COPING WITH AND MITIGATING THE EFFECTS OF SHORTAGES OF EMERGENCY MEDICATIONS

November 2012 (v.24Nov12)

Acknowledgements

This report was made possible with funding provided to the Association of State and Territorial Health Officials (ASTHO) from the US Department of Health and Human Services' Office of the Assistant Secretary from Preparedness and Response through contract #HHS100201100050C, "Strengthening ASTHO/HHS-ASPR Collaboration to Improve All Hazards Readiness."

ASTHO recognizes and thanks the many who served on the drug short national work group and gave freely of their time and expertise which dramatically helped to inform the examination of the current drug shortage issue and in creating the content found in this paper.

This project was conducted under the technical direction and oversight of ASTHO by James S. Blumenstock, M.A., Chief Program Office, Public Health Practice. ASTHO staff members Meredith Allen, Dr.PH, MS, Director of Preparedness and Strategic Partnerships and Lisa J. Peterson, MPH, MPA, CPH, Senior Analyst, Public Health Preparedness significantly contributed to this project.

ASTHO is the national nonprofit organization representing public health agencies in the United States, the U.S. Territories, and the District of Columbia, and over 100,000 public health professionals these agencies employ. ASTHO members, the chief health officials of these jurisdictions, formulate and influence sound public health policy and ensure excellence in state-based public health practice. ASTHO's primary function is to track, evaluate, and advise members on the impact and formation of public or private health policy which may affect them and to provide them with guidance and technical assistance on improving the nation's health.

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THE EMERGENCY CARE DRUG SHORTAGE ISSUE-COPING OPTIONS FOR THE PUBLIC HEALTH, EMERGENCY MEDICAL SERVICES AND EMERGENCY CARE/TRAUMA COMMUNITIES

November 2012

BACKGOUND

According to the US Department of Health and Human Services, over the last six years shortages of key cardiovascular, anesthetic, analgesic and anti-infective drugs have quadrupled and are often in short supply. It is estimated that nearly 40% of the drugs in shortage impact the delivery of emergency care due principally to the lack of sufficient and timely availability of sterile injectable drugs used in the emergency care setting[1]. While the emergency care drug shortage impact is not being felt equally in all jurisdictions (it is generally acknowledged that distributors can react very quickly to ameliorate truly local spot shortages), it, nevertheless, has escalated to a point of being considered a national public health and homeland security concern. At times, the impact of the drug shortages situation is so acute that it has been reported that a facility's management first becomes aware of a "crisis" when ordered drugs are missing from a shipment and put on back order and the hospital or EMS it finds themselves without any inventory of that medication. Patient comfort and safety can be put at risk when emergency care providers are forced to delay treatments, reallocate scarce resources or resort to backup treatment regimens. This would include using third or fourth line agents that may not be as effective and for which healthcare workers are unaccustomed to using and may not be competent to administer without education and training when the sufficient amount of the preferred drug is not available. As illustration, the results of a 2011 survey of hospital pharmacy staff conducted by the Institute of Safe Medication Practice was summarized in a April 2012 Medication Safety Alert which stated in pertinent part "Nearly a hundred practitioners took our short survey and strengthened our belief that the ongoing drug shortage crisis is exacting a significant toll on patient safety"[2]

The US Food and Drug Administration (FDA) continues to work with the drug manufacturers to address and prevent drug shortages, which can occur for many reasons, including manufacturing and quality problems, delays, and discontinuations; and to communicate the issue and help restore availability. Executive Order 13588 entitled "Reducing Prescription Drug Shortages" signed by President Obama on October 31, 2011 and Title X of the Food and Drug Administration Safety and Innovation Act of 2012 signed into law on July 7, 2012 have increased industry notification to FDA of impending shortages to provide additional lead time to respond to thwart potential shortages or at least lessen their impact. Despite these best efforts, this problem is not a transient one and is expected to exist for some time (measured in months, maybe even years) until such time as the root causes associated with domestic and global drug production capacity and product quality are addressed. As such, government officials and providers of emergency medical services and trauma care must work together to face and cope with the challenges presented by drug shortages to mitigate to the fullest extent possible, if not eliminate, the adverse impact on patient care, while working within a regulatory framework intended to also

[1] ASPR Proceedings Report: The Impact of the National Drug Shortage on Emergency Care. April 2012

[2] Institute of Safe Medication Practices (ISMP) Medication Safety Alert; *"A Shortage of Everything Except Errors: Harm Associated with Drug Shortage", April 19, 2012*

protect healthcare consumers but one which may not be readily adaptive to this current and unanticipated situation.

PURPOSE

Until such time when the root causes of the emergency care drug shortage are addressed and sufficient, reliable supplies of first-line medications are readily available, public health and other governmental officials, emergency medical services personnel, and emergency/trauma care providers must work collaboratively to identify and apply reasonable coping strategies and tactics to mitigate the impact of the shortage on patient care. This document attempts to capture and summarize the current best thinking of national thought leaders in these fields and is intended to serve as a guide or possible choices of various actionable options for consideration. It must be stressed that this document does not reflect a consensus and should not be construed as formal guidance. Rather, it is a compendium of various "coping" approaches currently being followed or being considered by certain practitioners in the field deemed worthy of sharing with the community of practice for individual assessment and consideration before being implemented. It is readily recognized that for a variety of reasons not every option will be viable for all entities and must be examined in the context of a facility's or agency's controlling policies and legal/regulatory construct.

The information in this paper was gleaned in large part from a two day work shop of national subject matter experts of physicians, paramedics, nurses, pharmacists and public health emergency planners (hereafter referred to as the "work group") which was conducted in mid-July 2012. Approximately 40 experts representing the following national organizations were convened for the express purpose of helping identify plausible coping strategies and tactics for consideration by public health, EMS, and emergency/trauma care sectors:

- American College of Emergency Physicians
- National Association of State EMS Officials
- National Association of Emergency Medical Technicians
- Association of State and Territorial Health Officials
- The Institute of Medicine
- American Pharmacists Association
- American Association of Poison Control Centers
- Trauma Center Association of America
- Federation of State Medical Boards
- Emergency Services Coalition for Medical Preparedness
- Association of Critical Care Transport
- National EMS Managers Association
- Emergency Nurses Association

Key federal agency representatives from relevant operating divisions/units also participated as observers and/or technical resources from the following departments:

- Department of Health and Human Services
- Department of Transportation
- Department of Homeland Security

This document is intended to serve as a guide (with links and references found in Appendix A) to a number of useful resources and tools identified during an environmental scan or provided by work shop participants.

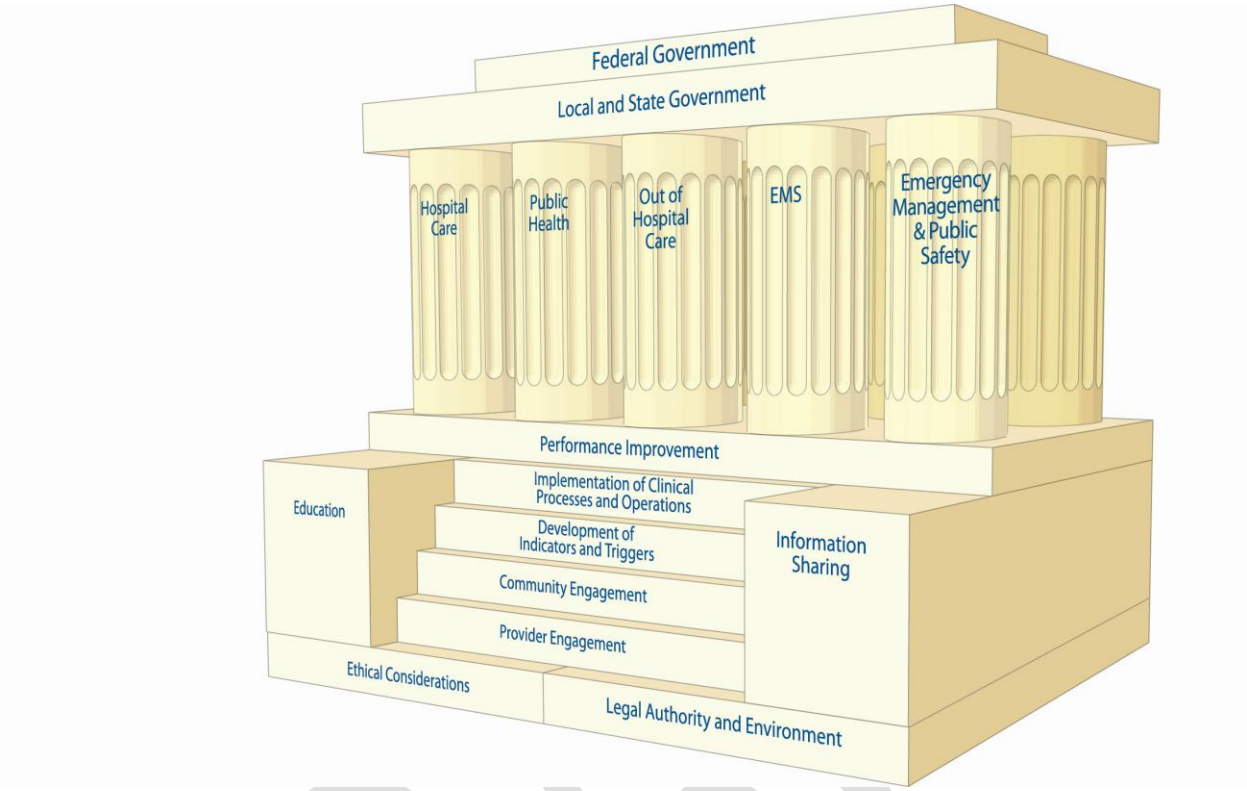
A FRAMEWORK FOR "COPING"

While principally drafted for the purpose of supporting broader disaster planning and response efforts, the work group recognized that the recently released Institute of Medicine report entitled "Crisis Standards of Care-A Systems Framework for Catastrophic Disaster Response" (the "framework") serves as the most appropriate and useful approach to systematically and methodically addressing the drug shortage issue and other health and medical matters when demand on needed resources far exceeds the availability of the resources. The framework reflects five key elements of crisis standards of care protocols:

1. Ethical considerations
2. Community and provider engagement, education, and communications
3. Legal authority and environment
4. Indicators and triggers
5. Clinical processes and operations

Depicted below is the conceptual model of the framework that would be very helpful in the development and implementation of plans to mitigate the effects of the drug shortage issue even though it makes specific reference to "catastrophic disaster response". The model depicts a strong foundation of the key guiding principles, the steps needed to successfully implement a response to the problem, the pillars of the system which clearly capture the three sectors of interest (public health, EMS and hospital based emergency/trauma care) and capped with the overarching authority for oversight and, in some cases, ensuring that plan development and execution occurs.

CONCEPTUALIZING A SYSTEMS FRAMEWORK FOR CATASTROPIC DISASTER RESPONSE



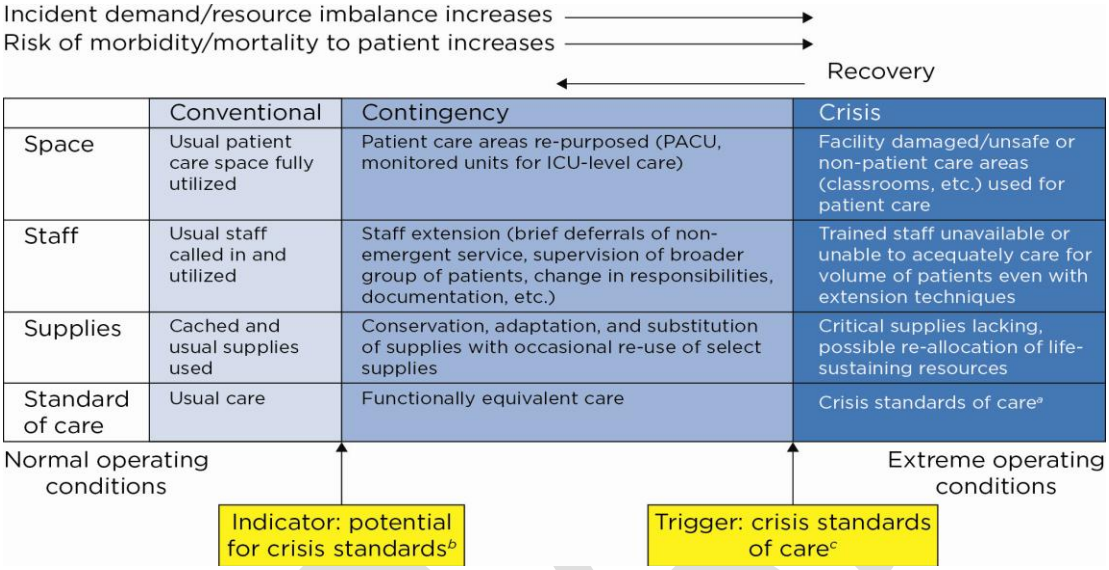
The framework also describes a very useful and adaptable continuum from conventional to crisis care, depending on the demands placed on the system and its component parts by the incident, in this case emergency care drug shortages. The three segments of the continuum are defined as follows:

> ***Conventional:*** The spaces, staff and **supplies** (emphasis added) used are consistent with the daily practices within the institution. These spaces and practices are used during a major mass casualty incident (or in this case a drug shortage situation) that triggers activation of the facility emergency operations plan.
>
> ***Contingency***: The spaces, staff, and **supplies** used are NOT consistent with daily practices but provide care that is functionally equivalent to usual patient care. These spaces or practices may be used temporarily during a major mass casualty incident or on a more sustained basis during a disaster (when the demands of the incident exceed community resources, in the case during emergency care drug shortages).
>
> ***Crisis***: Adaptive spaces, staff, and **supplies** are not consistent with usual standards of care but provide sufficiency of care in the context of a disaster (i.e. provide the best possible care to patients given the circumstances and resources available.) Crisis capacity activation constitutes a significant adjustment to standards of care.

It was the judgment of the work group that at the present time, the national EMS/emergency-trauma care system is in the ***contingency*** phase of this continuum (recognizing that there may be some regional and even facility to facility variation) and a concerted effort, through the possible use of the various

coping options presented in this paper, would be beneficial in stabilizing the shortage's impact and retarding, even preventing, the situation from escalating to the crisis phase through effective conservation, adaptation, and substitution. As visually portrayed in the graphic below, the goal is to intervene and cope early to stabilize the situation and avoid escalation of the problem (e.g. moving to the right into the "crisis" phase") which would cause more deviation from the normal/conventional standard of care.

ALLOCATION OF SPECIFIC RESOURCES ALONG THE CARE CAPACITY CONTINUUM



The IOM frame work is presented as a seven volume set of stand-alone resource manuals for all stakeholders involved in disaster response. Three of the volumes directly target the sectors of interest regarding emergency drug shortages: State and Local Government (public health), EMS, and hospitals. (http://www.iom.edu/Reports/2012/Crisis-Standards-of-Care-A-Systems-Framework-for-Catastrophic-Disaster-Response.aspx). The work group strongly recommends that use of this resource to guide planning and mitigation efforts to manage and minimize the impact of drug shortages.

The framework can be used to assist states and local jurisdictions in stabilizing the drug shortage situation and avoid escalation of the problem to the crisis stage. One key foundational element of the framework is the suggestion that state and local jurisdictions form a medical advisory committee. This committee, consisting of regional representatives from public health, emergency management, EMS, health care systems, community-based practitioners, and public safety, will be tasked with examining and developing a complete picture the current local and regional drug shortage situation. The inclusion of neighboring states in the shortage analysis will not only ensure the comprehension of the complete picture but will also assist in the development of regional approaches to coping strategies that address the drug shortage, paying close attention not to deplete the supply chain.

The medical advisory committee can also be used as technical advisors to provide analysis for potential modification of medical treatment, triage, and protocols. An example of this may involve the approval of medication alternatives due to drug shortages. The state EMS agency and/or medical director can use the subject matter expertise in the committee to determine the new medication recommendation and ensure legality. The committee can also be used to not only provide recommendations on specific

medications but can also provide state EMS agencies and other impacted healthcare entities with an understanding of their jurisdictional authority.

ACTIONABLE COPING STRATEGIES AND TACTICS-A MENU OF OPTIONS TO BE CONSIDERED TO HELP ALLIVIATE THE IMPACT OF A DRUG SHORTAGE

In the face of a shortage of critical emergency care drugs, systems, facilities and practitioners will need to promptly and responsibly act in order mitigate potential adverse consequences and provide the best possible care to patients. For many, this will be a new type of "crisis" to manage. It is also confounded and complicated by a series of legal/regulatory and institutional policy/practice barriers and considerations that must be successfully navigated with the ultimate objective of providing the best quality care to the patient while still remaining compliant with and true to the spirit of controlling laws, regulations, policies and clinical standards of care and practice.

To assist policy makers, emergency planners, and clinicians/ practitioners in this sometimes daunting task, the work group identified a series of strategies and tactics that, in their professional judgment, could be actionable and worthy of consideration. They are presented as just one resource to support ongoing planning and decision-making in this regard; they are not proffered as recommendations nor do they carry with them any formal endorsement from the participating organizations and agencies. Use of this resource should be done with conscious attention to and in the context of the prevailing jurisdictional and institutional legal, ethical, clinical and administrative doctrines. Furthermore, the options presented do not carry with them any legal advice, prioritization nor are they weighted with regard to importance or impact.

Get Ahead of the Curve-Increase Your Situational Awareness and Visibility of Supply Availability

Heavily embracing the old adage "knowledge is power", it is imperative that all three sectors increase their awareness, understanding, and visibility of the drug shortage issue, both nationally and, more importantly, locally. This is a dynamic, not static, situation. Different types of drugs will go in and out of shortage and there may also be geographic variation on the extent and duration of a shortage.

At the national, even global, level there are two highly regarded and heavily utilized resources that provide relatively real-time information on reported shortages. They are:

- The US Food and Drug Administration's Drug Shortage Program: http://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm. Here you will find an index of drugs in shortage as reported by the drug industry, resources and fact sheets for consumers and health professions, and a portal to report a drug shortage being experienced.
- The American Society of Health-System Pharmacists: http://www.ashp.org/shortages. The ASHP maintains a resource center containing a list of current and resolved drug product bulletins, as well as bulletins on drugs no longer available.

Interested parties are encouraged to periodically visit these sites for updates and utilize the various social media services available to receive information. Additionally, health care providers are reminded and encouraged to report shortages to the FDA Drug Shortage Program, particularly if they are experiencing a shortage of a drug that is not already listed on the drug shortage website.

Closer to home, planners, responders and clinicians should consider treating potential or real emergency care drug shortages as a standing element of national security preparedness and readiness and should utilize existing infrastructures and relationships of public health, EMS, and emergency/trauma care to exchange information and collaboratively plan and initiate mitigation actions, to the extent possible. This could include:

- *Advisory Committee(s)*: In order to ensure integrated preparedness efforts across jurisdictions, state and territorial health agencies receiving federal public health and health care preparedness funds, are required to establish and maintain advisory committees comprised of senior officials from governmental and nongovernmental organizations involved in homeland security, healthcare, public health, and behavioral health to integrate preparedness efforts across jurisdictions. These well-established advisory committees include senior jurisdictional officials directly responsible for the administration of Department of Homeland Security preparedness grants and ASPR and CDC preparedness cooperative agreements as well as representation from emergency medical services, emergency management, medical examiner's office, hospital association or local system, and quite often additional disciples such as legal counsel and finance, local officials, and citizens.

- *Healthcare Coalition(s)*: Healthcare coalitions exist and consist of one or more hospitals, at least one of which shall be a designated trauma center; one or more other local healthcare facilities, including clinics, health centers, primary care facilities, mental health centers, mobile medical assets, and/or nursing homes; and one or more political subdivisions. Healthcare Coalitions focus on collaboration during preparedness and develop priorities, goals, and objectives, which could also capture emergency care drug shortages.

- *Partnerships and other Standing Committees*: Additionally, many formalized partnerships exist between governmental public, healthcare and non-healthcare interested parties that provide an appropriate forum for information exchange as do other standing bodies such as Medical Coordination Centers/Committees and Regional Disaster Medical Advisory Committees.

One other way to increase situational awareness is to include drug shortage status as one of the data reporting elements in existing jurisdictional databases and dashboards (e.g., the State Medical Asset Resource Tracking Tool (SMARTT), or a "home grown" platform such as New Jersey's Hippocrates) that systematically capture, manage, display and disseminate important information on facility status, asset availability, service disruption, etc. and provide valuable decision support to public health and healthcare planners and responders. Given the potential impact of emergency care drug shortages or scarcity on national health security, if conditions worsen, field intelligence on shortage conditions should also be considered reportable to state fusion centers for information analysis and sharing.

It is also important that EMS and emergency/trauma care personnel make it known when a drug shortage situation has occurred which may have had a deleterious impact on the care and treatment of a patient. Such incidents should be immediately reported through established employer procedures and chain of command and also to the relevant jurisdictional regulatory agency, in accordance with established regulation, directives, and/or policies and protocols, when applicable. For example, one California jurisdiction requires the medical director be notified when treatment standards were alternated due to drug shortages. In turn, the medical director will inform in writing, the patient, the receiving hospital, FDA and DEA of the incident.[3] Additionally, the National Association of Emergency Medical Technicians (NAEMT), in collaboration with the Center for Leadership, Innovation and Research in EMS, has developed an anonymous system for EMS practitioners to report patient safety incidents by answering a series of questions in an online format. The purpose of the system is to collect and aggregate data that will then be analyzed and used in the development of EMS policies and procedures, and for use in training, educating, and preventing similar events from occurring in the future. This reporting system is called the EMS Voluntary Event Notification Tool (E.V.E.N.T.). For more information and to view the tool, please visit www.emseventreport.org. EMS providers experiencing drug shortage incidents having an impact on patient safety should consider reporting the details of the occurrence to E.V.E.N.T.

Remember, we all have a professional duty to anticipate, plan, and communicate.

Actions to Take to Avoid Shortages

The FDA defines a drug shortage as "a situation in which the total supply of all clinically interchangeable versions of an FDA-regulated drug is inadequate to meet the current or projected demand at the user level…"[4] Stated another way, it's not having what you need (the preferred course of treatment), in the indicated dosage and formulation, when it must be administered. Many anecdotes have been shared such as hospital administrators not learning of shortages until shipments are received with a back order "not available" notice or clinician goes on shift and discovers that what was available "yesterday" is not available "today." There are several steps EMS and hospital administrators should consider to avoid or delay shortages of preferred drugs. They include:

- *Set up "sentinels" in your inventory management system*: Have the necessary triggers and indicators properly calibrated so that you will get sufficient advanced warning of a drug that is approaching depletion with enough lead time to take action.

[3] A California jurisdiction requires its Advanced Life Support (ALS) providers to request the use of expired medications for patient care. Following Medical Director approval, the most recently expired medications are to be used for 30 days or less. Additionally, the Medical Director will inform, in writing, the patient, receiving hospital, USDA and DEA, as appropriate, that an extended expiration drug was administered during care.

[4] FDA Manual of Policies and Procedures (MAPP 6003.1, Office of New Drugs; *Drug Shortage Management,* February 3, 2012.

- *Modify purchase amounts*: Just-in-time procurement practices are very sensitive to fluctuations in product availability from manufacturers and distributors. Facilities should consider purchasing more liberal amounts of key drugs as a way to possibly mitigate some of the impacts of "no notice" shortages (benefit from a little more time to plan and initiate contingencies or possibly "ride it out" if it is a short term transient shortage.) A word of caution, ***do not hoard***. Over purchasing quantities key drugs is counterproductive given its impact on supply and will exacerbate the "have and have not" scenario. It also puts extra strain on material managers to ensure that products are used before their expiration date, should in-house demand not be in sync with the increased supply.

- *Broaden procurement options*: Facilities/systems could consider expanding their business relationships beyond their current suppliers. This may pay dividends in that end users have additional sources of product to then turn to. Group purchasing cooperatives, including larger regional collaboratives, may also be a path to explore, possibly garnering more favorable consideration from manufacturers and suppliers (preference given due to size of procurement action(s) and more favorable volume-based pricing to help with cost containment) and could also leverage the influence of existing and maturing healthcare coalitions, and possible improved material management resulting in waste reduction. Another collateral benefit mentioned is improved coordination and communication among state and private healthcare sector players. Procurement officials may also want to consider remaining in closer contact with manufacturers' representatives to get direct updates on supply availability and also to directly communicate to them the facility/system status and the level of criticality that may exist due to actual or impending shortages. Of course, there are down sides to this approach, the most obvious one being that with an insufficient, finite supply of drug(s), these approaches may provide relief to some but may increase the magnitude of the shortage on others.

- *Share*: It is quite possible that situations will be encountered where the transfer of drugs from one facility to another (or from a hospital to an EMS unit) to alleviate a facility shortage is not only necessary but feasible, intra- and interfacility-wise. In many areas of the country, EMS units may be struggling to maintain sufficient supplies of emergency care drugs necessary for advance life support. Hospitals should consider giving priority assistance to EMS units by making available caches of critical drugs that are in shortage. This option is based on the premise that proper and sufficient pre-hospital care is essential to the ultimate patient outcome and if accomplished, would lessen the burden on hospital's emergency department/trauma care team. In addition, EMS personnel, unlike physicians and hospital staff, have less latitude for alternative medication options due to scope of practice, education, and training requirements and resources. This type of mutual aid should be supported by the development of pre-event policies, procedures, and agreements between parties. The inter-facility transfer of certain drugs is also governed by state and federal regulation. As such, an examination of the prevailing and situation relevant laws and regulations should be done to ensure that noncompliant actions are not knowingly taken. The Department of Justice's Drug Enforcement Agency (DEA) does permit the inter-facility transfer of certain scheduled controlled dangerous substances between two DEA registrants as long as sufficient documentation is maintained in accordance with 21CFR13.05.11 et seq. (http://www.deadiversion.usdoj.gov/21cfr/cfr/2105cfrt.htm). For C-2 drugs a form # 222 must be completed and for C-3 through C-5 drugs, an invoice must be completed to document the transaction[5]. Facilities considering this approached are strongly

[5] November 14, 2012 telephonic conversation with the DEA Office of Drug Diversion, Liaison and Policy Unit

encouraged to consult with this local DEA office prior to initiating transfers (http://www.justice.gov/dea/about/Domesticoffices.shtml).

Tapping into Existing Federal and State Stockpiles

Utilizing existing "disaster" stockpiles affords one other option for very limited, temporary relief of a drug shortage. The Strategic National Stockpile (SNS) is a national repository of antibiotics, chemical antidotes, antitoxins, life-support medications, IV administration, airway maintenance supplies, and medical/surgical items. The SNS has two main features: the 12 hour "push pack" and the vendor managed inventory (http://www.cdc.gov/phpr/stockpile/stockpile.htm). A companion program, CHEMPACK, provides forward placement of caches of chemical antidotes to hospitals and EMS. This program is jointly administered by CDC and the state and territorial health departments. A formal request must be made by the jurisdiction and permission granted by CDC before SNS assets can be accessed. Some states also maintain supplemental supplies of medical supplies referred to as state stockpiles. Recognized benefits of using disaster stockpiles include: they are readily available, it addresses the immediate patient safety needs, they are either pre-deployed or can be made available within 12 hours, and they are largely under government (public sector) control ensuring equitable and objective allocation. Limitations include not a very good correlation between SNS formulary and emergency care drugs typically in shortage so not much relief should be anticipated through this route, restocking challenges to ensure that the SNS is readily replenished for future, potentially more serious emergencies, and complexity of billing for costs of the drug since facilities are not allowed to charge for equipment and supplies drawn from the SNS. It should be mentioned that on March 16, 2012, CDC's Division of Strategic National Stockpile issued a memorandum to clarify procedures for accessing diazepam and atropine sulfate included in the CHEMPACK containers forward deployed across the nation. In face of the reported shortage, CDC did grant permission to use CHEMPACK countermeasures under the following conditions:

1. The removal of stockpile material is for a life-saving measure.
2. An alternative means of procurement is not available in a timely manner to support a medical emergency.
3. Product removed and used from CHEMPACK cache cannot be charged to patient.
4. Product removed by the case(s) only. Any unused portion of product will not be returned to CHEMPACK container.

EMS and hospital emergency planners are encouraged to discuss this option with their respective state or territorial Strategic National Stockpile Coordinator.

Establish and Institutionalize a Suite of Contingencies for Clinical Care

EMS and emergency/trauma care professionals must be prepared with a "Plan B" should they face a drug shortage, despite their best efforts to avoid one. This plan should serve as a reliable decision-support tool by clearly articulating the various options, an indication of priority or criticality, conditions by which they will be executed, and other operational considerations. One such guideline developed in California is shown below and was discussed during the work group meeting in July. While the work group does not endorse this specific tool, it does, however, illustrate an approach of careful examination

and consideration and one way to facilitate structured and informed decision-making and action when a drug shortage coping intervention needs to be initiated.

Drug Shortage Mitigation Algorithm
(Prioritized by Patient Safety)

Decision Point	Comment	Intervention/Contingency
1	Baseline SOP	None: continue with current Policies / Procedures
2a	Does not require Medication changes	Utilize Expired Medications
2b	Does not require Medication changes	Utilize Compounded Medications
2c	Does not require Medication changes	Discontinue use of Medication for interventions with questionable utility
3	Requires New Dose Calculations & Training	Utilize the Same Drug with a Different Concentration
4	Requires New Dose Calculations & Training	Utilize the Same Drug given via a different route (oral vs. IV)
5	Requires New Dose Calculations & Training	Utilize a different drug from the same class (versed vs. valium)
6	Requires New Dose Calculations & Training	Utilize a different drug from a different class (Phenergan vs. Zofran)
7	Does Not Require Medication Changes	Stay in Service without the Medication (Failed Mitigation)

As can be seen from examining this algorithm, a number of interventions or contingencies have been listed which were also identified by the work group as being potentially feasible and actionable. A brief discussion of each of these contingencies follows.

- *Using Expired Medications*-The work group held a fairly strong opinion that under proper conditions and if clinical circumstances dictated, using out of date drugs would be one potentially viable option, especially if the clinician was faced with the decision of "using an expired drug vs. no drug at all", taking into account the effectiveness of the drug and the

seriousness of the patient's condition. The work group felt that favorable data exist for many classes of drugs regarding stability and efficacy beyond expiration, and that this option provides dosing consistency, that the drug would be readily available thus avoiding delays in administration, and would generally aid in reducing unnecessary waste of a limited resource. The problems associated with this approach include safety and effectiveness issues, potential regulatory non-compliance issues, public perception and mistrust, fear of potential liability, and the impracticality of facility's sponsoring and conducting their own product stability tests to determine the acceptability of the expired drug.

When considering this option, it is important to have a full understanding of the fairly complex regulatory framework, both at the federal and state levels, which should be factored in to your assessment before this approach is initiated. Federal law and FDA regulations require that drug product manufacturers assign an expiration date for drugs marketed in the United States. For drugs approved by the FDA, the expiration date is determined based on FDA review of stability data from studies performed by the manufacturer. These studies are designed to show that a properly stored drug does not degrade to the point that it no longer meets its stability specifications within the labeled expiry period, that is, it can be expected to remain safe and effective for the labeled period of time when properly stored.

Experience has shown that, in some cases, drug products may remain stable beyond their labeled expiration date. For instance, in some cases a drug product manufacturer may have stability data which supports a longer shelf life than what is initially established. In limited instances, where adequate stability data can be obtained, FDA has exercised enforcement discretion on a case-by-case basis to enable distribution and use of a product beyond its labeled expiration to alleviate drug shortages of medically necessary products. In these cases, FDA reviewed stability data showing that the product would remain safe and effective for a certain time frame beyond expiry, and Dear Healthcare Provider letters were sent out to notify practitioners of the expiry extension and the overlabeling of product (reflecting a revised expiration date). FDA cannot, however, support an "across the board" extension for all products, or particular classes or categories of products in absence of such data.

In addition to FDA jurisdiction and interests, the Center for Medicare and Medicaid Services (CMS), regulations, 42 CFR 482.25 (b) (3), states "Outdated, mislabeled, or otherwise unusable drugs and biologicals must not be available for patient use and the Joint Commission's Medication Management Standards requires that a hospital safely store medications (Standard MM.03.01.01) its Element of Performance 2 requires that hospitals safely store all medications according to the manufacturers' recommendations or in the absence of such recommendations, do so in accordance with a pharmacist's instructions. It is the Joint Commission's interpretation that if an expired medication is present (e.g. "stored") in a covered facility, even if sequestered from other "in date" medications, it would be a violation of the above cited Commission standards since it is available for use.

Because State pharmacy laws also govern the dispensing and dating of pharmaceuticals, they should also be considered in any approach that involves use of medicines past their labeled expiration date. In particular, state/local professional (e.g. medical, pharmacy, nursing, etc.) boards should be consulted. Some states have exercised its regulatory discretion authority to relax or waive regulations to allow providers such as EMS units to use expired medications

under certain conditions. For example, the state of Utah has approved an expiration date extension program for critical medications in short supply. Under this procedure, approved medications are authorized to be used for up to six months following their labeled expiration. The protocol allows each Utah EMS agency and its medical director the discretion to approve or deny the use of expired medication use in a shortage. [6]

Regarding the stability of drugs beyond its expiration date, drug product stability characteristics can differ from product to product. Product stability is also dependent on storage conditions (e.g., light, temperature, humidity, etc.), with some drugs more sensitive than others. In the case of emergency care drugs, storage conditions might vary significantly (e.g., storage in an ambulance compared to storage in a pharmacy). In the absence of acceptable stability data and information about product storage, the strength, quality, and purity of an expired product at the time of use cannot be assured. That being said, facilities faced with the challenge and choice of using an expired drug when medically necessary should, to the fullest extent possible, make an evidence-based decision. Drug manufacturers should be contacted for beyond expiration product stability data. If this cannot be accomplished, peer reviewed journals and compendia should be consulted. Two that are widely used are: 1) the American Hospital Formulary Service (AHFS) *Drug Information*, 2) Trissel's 2 *Clinical Pharmaceutics Database*, 3) Trissel's *Handbook on Injectable Drugs*, and 4) the *King Guide to Parenteral Admixtures*[7].

When considering this option:

- Inventory management practices should be examined and refined to minimize the amount of expired drugs on hand
- Determine the regulatory requirements of, and level of enforcement discretion being exercised by your jurisdiction's professional board(s)
- Establish clear documented institutional guidance and authority governing this practice
- Contact the drug manufacturer to learn more about the stability characteristics as a means to make a more informed decision on a drug by drug basis
- Maintain patient record documentation including a reference to a clinical assessment determination of medical necessity and that patient benefit clearly outweighed known or theoretical risk(s)

- *Using Compounded Medications*-The increased use of compounding pharmacies has been identified as one other means to increase drug availability. It too can result in immediate availability of a product that is not commercially available and is especially useful as it pertains to addressing the individual medical needs of certain special populations. The disadvantages identified include product safety and efficacy concerns due to poorly compounded drugs as evidenced by the recent multistate fungal meningitis outbreak associated with mass produced commercially compounded drugs

[6] Utah Bureau of EMS and Preparedness Drug Shortage Protocol October 2012

[7] Medication Safety Alert: "Results of Our Survey on Drug Storage, Stability, Compatibility, and Beyond Use Dating", Institute of Safe Medication Practices; March 22, 2012

(http://www.fda.gov/Drugs/DrugSafety/FungalMeningitis/default.htm#), increased expense, a shorter shelf life possibly resulting in potential wastage, and it is an option not widely or readily available to all (regional and geographic limitations). Other general concerns expressed by the work group worthy of consideration when exploring this option were potential liability due to human error in the compounding process resulting in impact on patient safety, the current framework of state regulatory oversight and FDA policy regarding this process and the concern that the compounded product is not produced in full accordance with current good manufacturing practices (CGMP) for drugs. If this avenue is being considered, it is strongly recommended that facilities consult with the State Board of Pharmacy having jurisdiction over the commercial compounding pharmacy of interest to ascertain the current level of regulatory oversight provided (e.g. adequacy of state regulations and inspection and enforcement program) and the compounder's compliance track record before making a decision. A list of the state boards of pharmacy contacts can be found at the National Association of Boards of Pharmacy website, http://www.nabp.net/boards-of-pharmacy/.

New Jersey has developed guidelines to assist its specialty care, mobile intensive care and air medical units in needing waivers associated with mandated on-board medications. Documentation must demonstrate a multi-tiered good-faith effort to obtain the needed medications. As an additional requirement, the agency must have used compounding as an alternate for at least 30 days with no indication of resupply in the near future. [8]

- *Conservation Including Tiered Utilization (Priority Given to Select Medically-necessary Patients), Discontinued Use of Medical Intervention with Questionable Utility, and Adjusting Dosage concentration ("titrate to effect") and/or route of delivery*-This approach allows for prudent conservation of a scarce resource with the goal of preserving sufficient preferred treatment courses for life threatening situations and/or special medical populations where treatment alternatives are limited or non-existent. It also allows treatment with the same drug thus avoiding the need to pursue substitution (discussed below). Potential areas of concern associated with this approach include managing perceptions of inequity, the need to have a strong ethical framework behind and supporting treatment decisions, sub-optimal treatment, and a fear of increased exposure to liability and potential litigation.

- *Substitution: Utilizing a Different Drug from the Same Class or a Different Drug from a Different Class*-By expanding your formulary of both in-class and out-of-class drugs, this option provides an alternative path for treatment when the preferred drug is not readily available or is being reserved for more medically-critical situations. In general same class drugs would be preferable to drugs from a different class as this should minimize differences in side effect profiles and staff training requirements. The benefit of this approach is that it does allow for timely treatment rather than delaying or forgoing drug administration. It may also reduce the potential from inappropriate hoarding of first order medications that are in limited supply. Drawbacks to this option that must be seriously considered are the possible lack of practitioner familiarity of and

[8] Waiver issued for New Jersey Administrative Code 8:41-6.1-014 on July 1, 2012

professional competence with rarely or never before administered 3rd and 4th line drugs possibly resulting in medical errors and jeopardizing patient safety (including side effects and drug interactions), the imperative need for additional clinician education and training that carry with it a cost and commitment of time, and burden of increased procurement costs and storage space and expense to accommodate the expanded formulary.

Massachusetts allows for substitute concentrations when typical dosage forms are unavailable. All temporary substitutions must be approved by the service provider's affiliate hospital's medical and pharmacy directors. The protocol requires that the use substitute deliver the standard amount of active medication and be packaged to prevent medication errors as best possible. [9]

- *Sparing: Using Multi-dose Vials of Medications on Multiple Patients*-When a EMS Unit or healthcare facility is faced with the dilemma of not having sufficient single-use vials of a scarce medication or not have any at all; consideration may be given to using multi-dose vials of that medication for multiple patients. Like some of the other options, this will result in a readily available drug of choice and could decrease costs and product waste. Some of the disadvantages or at least challenges that must be overcome are the potential for product contamination, dosing errors, potential for diversion, establishing guidelines and improved practices for proper vial storage once opened and maintaining increased documentation requirements.

Establish a Culture of Awareness and Understanding and a Discipline of Inclusion and Integrated Response to Drug Shortages

Drug shortages impact all levels and components of a healthcare enterprise (i.e., executives, operations, clinical care, communications and outreach, and the healthcare consumer.) Every effort should be taken to prevent being caught short or taken by surprise. Furthermore, the EMS and emergency/trauma care sectors should seize every opportunity to leverage existing resources and infrastructures to support drug shortage mitigation and coping strategies. Ideas generated by the work group include:

- *Proactively maintain and share with all who have a need to know a real-time list of drugs in shortage*: This will undoubtedly allow clinicians to anticipate possible practice adjustments and consider alternative treatments prior to an emergent need, will achieve better than just-in-time (or "at the moment") notification of the shortage, facilitate resource sharing to the extent possible, and inform future policy decisions. It would be useful to have a pre-designated list of suggested substitutions collaboratively developed by the pharmacy and medical staffs. A brief summary of side effects and contraindications should also be listed for those substitution medications that are uncommonly used.

- *Optimize use of decision-support tools:* Modify electronic medical records (EMRs) to provide and capture important information on alternative drug treatment regimens during times of

[9] Memorandum from Massachusetts State EMS Director dated January 17th, 2012.

shortage. Expanding data sets could also be considered as a way to record use of alternative treatment modalities resulting from a drug shortage which could have value as it pertains to potential concerns over malpractice and other liabilities, inform future policy-making, support future research, and serve as one means to trigger escalated (or deescalated) contingency planning.

- *Address drug shortage Issues as a standing part of the curricula for in-service training and continuing education activities for nurses, physicians, pharmacists, and EMS personnel-* Expanded education and training is considered the lynchpin to successful implementation of any and all of the coping strategies identified in this paper. It is proactive and progressive; it will minimize confusion, frustration, and conflict; and will reduce medical errors and adverse patient outcomes. It will also build stronger collaboration between hospital and pre-hospital care providers. The development and sharing of model protocols and training modules would result in increased consistency across healthcare systems and geopolitical jurisdictions, save time and improve coordination, and, with more rigorous development, could contain extremely valuable and helpful evidence-based options. Additionally, the engagement of medical specialty organizations in communicating recommendations of preferred alternative medications when the primary or preferred drug is unavailable enhances patient safety especially for patient populations with functional or other special needs.

- *Institute awareness level training for the non-clinician:* Policy and decision-makers at the executive and senior management/operations level must have a full appreciation of the impact drug shortages will have on a facility or operation. This awareness will provide them with the requisite sensitivity to the issue and empower them to support, maybe even champion, appropriate policy development, procurement actions, and advocacy efforts.

- *Engage the public:* It is important for the public to receive timely, accurate and objective information on the status of the emergency care drug shortage issue and its potential impact on patient care and safety. Too much is at stake to allow public trust to erode simply as a result of the inability, unwillingness, or failure to communicate and help the public understand the issue, recalibrate their expectations under these conditions, and if necessary, make informed decisions as a healthcare consumer. Be “upfront” about this issue and let the public know what your facility/unit is doing to cope with and counter the shortage with the assurance that patient comfort and safety is the paramount consideration. Volume 6 of the aforementioned Crisis Standards of Care Framework addresses Public Engagement and contains very useful guidelines and templates to assist in this important activity.

Regulatory Considerations

A discussion on drug shortage issues would not be complete without a brief review of the state regulatory implications. It is vital that regulated entities such as EMS providers and hospitals maintain direct frequent contact with their jurisdictional regulatory bodies such as the department of public health and boards of medicine and pharmacy to discuss the impact caused by the shortage, difficulties in complying with applicable rules and regulations, and the potential need for regulatory relief to allow for contingencies to be operationalized when it is determined to be in the best interests of the patient.

Conversely, state regulatory agencies, after validating the "ground truth", should consider using proper enforcement discretion and other authorized means to provide assistance in the form of regulatory relief when the benefits of such relief (e.g. temporary suspension or modification or specific requirements) is determined to outweigh the perceived risk. Two specific areas of interest include the authorized use of expired drugs and waiving the par requirements for medical caches during times of document shortage. Regarding the former, many state regulatory agencies do not have the authority to issue a blanket waiver, nor would it be prudent to do so, to allow for the use of expired medications. They will, however, use discretion before taking an enforcement action if the attempts to acquire the subject drug(s) are documented properly by the EMS provider. For example, in Texas, the state regulatory agency requires providers to have a statement from their medical director which will demonstrate to the department that the medical director is aware of the situation: *"If the department receives a complaint that a provider is using expired drugs or expired drugs are found on an ambulance during an inspection, the department will require the EMS organization to provide documentation from the manufacturer and the provider's medical director regarding the shortage of the specific drug(s) before considering an enforcement action. DSHS is recommending that the documentation is on any ambulance that has expired drugs approved by the Medical Director."*[10]

Arizona[11] and Tennessee [12] have also used discretion for would-be citations issued during inspections. Arizona will allow the suspension of a citation during inspection if the EMS agency provides documentation showing a good faith effort to obtain the needed medications with no success. If the request meets the required documents, the EMS Bureau will not cite the deficiency for 90 days. Tennessee also requires good faith effort documentation. In addition, if a therapeutic equivalent substitution is written by the Medical Director, the new protocol must be placed in each unit's onboard protocol book for reference.

In Closing…

It is our sincere hope that this collection of peer-generated suggestions for coping with the ongoing emergency care drug shortage issue will be of assistance to you and your facility as you continually attempt to mitigate its consequences. It is also our plan to periodically update this document as more is learned about the impacts of the shortage and an evidence-base for impactful coping strategies and tactics is developed. As such, we welcome your feedback on the utility of this guide and suggestions for enhancement and improvement. Additionally, we hope to soon establish a compendium of resources from the field that can be shared among the public health, EMS, and emergency/trauma care community of practice. All comments and submission of candidate resources should be forwarded infocenter@astho.org .

[10] Statement found on the Texas Department of Health Services website: http://www.dshs.state.tx.us/Layouts/ContentPage.aspx?PageID=35824&id=3979&terms=drug+shortage+statement

[11] Arizona Guidance Document 104-PHS-EMS; Drug Shortages http://www.azdhs.gov/diro/admin_rules/guidancedocs/GD-104-DrugShortages.pdf

[12] Tennessee memo from State Medical Director and EMS Director to all EMS Service Directors and Medical Directors

Appendix A

State Resources

Citation Waivers

Arizona

- State of Arizona EMS and Trauma System Drug Shortages
  http://www.azdhs.gov/diro/admin_rules/guidancedocs/GD-104-DrugShortages.pdf

Tennessee

- Memo from State Medical Director & State EMS Director to Service Directors on National Drug Shortage, Jan. 20, 2012

Texas

- Department of State Health Services Statement
  http://www.tmb.state.tx.us/news/press/2012/120224.php

Expiration Date Extension

California

- Emergency Extension of Expiration for Selected Field Medications (from unnamed local jurisdiction in California)

Utah

- Utah EMS Medication Shortage Procedure: For emergency medication use up to six months beyond labeled expiration date

Medication Substitutions

Maryland

- Emergent Addition of Diazepam for Active Seizure Management, May 18, 2012
- Emergent Addition of Fentanyl to 2012 Protocols, June 12, 2012
- Altered Mental Status: Seizures (new May 2012)
- Updated Bucking Dose for Ketamine
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Massachusetts

- Advisory: Immediate change to Paramedic-level ambulance required medication list to make Morphine optional, Nov. 15, 2011

- Memo: Drug Supply Shortages: D50, furosemide and substitutions in temporary shortages, Aug. 10, 2010
- Memo: shortage of Diazepam/Lorazepam and Magnesium Sulfate, Sept. 1, 2011
- Memo: Drug Supply Shortages: Epinephrine 1:10,000 and Morphine Sulfate, June 30, 2010
- Memo: shortage of Midazolam and other injectable Benzodiazepines, Jan. 25, 2012
- Memo: shortage of Metoprolol, Jan. 17, 2012
- Memo: shortage of Ondansetron shortage, Jan. 12, 2012

Michigan

- Michigan Guidance Email ASPR Drug Shortage Mitigation, July 11, 2012
- Michigan Medication Shortage Protocol

New Jersey

- Medication Waiver Extension
- New Jersey OEMS Guidance Email, July 10, 2012

Ohio

- Announcement of Drug Shortages, Mar. 1, 2012

Other

Virginia

- Drug Kit Statute 18VAC110-20-500, State of Virginia http://leg1.state.va.us/cgi-bin/legp504.exe?000+reg+18VAC110-20-500

Additional Resources

- Institute for Safe Medication Practices; Medication Safety Alert-"Weathering the Storm: Managing the Drug Shortage Crisis", October 7, 2010 (includes a Failure Mode and Effects Analysis tool) http://search.ismp.org/cgi-bin/hits.pl?in=517791&fh=80&ph=1&tk=cHEez%20HEezyq%20qnWEPczg%20qnWEPczgyq%20HEezq%20qnWEPczgq&su=kKQQwHgg___.VbPw.upWg%2F%3F_bk%3FQQ%3FpbgA-rQ%3F-Ap%3FgApQV-k%3Fbg20101007.Abw&qy=ypfMQ%20jrXfsuQb&pd=1)
- Archives of Internal Medicine; "Coping with Critical Drug Shortages: An Ethical Approach for Allocating Scarce Resources in Hospitals, *Arch Intern Med. 22012; ():1-6. Doi: 10.1001/archintermed.2012.4367;* Rosoff PM, et al. (provides 10 accountability for reasonableness steps)
- American Society of Health-System Pharmacists; "ASPH Guidelines on Managing Drug Shortages", Am J Health-Syst Pharm; 2009; 66: 1399-406 (http://www.ashp.org/DocLibrary/Policy/DrugShortages/ASHP_shortage_guide09.pdf)