Report on the Department of Defense Pharmaceutical Supply Chain Risks

Office of the Under Secretary of Defense for Acquisition and Sustainment

November 2023

Pursuant to Section 860(a) of the National Defense Authorization Act for Fiscal Year 2023 (Public Law 117-263)

The estimated cost of this report or study for the Department of Defense is approximately $906,253 for the 2023 Fiscal Year. This includes $858,372 in expenses and $47,881 in DoD labor.

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CONTENTS

Executive Summary

Section 860(a)(3) of the James M. Inhofe National Defense Authorization Act (NDAA) for Fiscal Year (FY) 2023 (Public Law 117-263) requires the Under Secretary of Defense for Acquisition and Sustainment to submit a report regarding the following information relative to the Department of Defense (DoD or Department) pharmaceutical supply chains:

> (A) existing information streams, if any, that may be used to assess the reliance by the Department of Defense on high-risk foreign suppliers of drugs;
> (B) vulnerabilities in the drug supply chains of the Department of Defense; and
> (C) any recommendations to address—
>> (i) information gaps identified under paragraph (2); and
>> (ii) any risks related to such reliance on foreign suppliers.

This report fulfills this requirement and provides an overview of the pharmaceutical supply chain roles and responsibilities, information streams, analysis and methodology, results, and future actions.

The Department of Health and Human Services (HHS) is responsible for industrial base management of U.S. pharmaceutical supply chains. DoD is supported by the defense medical industrial base and provides medical treatment and care for the U.S. Military. The Defense Health Agency (DHA) manages the personnel, facilities, treatment protocols, and requirements of the military healthcare system. The Defense Logistics Agency (DLA) serves as DoD's most significant pharmaceutical procurement organization to fulfill the military healthcare system material requirements. DLA procures approximately $5.4 billion annually which represents approximately 2 percent of the U.S. commercial marketplace. Out of 17,555 total generic sequence numbers (GSN) that HHS has identified for the U.S. marketplace, DLA procures 6,589 (approximately 37% by drug family) annually for use by DoD.

In alignment with Executive Order (EO) 14017, Improve Resiliency of Key American Supply Chains and EO 13953, Address Threat to Domestic Supply Chain from Reliance on Foreign Adversaries, DoD is developing a supply chain risk management (SCRM) framework to help ensure coordination and communication within DoD as well as with other federal agencies. As part of this effort, and to address DoD pharmaceutical supply chain management requirements more effectively, DoD is developing and sustaining the Pharmaceutical Provenance Solution (PPS) which will provide a means and method to identify active pharmaceutical ingredients (API) with associated risks and dependencies. This is a developing program that will require continuous monitoring and information updates to sustain as a relevant source of risk and dependencies. The PPS effort will be incorporated into the general DoD SCRM Framework to allow the Department to consider specific pharmaceutical sourcing risk considerations as part of SCRM analysis.

The findings in this report are based upon the results of an initial DoD pharmaceutical supply chain analysis. DoD analyzed 1,744 GSNs (drug families), which equates to 12,917 national drug codes (specific drugs), or about 10% of the total U.S. marketplace. The pharmaceuticals analyzed are identified in the Food and Drug Administration (FDA) Essential Medicine List. Although this

analysis provides a view of essential medicines, it does not provide a complete picture of the DoD risk assessment for all pharmaceutical supply chains. DoD is scheduled to address the balance of DoD generic sequence numbers in calendar year 2023 and beyond. Additional efforts will be required by HHS to identify risks and vulnerabilities in the remaining 63% of the U.S. commercial marketplace that is for other than DoD utilization.

Based on the 1,744 GSN analyzed in this report, DoD has a high dependence on foreign material and trade agreements to maintain current pharmaceutical capabilities. Although 28% of the APIs are sourced from North America and are considered at least moderately secure, 5% are sourced from China, and 22% are unknown. In total, DoD has identified that 54% of the DoD pharmaceutical supply chain is considered either high or very high risk, with dependency on non-Trade Agreements Act (TAA) compliant suppliers, sourcing from China and India, or unknown.[1]

DoD is using the findings from PPS to develop internal mitigation strategies. Expansion of PPS within the 2023 calendar year will include 539 GSNs critical to DoD operations in the event of armed conflict requiring surge capability, 1,829 GSNs representing the balance of the Joint Deployment Formulary (JDF), and 665 GSNs representing the top high-volume drugs purchased by DLA annually. Additionally, DoD intends to share the information with HHS to enable management of the industrial base, thereby assuring national security through the health and readiness of DoD.

In addition to increasing information sharing, DoD intends to pursue the following steps to help address and mitigate the supply chain risks identified in this report. These actions target short-, mid- and long-term goals:

1. DLA will continue to work with the Military Services and other supported DoD Components and recommend/facilitate transition to TAA-compliant viable therapeutic alternatives.

2. DLA will continue to enhance event mapping capability in PPS to anticipate supply disruption and work to validate sources of supplies/production capacity from industry.

3. DLA will continue to support domestic manufacturing supply and partner with the FDA and other Federal stakeholders to compel industry to provide the necessary business intelligence to determine the source for the finished drug, API and key ingredients acquired by the federal government.

Utilizing the identified risks coupled with the SCRM framework, DoD also intends to develop needed mitigation strategies to address sourcing and dependency risks associated with the 1,744

[1] DoD recognizes that country of origin determinations for pharmaceutical ingredients is a nuanced and fact-specific inquiry. For the purposes of this report, the term "TAA (Trade Agreement Act) Compliant" means that the sources of both finished pharmaceuticals and APIs or key ingredients are U.S.-made or a qualifying country or designated country item and API. The term "TAA Non-Compliant" for purposes of this report does not include application of the definition of U.S.-made end product as defined in Defense Federal Acquisition Regulation Supplement (DFARS) clause 252.225-7021. If the API or key ingredients have not been substantially transformed in the U.S., a qualifying country, or designated country, then the item is "TAA Non-compliant" for the purposes of this report.

GSNs referenced in this report. Additionally, this information will be provided to the HHS Joint Supply Chain Resilience Working Group (Joint SCRWG) to facilitate inter-departmental communications and enable HHS to manage the medical industrial base.

With the strict focus of the DoD pharmaceutical requirements to review the essential medicine lists for the JDF, the scope of this analysis looks to explore risk exposure due to availability. This analysis utilizes the DoD's newly established effort through the taxonomy to measure the identified risks and vulnerabilities from lines of effort of acquisition and sustainment. From the identified vulnerabilities and gaps, DLA makes the recommendation for the Administration and Congress to work together to develop, enact, and enforce legislation that compels all manufacturers of pharmaceuticals sold in the U.S. to provide the FDA with definitive information on the production location of all their finished drugs and the source of all APIs and key ingredients, and the percentages of APIs and key ingredients coming from each source, for each lot of drugs they produce. In turn, the FDA should array and store this sourcing data in an appropriate repository and make it available to all Federal stakeholders responsible for assessing and mitigating vulnerabilities to the nation's pharmaceutical supply chain.

Background

DoD operates many supply chains fulfilling requirements through the acquisition, maintenance, transportation, storage, and delivery of materiel. DoD also manages materiel returns, movement of reparable materiel to and from maintenance facilities, and ensures the exchange of information among customers, maintainers, supply chain managers and suppliers. Identifying and managing risks is an important function within these processes to maximize the security, integrity, and uninterrupted flow of materials, products, and services. Management and mitigation of risks is largely conducted within respective elements of DoD, thus may not always result in a holistic or systematic approach. DoD recognizes the limitations of a non-coordinated approach and is taking action to develop a deliberate, holistic, and coordinated construct to managing the disparate risks associated with the supply chains of the defense industrial base (DIB). The risks within the DoD and DIB supply chains include counterfeit items, diminishing manufacturing sources and material shortages (DMSMS), obsolescence, supply chain disruptions, cyber vulnerabilities, foreign sourced components, foreign investments, financial distress, and sourcing of critical technologies from entities within or associated with potentially adversarial nations. This approach to SCRM will enable cross-functional coordination and sharing of common supply chain information or initiatives across the myriad DoD organizations managing risk through use of a common supply chain risk terminology and data sharing.

The first year of DoD's coordinated effort resulted in a risk framework and taxonomy from examination of eight lines of effort including: acquisition, sustainment, intelligence and security, industrial base capabilities, installations and critical infrastructure, technology protection, cyber, and information and communications technology. Phase II of this effort encompasses refining and developing the DoD supply chain ecosystem and incorporating additional lines of effort such as transportation, pharmaceutical/medical, environment, agriculture, data analytics, and chemical. Phase II also includes the integration of metrics, climate, and operational considerations.

Pharmaceuticals are one element of DoD's effort to understand risks, dependencies, and vulnerabilities present in the global manufacturing and distribution supply chains. Pharmaceuticals are used to enable DoD's treatment and care of the members. Pharmaceuticals are comprised of many ingredients including APIs. An API is the component of an over the counter (OTC) or prescription medication that produces intended health effects. Combination therapies have more than one active ingredient, each of which may act differently or treat different symptoms.

HHS is responsible for industrial base management of the U.S. pharmaceutical supply chains. DoD is supported by the defense medical industrial base in providing medical treatments and care for the U.S. Military. DLA is the most significant pharmaceutical procurement arm for the DoD, procuring approximately $5.4 billion annually which represents about 2% of the total U.S. commercial pharmaceutical market.

In alignment with statutes, regulation, and policy, the DoD is pursuing methods to positively identify the source of APIs and dependencies. To accomplish this, DoD developed PPS to identify sources of supply, dependencies, and risks. PPS was developed as a Small Business Innovation Research project concluding in April 2023 and transferred to sustainment through a General Services Administration contract. PPS uses a third-party secure, web-based platform that automatically maps all known suppliers of drug ingredients and chemical precursors. It assists with providing persistent situational awareness, a common operating picture, and early warning of risks

and potential supply disruptions. PPS additionally provides certain insights into supplier risk, product risk, formulary risk, active and inactive pharmaceutical ingredients, known n-tier suppliers, countries of origin, and TAA compliance. PPS also accounts for attributes for each drug including strength, dosage form, pharmacologic category, and packaging information.

DoD recognizes that country of origin determinations for pharmaceutical ingredients is a nuanced and fact-specific inquiry. For the purposes of this report, the term "TAA Compliant" means that the sources of both finished pharmaceuticals and APIs or key ingredients are U.S.-made or a qualifying country or designated country item. API. The term "TAA Non-Compliant" for purposes of this report does not include application of the definition of U.S.-made end product as defined in Defense Federal Acquisition Regulation Supplement (DFARS) clause 252.225-7021. If the API or key ingredients have not been substantially transformed in the U.S., a qualifying country, or designated country, then the item is "TAA Non-compliant" for the purposes of this report.

RISK, INFORMATION STREAMS, AND METHODOLOGY

The primary focus of this report is the domestic pharmaceutical supply chains dependance on foreign sources. DoD uses a "just-in-time" ordering concept that is prevalent throughout the commercial marketplace and does not store additional finished drug products. Therefore, supply disruptions, such as transportation delays, adversarial actions, or other events could cause a drug shortage that impacts operations.

There are multiple information streams and data sources that may be used to analyze APIs. Currently, PPS includes the following information streams, although this list may expand or change subject to data availability and cost:

- American Society of Health System Pharmacist Drug Shortage Database
- Food and Drug Administration Drug Shortage Database
- United States (US) Pharmacopeia Database
- Food and Drug Administration Drug Data Resource
- Supply Dynamics Explore Rx

|*Note: Each organization defines drug shortages and reports them differently.*

DLA utilized PPS to examine the pharmaceuticals on the FDA's Essential Medicine List. DLA reviewed a total of 211 Essential Medicines and Medical Countermeasure items including fractionated plasma products, antivenoms and volume expanders. DLA excluded blood products, medical devices, and non-pharmaceutical items from the list.

The resultant 211 drugs equated to 1,744 GSNs, a drug classification system that groups together pharmaceutical products having the same ingredients, route of administration, drug strength, and dosage form.

DLA's analysis of the 1,744 GSNs resulted in a total of 12,917 National Drug Codes (NDC). The NDC is a unique number assigned to identify specific drugs in the US. DLA used the total NDC count as the denominator to calculate the percentages it provides in the results section below.

RESULTS

- Percentage of pharmaceuticals with an API domestically sourced in the U.S.
  - **25% (3,272 NDCs)**
- Percentage of pharmaceuticals with an API sourced to Canada and Mexico
  - **3% (345 NDCs)**
- Percentage of pharmaceuticals with an API sourced to TAA compliant countries outside of North America.
  - **18% (2,373 NDCs)**
- Percentage of pharmaceuticals with an API sourced from India.
  - **26% (3,349 NDCs)**
- Percentage of pharmaceuticals with an API sourced from China.
  - **5% (650 NDCs)**
- Percentage of pharmaceuticals with an API from other non-TAA compliant country.
  - **1% (108 NDCs) includes Brazil, Jordan, Malaysia, and Thailand**
- Percentage of pharmaceuticals with an Unknown for its API country of origin.
  - **22% (2,820 NDCs)**

Using the results above, DLA developed a Hierarchy of Drug Security as outlined below. In its approach to gauge the risks associated with the sources of drugs, APIs and key ingredients required by DoD, DLA developed an ideal sourcing hierarchy. This hierarchy is outlined in Figure 1 of the report.[2] Given no other limitations, DLA's preference for all drugs, APIs and key ingredients would come from the following sources in the priority/order presented:

1. US Domestic sources.
2. Sources in the Americas (Canada & Mexico).
3. TAA-Compliant sources outside the Americas.
4. Non-TAA compliant sources except for China.
5. China

- Most Secure (U.S. Only):
  - Multiple domestic manufacturers; use of domestic APIs.
  - **25% (3,272 NDCs).**
- Moderately Secure (Canada and Mexico):
  - Multiple manufacturers in North America; APIs sourced in North America.

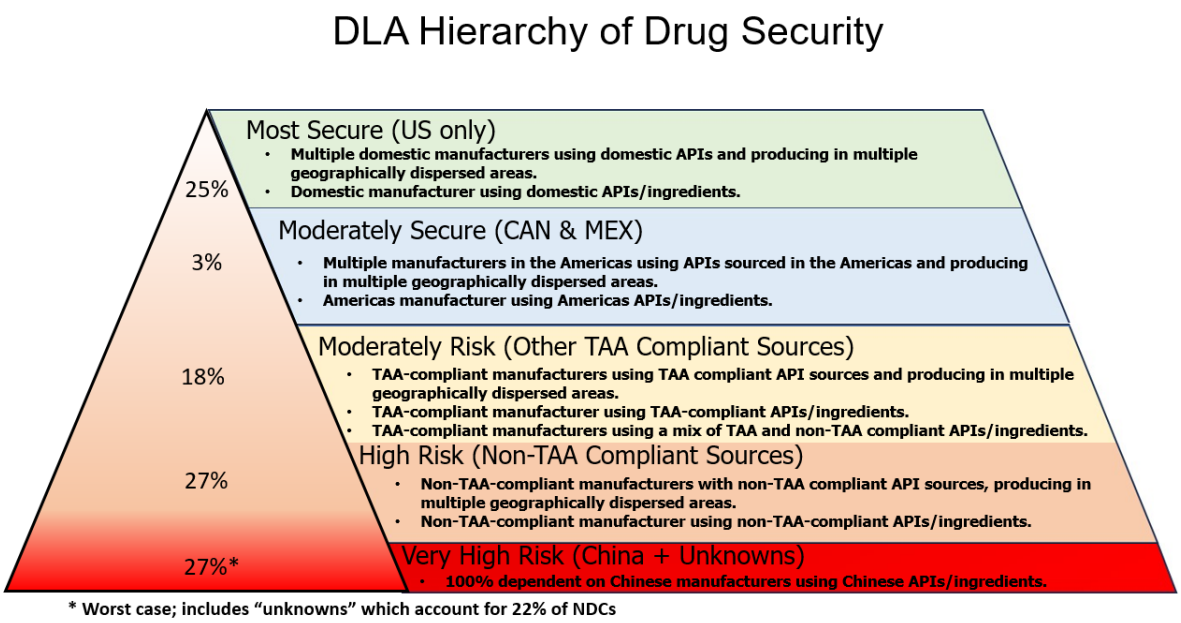
[2] Although China is specifically identified in this hierarchy, other countries are also considered a significant source of risk, to include countries such as Russia, North Korea, and Iran. As of this report, DLA is unaware of any APIs that are sourced from those countries, so they have been excluded from this sourcing hierarchy. As international relations, trade agreements, and other dynamics evolve, the hierarchy may change accordingly.

  - **3% (345 NDCs).**

- Moderate Risk (Other TAA compliant Manufacturers)
  - Multiple TAA compliant manufacturers using TAA compliant APIs.
  - **18% (2,373 NDCs).**

- High Risk (Non-TAA Compliant Manufacturers excluding China)
  - Multiple non-TAA compliant manufacturers excluding China.
  - **27% (3,457 NDCs).**

- Very High Risk (China; Unknowns)
  - Dependence on Chinese manufacturers using Chinese APIs
  - Includes drugs with Unknown sources.
  - **27% (3,470 NDCs).**



Hierarchy of Drug Security. Note: Other countries may be identified as high-risk, such as North Korea, Iran, and Russia. As of this report, APIs are not sourced from those countries and are not included in the hierarchy.

FINDINGS

How reliant is DoD on China when it comes to procurement of pharmaceuticals for CY22?

Based on the pharmaceuticals procured by DLA for CY22, DoD has purchased 46 drugs (684 NDCs) from the FDA Essential Medicine List and other pharmaceuticals with API that were sourced from China (Illustrated on Fig.1).

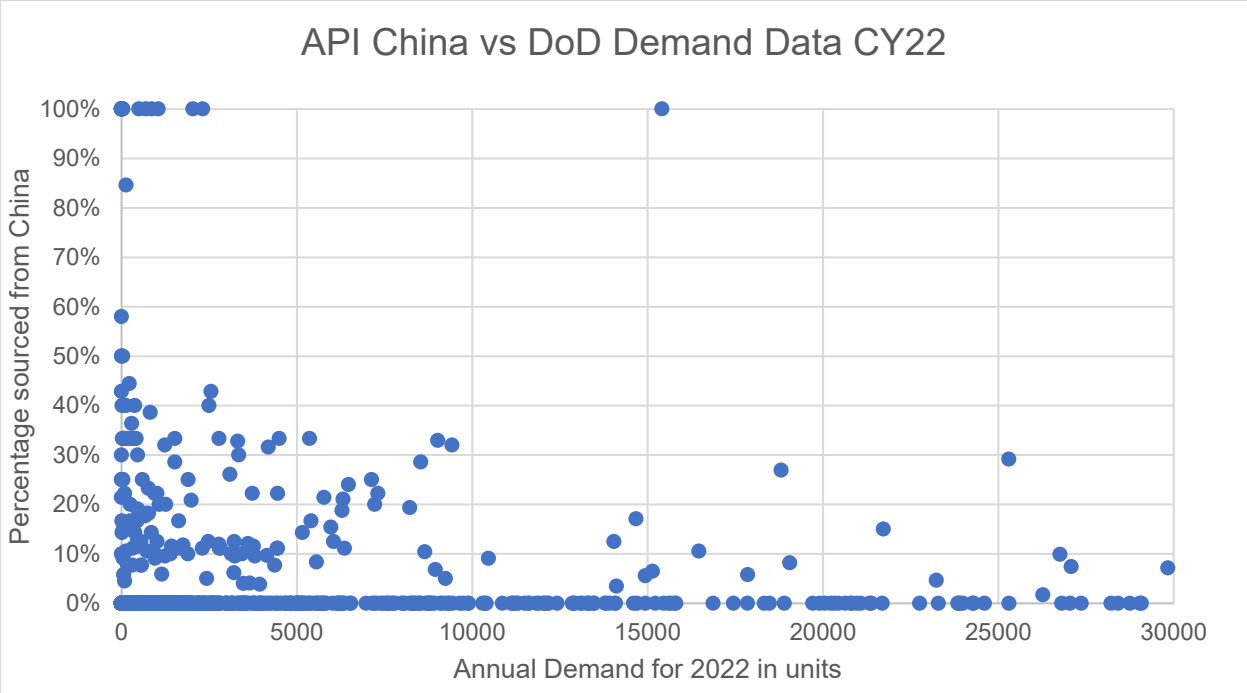


Figure 1. Depicts APIs from all 46 drugs (684 NDCs) from the FDA Essential Medicine List and other pharmaceuticals purchased by DLA in CY22 that were sourced from China. This figure illustrates that demand has a large correlation to production and sourcing of APIs from other than China.

In addition, seven out of the 46 drugs (20 NDCs) procured had APIs that were solely sourced from China for a total quantity of 22,957 units. These pharmaceuticals were used for anti-microbials, antivirals, human granulocyte colony-stimulating factor and glycemic control agents.

	API from China				
GSN - DESCRP	No	Yes	Total NDC	% API from China	Demand 2022
042076 - INSULIN LISPRO PROTAMINE AND INSULIN LISPRO - 75-25/ML - INSULIN PEN (ML)		4	4	100%	15409
047172 - INSULIN LISPRO PROTAMINE AND INSULIN LISPRO - 75-25/ML - VIAL (ML)		1	1	100%	2318
043242 - INSULIN LISPRO PROTAMINE AND INSULIN LISPRO - 50-50/ML - INSULIN PEN (ML)		2	2	100%	2036
029753 - CEFAZOLIN SODIUM - 2 G - VIAL (EA)		2	2	100%	1047
049872 - PEGFILGRASTIM - 6 MG/0.6ML - SYRINGE (ML)		1	1	100%	862
061721 - INSULIN LISPRO PROTAMINE AND INSULIN LISPRO - 50-50/ML - VIAL (ML)		1	1	100%	691
073319 - PEGFILGRASTIM - 6 MG/0.6ML - SYRINGE, WITH WEARABLE INJECTOR		1	1	100%	496
073201 - TOBRAMYCIN/NEBULIZER - 300 MG/5ML - AMPUL FOR NEBULIZATION (ML)		1	1	100%	38
076321 - DOXYCYCLINE HYCLATE - 120 MG - TABLET, DELAYED RELEASE (ENTERIC COATED)		1	1	100%	33
065760 - PERAMIVIR/PF - 200MG/20ML - VIAL (ML)		4	4	100%	22
059747 - CEFTAZIDIME - 1 G - VIAL WITH THREADED PORT (EA)		2	2	100%	5
Summary: 7 Drugs	**0**	**20**	**20**	**100%**	**22957**

Figure 2. List of pharmaceuticals purchased by DLA in CY22 with APIs that were solely sourced from China.

How reliant is DoD on India when it comes to procurement of pharmaceuticals for CY22?
Based on the pharmaceuticals procured by DLA for CY22, DoD has purchased 126 drugs (4,107 NDCs) from the FDA Essential Medicine List and other pharmaceuticals with APIs that were sourced from India (illustrated on Fig.3).

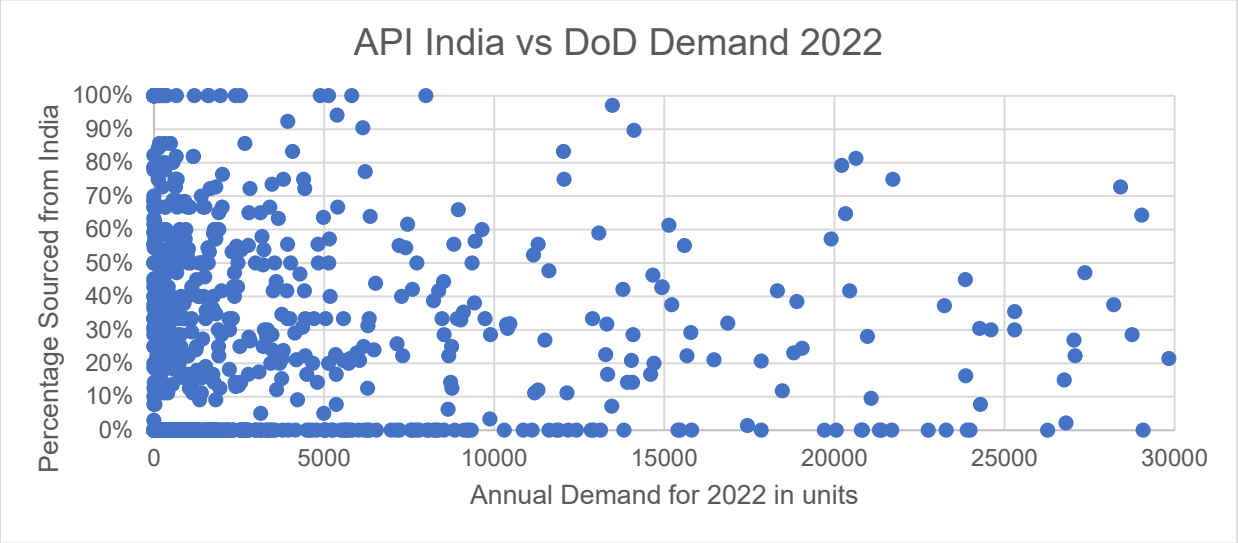


Figure 3. Depicts APIs from all 126 drugs (4,107 NDCs) in the FDA Essential Medicine List and other pharmaceuticals purchased by DLA in CY22 sourced from India illustrating a large demand correlation to API production and sourcing.

Furthermore, twenty of the 126 drugs (105 NDCs) procured had API that were solely sourced from India for a total quantity of 107,587 units. These pharmaceuticals were used for as anti-microbials, antivirals, anticonvulsants, human granulocyte colony-stimulating factor and agents used for cardiovascular, endocrine, and gastrointestinal conditions.

	API from India				
GSN - DESCRP	No	Yes	Total NDC	% API from India	Demand 2022
047525 - ESOMEPRAZOLE MAGNESIUM - 20 MG - CAPSULE,DELAYED RELEASE (ENTERIC COATED)		3	3	100%	39950
016266 - HYDROCORTISONE/ALOE VERA - 1 % - CREAM (GRAM)		1	1	100%	30053
007670 - ACYCLOVIR - 5 % - OINTMENT (GRAM)		2	2	100%	7997
072532 - CYANOCOBALAMIN (VITAMIN B-12) - 500MCG/SPR - SPRAY, NON-AEROSOL (EA)		1	1	100%	5816
046771 - LEVOFLOXACIN - 750 MG - TABLET		10	10	100%	5134
080790 - BEMPEDOIC ACID/EZETIMIBE - 180MG-10MG - TABLET		1	1	100%	4893
065336 - EPINEPHRINE - 1 MG/ML(1) - VIAL (ML)		5	5	100%	2545
031610 - DESMOPRESSIN ACETATE (NON-REFRIGERATED) - 10/SPRAY - AEROSOL, SPRAY		2	2	100%	2396
000571 - DILTIAZEM HCL - 60 MG - CAPSULE, EXTENDED RELEASE 12 HR		4	4	100%	1958
000570 - DILTIAZEM HCL - 120 MG - CAPSULE, EXTENDED RELEASE 12 HR		4	4	100%	1619
062053 - DEXAMETHASONE SODIUM PHOSPHATE/PF - 10 MG/ML - VIAL (ML)		19	19	100%	1590
029927 - LEVOFLOXACIN - 250 MG - TABLET		14	14	100%	1189
000572 - DILTIAZEM HCL - 90 MG - CAPSULE, EXTENDED RELEASE 12 HR		4	4	100%	662
049444 - PHENYTOIN SODIUM EXTENDED - 300 MG - CAPSULE		6	6	100%	372
078661 - VANCOMYCIN HCL - 1.25 G - VIAL (EA)		2	2	100%	357
078119 - METOPROLOL SUCCINATE - 25 MG - CAPSULE SPRINKLE, EXTENDED RELEASE 24 HR		1	1	100%	285
078120 - METOPROLOL SUCCINATE - 50 MG - CAPSULE SPRINKLE, EXTENDED RELEASE 24 HR		1	1	100%	203
049445 - PHENYTOIN SODIUM EXTENDED - 200 MG - CAPSULE		6	6	100%	179
078121 - METOPROLOL SUCCINATE - 100 MG - CAPSULE SPRINKLE, EXTENDED RELEASE 24 HR		1	1	100%	113
067533 - AZITHROMYCIN - 500 MG - VIAL WITH THREADED PORT (EA)		2	2	100%	78
078537 - PEGFILGRASTIM-JMDB - 6 MG/0.6ML - SYRINGE (ML)		1	1	100%	68
009245 - ERYTHROMYCIN ETHYLSUCCINATE - 400 MG - TABLET		4	4	100%	67
078122 - METOPROLOL SUCCINATE - 200 MG - CAPSULE SPRINKLE, EXTENDED RELEASE 24 HR		1	1	100%	20
083071 - VASOPRESSIN - 20/100 ML - INFUSION BOTTLE (ML)		2	2	100%	20
008207 - FUROSEMIDE - 40MG/5ML - SOLUTION, ORAL		1	1	100%	12
083330 - PHYTONADIONE (VIT K1) - 1MG/0.5ML - VIAL (ML)		2	2	100%	5
067217 - MOXIFLOXACIN HCL - 0.5 % - DROPS, VISCOUS (ML)		1	1	100%	4
002304 - PHYTONADIONE (VIT K1) - 10 MG/ML - VIAL (ML)		2	2	100%	1
083072 - VASOPRESSIN - 40/100 ML - INFUSION BOTTLE (ML)		2	2	100%	1
Summary: 20 Drugs	**0**	**105**	**105**	**100%**	**107587**

Figure 4. List of pharmaceuticals with APIs purchased by DLA in CY22 with APIs that were solely sourced from India.

How do the current drug shortage issues affect the availability of the pharmaceuticals from the FDA Essential Medicine List?

Using the data from the FDA Drug Shortage resource and the American Society of Health System Pharmacists (ASHP) Drug Shortage database, DoD was able to determine how the current nation-wide drug shortages affect the FDA Essential Medicine List. The FDA shortage list is usually smaller in scale compared to the ASHP's drug shortage data due to differences in scope, audience, and criteria. Below are the notable differences between the two references.

Contrasting the FDA (CDER) and ASHP Drug Shortage Websites: What are the differences?		
	FDA	**ASHP**
Purpose	Provides information obtained from manufacturers about current shortages, estimated duration, and discontinuations and provides information about FDA's and other stakeholders' roles in addressing and preventing shortages	Notification of new shortages and status of ongoing shortages; drug shortage management resources
Audience	Public	Healthcare practitioners
Scope of shortage list	All drugs are listed that are confirmed to be a national shortage by FDA. A shortage is considered to be the period of time when the demand for the drug within the United States exceeds the supply of the drug. **Note:** A separate shortage webpage[i] for vaccines and some biologics is maintained by the Center for Biologics Evaluation and Research.	All drug and biologic shortages reported and confirmed with manufacturer that are national in impact. **Note:** ASHP frequently lists more shortages than FDA.
Source of shortage report	Manufacturers notify FDA of production disruption and voluntarily provided updates. Reports are also received from ASHP and from public via drugshortages@cder.fda.gov **Note:** Manufacturer-provided information represents shortage status at drug firm level	Voluntary reports from practitioners, patients, pharmaceutical industry representatives and others **Note 1:** Information is updated based on release dates from manufacturers. **Note 2:** Reports reflect status at healthcare provider level.
Criteria for inclusion on list	Manufacturers cannot meet current market demand for the drug based on information provided by manufacturers and market sales research	(1) Shortage is verified with manufacturers and (2) affects how pharmacy prepares or dispenses a product, or (3) requires use of alternative drugs, which may affect patient care
Criteria for resolving shortage	One or more manufacturers are in production and able to meet full market demand	All manufacturers of the drug restore all formulations and dosage sizes to full availability. **Note:** Product are listed despite partial or restricted availability as supply chain disruptions can result in intermittent shortages at the provider or patient level
Reason for shortage	Provided by manufacturers using reasons required by legislation.[ii] FDA encourages firms to provide additional information about reasons and other information which, if proprietary, is nondisclosable without the firms' permission.	Provided by manufacturer, if willing to disclose. **Note:** May differ from FDA's due to different sources of information and legislation requiring FDA to use specified reasons
Other information	Estimated duration, links to regulatory information such as recalls and Dear Healthcare Provider Letters	Estimated duration, list of available products, implications for patient care and safety, shortage management strategies, therapeutic alternatives

Developed by: Food and Drug Administration Drug Shortage Staff, American Society of Health-System Pharmacists, and the University of Utah Drug Information Service. August 2014

As of August 15, 2023, which is when DLA conducted its analysis, 36 out of 211 drugs (17%) from the FDA Essential Medicines List were experiencing availability issues according to the FDA drug shortage list. Similarly, the ASHP drug shortage resource indicates 68 out of 211 drugs (32%) from the FDA Essential Medicines List are also having availability issues. See Appendix A for additional shortage information.

Based on the analysis of the FDA Essential Medicine List, what is the level of risk to the Warfighters?

From the 5% (650 NDCs) of pharmaceuticals with an API sourced from China, there are 113 NDCs that are currently being used in the JDF, which is a list of Joint Service reviewed and

approved pharmaceuticals to support Roles of Care I through III during the first 30 days of a contingency operation.

REPORT CONSIDERATIONS and GAPS

The PPS vendor is currently in the process of incorporating and validating its data with the limited biannual data FDA shared with DLA. The numbers presented in this report may change slightly once the validation is completed. In addition, the PPS vendor is also working on adding another data array depicting the country-of-origin site of final formulation. Although these data are resident in PPS, the current functionality does not afford easy access.

PPS is significantly limited through the lack of definitive data on the sources of drugs, APIs, and other key ingredients sold in the U.S. Current PPS functionality is sufficient to meet DoD's risk assessment need if the data were available. This report quantifies the current data limitation by highlighting the 22% of "unknown" sources in the PPS results analyzed for this report. DLA continues to work with the public commercial sources and the FDA to close this 22% gap. A less significant limitation of PPS is it does not yet have the capability to determine production percentage of a given drug, API, or ingredients. Again, this limitation is related to the lack of data specifying exact sources of these products, and DLA is working to address by adding and refining additional commercial data sources.

This report focuses on the foreign dependance of APIs which is only one of many potential risks and vulnerabilities within the supply chain. Other areas include manufacturing capabilities, regulatory, distribution, and other risk areas. DoD is in process of developing the SCRM Framework and Taxonomy with implementation guidance, as well as the SCRM governance process. Once developed and implemented, these additional areas of risk will be able to be considered more fully to include mitigation efforts.

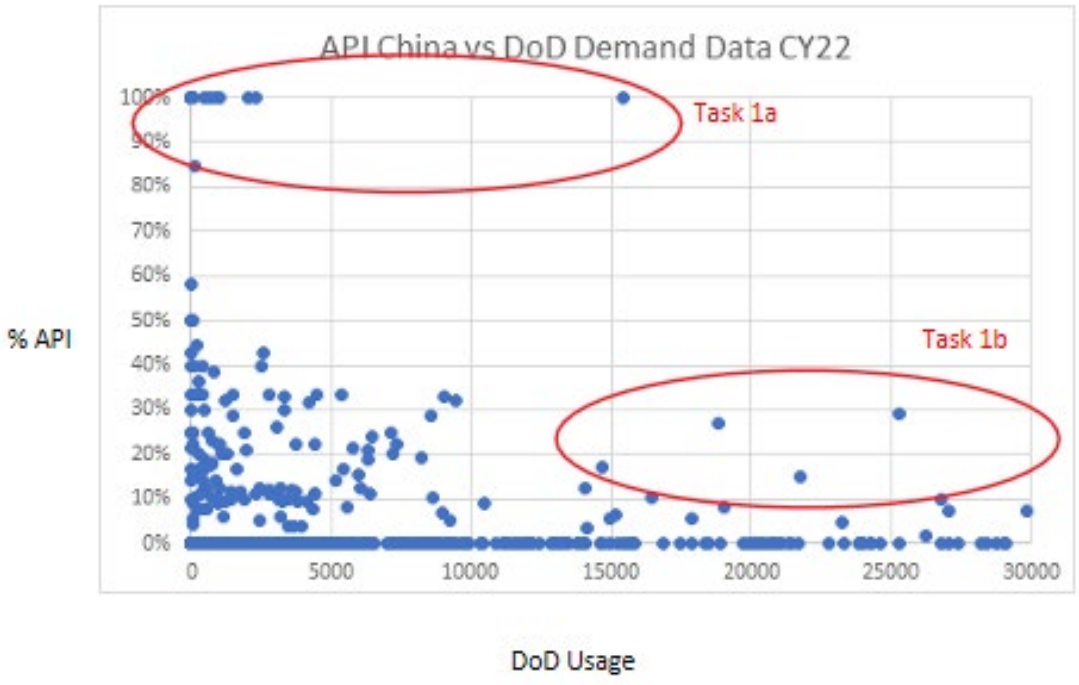
FOREIGN INFLUENCE MITIGATION and RECOMMENDATIONS

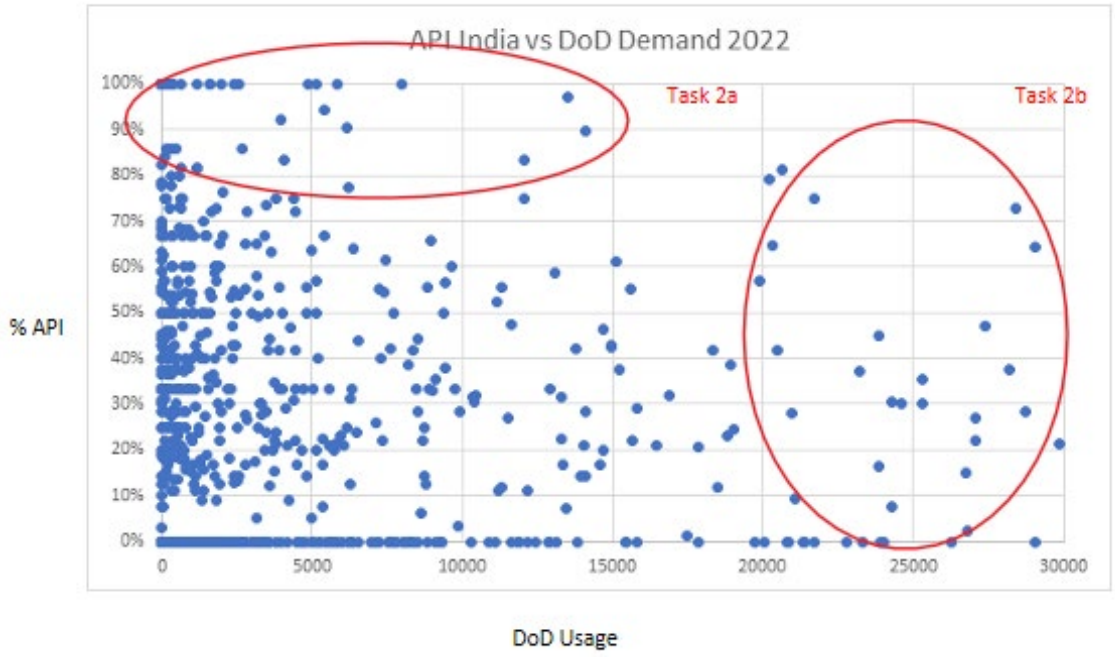
DOD identifies the following mitigations and recommendations in consideration of mitigating risk on foreign dependance. While DOD has limited authorities to stop buying end products and less authority to restrict sourcing of underlying components from any particular country, DOD does have authorities to determine preference and requirement generation. The mitigations and recommendations presented are in three categories reflecting developing efforts to minimize foreign influence risks. Specific resource assignment, timeframes, and completion criteria are to be determined for each.

Short Term

- DLA will work with the Military Services and other supported DoD Components and recommend/facilitate their transition to TAA-compliant viable therapeutic alternatives focusing on:

    1. Drugs with sole-sourced APIs from China (Task 1a) and then drugs, with significant percentages of Chinese APIs, and high DoD usage rates (Task 1b),
    2. Drugs sourced from China that are used in the JDF,
    3. Drugs with APIs sole-sourced to India (Task 2a) as well as drugs with significant percentages of Indian APIs, and high DoD usage rates (Task 2b).





Mid-term

- DLA will:
  1. Pursue efforts to validate sources of supplies/production capacity from industry.
  2. Continue to enhance event mapping capability in PPS to anticipate supply disruption.
  3. Focus on products from domestic and TAA compliant sources, depending on global supply availability.
  4. Engage suppliers of pharmaceuticals with Unknown country of origin to determine source of API and update in PPS database.

Long-term

- DLA will:
  1. Work with relevant federal stakeholders to support domestic production of finished generic drugs, APIs, and key ingredients.
  2. Focus on utilization of secure ingredient sources following DLA's sourcing hierarchy.
  3. Partner with FDA and other federal stakeholders to require industry to provide the necessary business intelligence to determine the source for the finished drug, API and key ingredients acquired by the federal government.

OTHER RECOMMENDATION ON INFORMATION GAPS

DLA has identified the lack of authoritative data on the sources of finished generic drugs, their APIs, and other key ingredients as a critical information gap representing a substantial vulnerability to its pharmaceutical supply chain. For example, with all its specialized expertise, available databases, and IT support tools and capabilities, DLA could not identify 22% of the sources of APIs for the 211 drugs (2,820 NDCs) on the FDA Essential Medicines list. DoD recommends that manufacturers of pharmaceuticals sold in the U.S. be required to provide the FDA with definitive information on the production location of all their finished drugs and the source of all APIs and key ingredients, and the percentages of APIs and key ingredients coming from each source, for each lot of drugs they produce. Manufacturers should also be required to update this production and sourcing data for each generic drug prior to selling the pharmaceutical in the United States. The FDA should array and store this sourcing data in an appropriate repository and make it available to all federal stakeholders responsible for assessing and mitigating vulnerabilities to the nation's pharmaceutical supply chain.

FUTURE WORK

DoD will complete Phase II of the SCRM effort resulting in a holistic baseline for use by all programs, systems, and supply chain managers. This will be further refined for specific medical pharmaceutical utilization.

DoD will utilize the identified risks and the developing SCRM framework to develop mitigation strategies and implementation plans. These will enable the DoD to address sourcing and dependency risks through acquisition strategies.

Additionally, this information will be provided to the HHS Joint SCRWG to facilitate inter-departmental communications and enable HHS to manage the medical industrial base. The Joint SCRWG is a formal Working Group under the authority of the Critical Infrastructure Partnership Advisory Council facilitating engagements between government representatives at the federal, state, local, tribal, and territorial levels and representatives from critical infrastructure owners and operators to conduct deliberations and form consensus positions to assist the Federal Government in developing resiliency.

Appendix A: Drug Shortage Information from FDA and ASHP

The FDA Drug Shortage resource and the ASHP Drug Shortage database provide information and status. DLA has provided the procured medicines on the lists and declaration times of the FDA and ASHP.

FDA Essential Medicine List			
Drug Name	Drug Shortage	FDA	ASHP
Gastrointestinal Agents			
Famotidine (IV)	Y		X (Since Dec 2019)
Pantoprazole (IV)	Y	X (Since May 2019)	X (Since Mar 2019)
Anticonvulsants			
Phenytoin (IV)	Y		X (Since Dec 2022)
Levetiracetam (IV)	Y		X (Since May 2015)
Antiemetics			
Ondansetron (IV)	Y		X (Since Mar 2015)
Anticoagulants/Antiplatelets			
Heparin (IV)	Y	X (Since Nov 2017)	x (Since Oct 2017)
Protamine (IV)	Y		x (Since May 2023)
Vitamin K (IV)	Y		x (Since Aug 2022)
Argatroban (IV)	Y		x (Since Nov 2018)
Antimetabolite			
Hydroxyurea (Oral)	Y		x (Since May 2023)
Antihistamines			
Diphenhydramine (IV)	Y		x (Since Mar 2022)
Antihypertensive/Cardiovascular			
Adenosine (IV)	Y		x (Since Apr 2023)
Atropine (IV)	Y	x (No data available)	x (Since Aug 2011)
Amiodarone (IV)	Y		x (Since Jan 2018)
Diltiazem (Oral/IV)	Y	x (Since Feb 2018)	x (Since Jun 2015)
Esmolol (IV)	Y		x (Jan 2022)
Furosemide (Oral/IV)	Y	x (Since Apr 2020)	x (Since May 2017)
Labetalol (IV)	Y		x (Since Jan 2022)
Mannitol (IV)	Y	x (Since Sep 2021)	x (Since Sep 2021)

Metoprolol (IV)	Y		x (Nov 2017)
Dobutamine (IV)	Y	x (Since Nov 2017)	X (Since Mar 2017)
Antimicrobial			
Amphotericin B (IV)	Y		x (Since Nov 2021)
Clindamycin (IV)	Y	x (Since Mar 2023)	x (Jun 2015)
Doxycycline (Oral)	Y		x (Since Nov 2021)
Metronidazole (Oral/IV)	Y	x (Since Nov 2022)	x (Since Oct 2021)
Penicillin G (IV)	Y		x (Since Feb 2023)
Rifampin (Oral/IV)	Y	x (Since Feb 2021)	
Vancomycin (IV)	Y		x (Since Jun 2015)
Psychiatric Agents			
Haloperidol (IM)	Y		x (Since Dec 2020)
Olanzapine (IV)	Y		x (Since Nov 2021)
Antipyretics			
Ibuprofen (Oral)	Y		x (Since Nov 2022)
Analgesics			
Fentanyl (IV)	Y	x (No data available)	x (Since May 2017)
Hydromorphone (Oral/IV)	Y	x (Since Oct 2017)	x (Since Jun 2017)
Morphine (IV/Oral Solution))	Y	x (Since Oct 2017)	x (Since Jun 2009)
Lidocaine/Epinephrine (Solution for SQ)	Y	x (Since Feb 2012)	x (Since Jun 2015)
Antivirals			
Valganciclovir (Oral)	Y		x (Since Feb 2023)
Oseltamivir (Oral)	Y		x (Since Nov 2022)
Pulmonary			
Albuterol (MDI/NEB)	Y		x (Since Mar 2020)
N-Acetylcysteine (IV Solution)	Y		x (Since Jun 2015)
Immunomodulator			
Mycophenolate (Oral/Suspension)	Y		x (Since Jul 2018)
Paralytics			
Rocuronium (IV)	Y	x (Since Feb 2023)	x (Since Feb 2017)
Vecuronium (IV)	Y	x (Since May 2020)	x (Since Sep 2015)

Glycemic Control			
Dextrose 50% Injection (IV)	Y	x (Since Jan 2022)	x (Since Dec 2021)
Reversal Agents			
Glucagon (IV)	Y		x (Since Oct 2022)
Hypnotic/Sedatives			
Dexmedetomidine (IV)	Y	x (Since Apr 2020)	x (Since Nov 2018)
Etomidate (IV)	Y	x (Since Oct 2022)	x (Since Oct 2022)
Ketamine (IV)	Y	x (Since Feb 2018)	x (Since Feb 2018)
Lorazepam (IV)	Y	x (Since May 2018)	x (Since Jun 2015)
Midazolam (IV/IM)	Y	x (Since Apr 2020)	x (Since Jun 2019)
Propofol (IV)	Y	x (Since Apr 2020)	x (Since Apr 2020)
Malignant Hyperthermia			
Dantrolene (IV)	Y		x (Since Feb 2022)
Steroids			
Dexamethasone (IV)	Y	x (Since Feb 2019)	x (Since Mar 2011)
Hydrocortisone (Oral/IV)	Y	x (Since Apr 2020)	x (Since Mar 2020)
Methylprednisolone (IV)	Y	x (Since Dec 2021)	x (Since Aug 2021)
Endocrine			
Levothyroxine (Oral/IV)	Y		x (Since Feb 2022)
Zoledronic Acid (IV)	Y		x (Since Jan 2022)
Vasopressors			
Epinephrine (IV)	Y	x (Since Apr 2020)	x (Since May 2018)
IV Fluids			
Sodium Chloride (Multiple Bag Size)	Y	x (Irrigation-since Apr 2023)	x (Since 2017)
Dextrose (Multiple Bag Size)	Y	x (Since 2022)	x (Since 2021)
Additives			
Calcium Gluconate (IV)	Y	x (Since Mar 2021)	x (Since Dec 2021)
Potassium Chloride (Oral/IV)	Y	x (Since Nov 2021)	x (Since Sep 2021)
Sodium Bicarbonate (IV)	Y	x (Since Mar 2017)	x (Since Feb 2017)
Sodium Phosphate (IV)	Y	x (Since Sep 2021)	x (Since Aug 2021)
Fractionated Plasma Products			

Albumin (IV)	Y		x (Since Sep 2022)
Animal Derived IG Product			
Black Widow Anti-Venin (IV)	Y		x (Since Oct 2021)
Amino Acids (IV)	Y	x (Since Dec 2020)	
Digoxin (IV)	Y	x (Since Jun 2021)	x (Since Jan 2023)
Biological Threat MCMs			
Amoxicillin (Oral)	Y	x (Since Oct 2022)	x (Since Oct 2022)
Ciprofloxacin (IV)	Y		x (Since Jan 2023)
Burn and Blast Injuries			
Oxycodone (Oral)	Y		x (Since Mar 2023)
		36/211	**68/211**
		17%	**32%**
		FDA	**ASHP**