can confirm the shortage, determine the anticipated duration, check current inventory in hand and with alternative suppliers, and investigate the use of alternative agents or the possibility of compounding the product on shortage (if possible). Phase 2 is a preparation phase that includes determining the patient population that will be affected, contacting providers to determine possible alternative therapies, communicating with stakeholders, and prioritizing patient care. Phase 3 is a contingency phase that entails considerations to risk management and liability, budget considerations, and coordination of information. Once a plan is created, it must then be effectively communicated and implemented.

While such plans are extremely useful for the multiprofessional team in preparing for several contingencies, these plans do not address the potentially serious ethical concerns related to drug shortages: the prioritization and rationing of care. These ethical concerns can be divided into those that pertain to the institution and those that pertain to direct distribution and administration of drugs to patients. It is essential for critical care practitioners to familiarize themselves with and prepare to handle these ethical concerns in order to minimize the potential disruptions to patient care.
Institutional Concerns

Most institutions deal with drug shortages on a reactionary or case-by-case basis with no formal guidance. In some instances, the institution may not be aware of the shortage until the current supply is at or near zero or when the procurement department attempts to place an order only to find out that the wholesaler does not have adequate supplies. ASHP has provided a guide to help institutions effectively plan for shortages, but many questions remain as to how institutions can properly prepare for these contingencies with minimal impact on patient care.

Several ethical concerns arise as institutions develop plans for managing drug shortages. These include the issues of stockpiling medication supplies and the use of nontraditional resources, or the so-called gray market. The issue of medication stockpiling arises during the drug acquisition process. When an order is placed for a product in short supply, the institution may attempt to order more supply than is actually needed for usual patient care or may even attempt to order all of the remaining supply from the wholesaler. This may lead to two distinct problems: (1) It can create an artificial shortage by draining the supply chain and exceeding manufacturing capabilities, and (2) the institution has to cover the increased costs of obtaining and storing the additional inventory that may not be needed. These potential problems have been studied with regard to medications used in the ICU. Seventeen medications listed on the ASHP Web site were reviewed at the Tufts Medical Center to determine the impact of the reported shortages. Of the 17 medications, 10 stayed at a minimum of 50% of the normal dispensing level. For the 7 that dropped to a dispensing level less than 50% of normal, this did not occur until a mean of 8 months after the shortage was first listed. While not an absolute, these results suggest that overordering or stockpiling of supplies may be unnecessary.

Stockpiling also can leave other institutions with shortages of a medication. In an editorial discussing this topic, Michael Manolakis, an associate dean at the Wingate University School of Pharmacy, writes, “It is unconscionable to think that a hospital could build a large inventory of a lifesaving medication while a patient in a nearby hospital suffers without access to the medicine.” It has been recommended that institutions advocate for,
and engage in, a regional medication sharing policy to adequately meet the needs of all patients.\textsuperscript{8,9}

Gray market is a term used to describe the use of alternative suppliers to meet inventory needs. These are typically licensed distributors or brokers that are able to acquire the products that are on shortages for the sole purpose of marketing them to institutions that cannot obtain the products from traditional resources.\textsuperscript{8} The use of this market creates several ethical dilemmas: The products are typically limited in supply and marketed at exorbitant prices, returns or refunds are not offered in the event of expiration or nonuse, the reliability of the original source may not be known (and the source may be outside of the United States), and the storage and handling may not meet the manufacturer’s standards.\textsuperscript{8,11} There are also concerns that the gray market may actually cause some drug shortages, and this has led to a call to cease the use of these distributors.\textsuperscript{9,11}

Patient Care Concerns

In addition to the ethical issues associated with acquisition of medications on shortage, issues related to the administration of these medications arise. This concept has been explored within the realm of medical ethics. Based on the “accountability for reasonableness” approach, Phillip Rosoff, MD, from the Department of Pediatrics at the Duke University Medical Center, has proposed that 5 components must be considered in order to develop an equitable and fair approach to the decision-making process with regard to drug shortages.\textsuperscript{12,13}

The first component is \textit{transparency}, whereby the rationale, development, and implementation of the entire decision process are open and available to public scrutiny. The second component is \textit{relevance}, such that unbiased observers can view the decision process as relevant to each situation. The third component is \textit{appeals}, referring to the availability of a timely and reversible process for any participants or others who feel that the process is unfair. The fourth component is \textit{enforcement}, the process of implementing and applying the process. The fifth component is \textit{fairness}; the rules must apply in all situations regardless of the individual circumstances, and the
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The entire process should be adaptable if needed as more experience is gained in these situations. These concepts have been incorporated into a reliable, workable, and acceptable policy for the clinicians, staff, and patients at the Duke University Medical Center.\textsuperscript{14}

While this process seems to be a reasonable approach for dealing with the ethical issues related to drug shortages, experts have identified several issues with regard to the Rosoff model that need to be addressed. The first issue regards the time frame of the shortage; the Rosoff model may work well with advance notice of a potential drug shortage but may not adequately address the issues of a sudden shortage due to, for example, product contamination.\textsuperscript{15} Therefore, a trial run is recommended to test the system prior to initiation. The second issue involves the intended use of the medication on shortage and whether there are viable alternatives. It may be somewhat easier to cancel elective procedures or discontinue nonvital medications, but additional planning is needed to adequately deal with agents used for life-threatening conditions and those for which substitutes may not exist.\textsuperscript{15} Third, individual need and efficacy should be clearly defined; in other words, how should it be determined whether one patient has more of a need for a medication on shortage than does another patient?\textsuperscript{16} This might include additional concerns such as clinical efficacy of the original medication and the possible alternatives, as well as the cost-effectiveness of these medications. The fourth issue is fairness and the potential for bias. This includes conscious and unconscious biases and conflicts of interest for those involved in both the decision and appeals process. It is further suggested as a part of this concept that a supportive care process is needed for those who do not receive the medication as well as to address possible feelings of guilt for those who do receive it.\textsuperscript{17} This also encompasses the concept of fairness—that those who significantly contribute to the healthcare process should not be given preferential treatment.\textsuperscript{18} Included in this list would be hospital employees, executives, celebrities, political figures, and donors to the institution.
Summary

While no perfect method exists for developing an ethical approach to dealing with drug shortages, the key is to have a well-defined plan in place that incorporates a multiprofessional approach for optimal patient care. In an ideal situation, this plan should be developed and tested before the shortage occurs, but this may not be feasible in all cases. Therefore, it is recommended that all stakeholders develop a plan to ensure that the 5 ethical components described by Rosoff are considered to make certain that all patients are treated fairly with minimal disruptions in care.

REFERENCES

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