

STRENGTHENING U.S. PHARMACEUTICAL SUPPLY CHAIN RESILIENCE THROUGH EVIDENCE-BASED POLICY AND REGULATORY REFORM

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ABSTRACT

The resilience of the U.S. pharmaceutical supply chain has become a central concern for healthcare continuity, economic security, and public policy. Drug shortages expose a system in which manufacturing concentration, upstream dependencies, low-margin markets, incomplete supply-chain visibility, procurement incentives, and regulatory constraints can interact to convert localized disruptions into prolonged access problems. This narrative policy review critically examines the structural, economic, operational, and regulatory determinants of pharmaceutical supply vulnerability in the United States and evaluates the limitations of current policy responses. It argues that shortage management and supply-chain resilience are related but distinct objectives: the former is predominantly reactive, whereas the latter depends on the capacity to anticipate, absorb, adapt to, and recover from disruption. Building on this distinction, the review develops an integrated resilience architecture organized around eight functions: Detect, Assess, Incentivize, Diversify, Buffer, Adapt, Recover, and Learn. The framework links predictive supply-chain intelligence with resilience-oriented procurement, targeted manufacturing support, adaptive regulation, strategic capacity, and continuous learning. The central policy implication is that durable resilience requires coordination across regulatory, procurement, manufacturing, economic, and emergency-preparedness functions rather than a series of isolated shortage interventions. The paper therefore reframes pharmaceutical resilience as a designed property of market governance: one that must preserve safety, quality, affordability, and efficiency while reducing the probability that foreseeable vulnerabilities become prolonged national shortages.

KEYWORDS: *pharmaceutical supply chain; drug shortages; resilience; health policy; pharmaceutical regulation; generic medicines; procurement; manufacturing; supply-chain intelligence.*

1. INTRODUCTION

The resilience of the pharmaceutical supply chain has become a matter of healthcare security, economic stability, and public policy rather than a narrow question of logistics. Medicines are produced through interconnected networks involving active pharmaceutical ingredients (APIs), excipients, manufacturing facilities, distributors, wholesalers, group purchasing arrangements, pharmacies, hospitals, and regulators. Disruption at one node can therefore propagate across the network and constrain access to clinically necessary products. U.S. medical-product supply chains are complex, multilevel, and globally distributed, creating exposure to production failures, quality problems, transportation interruptions, geopolitical events, and demand shocks.^[1,2]

Drug shortages are the most visible manifestation of this vulnerability, but they are not equivalent to resilience itself. Shortage management begins after a disruption has become observable and focuses on preserving remaining supply, accelerating alternatives, and restoring availability.^[3] Resilience is broader and more anticipatory. It concerns whether the system has sufficient information, economic incentives, productive capacity, regulatory adaptability, redundancy, and institutional coordination to absorb disruption without disproportionate loss of access. This distinction matters because a decline in the number of newly reported shortages can coexist with longer shortage duration or slower recovery.^[1]

The persistence of shortages despite repeated interventions suggests that the problem is structural rather than episodic. Federal analyses have identified interacting vulnerabilities that include limited transparency, concentrated manufacturing and intermediary structures, weak incentives for redundancy, and generic-drug prices that may be insufficient to sustain resilient production and purchasing practices. Generic sterile injectables are a particularly important illustration because they combine demanding manufacturing requirements with limited substitutable capacity and, in many cases, weak commercial returns. One federal analysis reported that a large share of recently launched generic injectable products in its sample had not reached profitability by the third year after launch.^[4]

Global production adds another layer of complexity. A substantial proportion of manufacturers supplying the U.S. market operate outside the United States, creating oversight and supply-risk challenges while also reflecting the efficiency gains and specialized capabilities of international production.^[5] Geographic dependence should therefore not be treated as synonymous with vulnerability. The more important question is whether critical products and inputs are diversified across genuinely independent suppliers and

production regions, and whether capacity can be substituted when one source is lost.^[1]

Current policy has strengthened surveillance, manufacturer notification, shortage response, and selected domestic-manufacturing initiatives. Yet these tools remain distributed across agencies and policy domains. A regulator may be able to detect and mitigate an emerging shortage without being able to change the procurement incentives, market structure, or capital economics that made the supply chain fragile in the first place.^[1] Likewise, manufacturing support can add capacity without ensuring that demand will remain sufficient to sustain that capacity after incentives expire.

This review therefore asks a broader question: how can U.S. pharmaceutical policy move from reactive shortage management toward anticipatory resilience governance? It critically examines the structural and economic determinants of supply vulnerability, evaluates the strengths and limitations of existing policy instruments, and develops an integrated policy architecture for aligning commercial incentives with public resilience objectives. The goal is not indiscriminate reshoring, permanent overcapacity, or weaker regulation. Rather, it is to identify where targeted interventions can improve diversification, visibility, adaptive capacity, and recovery while preserving the safety, quality, affordability, and efficiency that pharmaceutical policy must also protect.

2. Review Approach and Analytical Scope

This article is a narrative policy review and conceptual synthesis examining pharmaceutical supply-chain resilience and drug shortages in the United States. Rather than employing a systematic-review methodology, the analysis draws on a purposively assembled body of peer-reviewed literature and policy-relevant evidence spanning pharmaceutical supply-chain management, health economics, pharmaceutical manufacturing, procurement, regulatory science, operations research, and drug-shortage management. Sources were included on the basis of their relevance to the principal mechanisms examined in the review, including manufacturing and upstream concentration, market incentives, supply-chain visibility, forecasting, regulatory adaptability, strategic buffering, procurement, and recovery capacity.

The evidence was synthesized thematically and organized around a causal-policy logic. First, the review examines structural conditions that can increase vulnerability to pharmaceutical supply disruption. Second, it considers how these vulnerabilities can translate into drug shortages and downstream healthcare and economic consequences. Third, existing policy instruments are examined in relation to the resilience functions they address and the structural limitations that may remain. Finally, recurring concepts and mechanisms identified across the literature are integrated into the proposed eight-function resilience architecture—Detect,

Assess, Incentivize, Diversify, Buffer, Adapt, Recover, and Learn.

The review treats resilience as a multidimensional policy outcome rather than as the absence of reported shortages alone. Relevant dimensions include exposure to common-mode supply failure, substitutability, production flexibility, supply-chain visibility, buffering capacity, recovery time, and the economic sustainability of production capacity.^[1,6,7] The proposed framework is therefore an interpretive synthesis intended to organize existing evidence and identify policy relationships and research priorities; it should not be interpreted as a formally validated measurement instrument or causal model. Because the review is narrative rather than systematic, no formal study-screening protocol, risk-of-bias assessment, or meta-analysis was undertaken.

3. The Structural Architecture of U.S. Pharmaceutical Supply-Chain Vulnerability

Pharmaceutical supply vulnerability is produced by the interaction of market concentration, geographically distributed production, weak incentives for redundancy, incomplete supply-chain visibility, and operational or regulatory constraints that can slow adjustment. These vulnerabilities become most consequential when they converge around medicines for which alternative suppliers are limited, production is technically demanding, and additional capacity cannot be mobilized quickly.^[8,9] Table 1 summarizes the structural mechanisms through which apparently localized weaknesses can become system-level risks.

3.1 Manufacturing and supplier concentration

Manufacturing concentration is one of the clearest pathways from local disruption to national shortage. Older generic sterile injectables illustrate the problem because a small number of facilities may account for substantial effective capacity, production lines may be highly utilized, and qualification of alternative capacity can take time. When a producer experiences a quality failure, prolonged outage, or market exit, nominally competing firms may be unable to expand output rapidly enough to offset the loss.^[4,10]

The relevant measure is therefore not simply the number of firms listed in a market. Effective resilience depends on independent production capability, spare or surge capacity, the location of facilities, and the extent to which manufacturers share upstream inputs. A market can be competitive on price while remaining highly concentrated in production capability. Strong price competition may simultaneously reduce acquisition costs and weaken incentives for spare capacity, facility modernization, redundant suppliers, and resilient sourcing.^[8,11]

Upstream concentration can create an additional layer of common-mode risk. Finished-dose manufacturers that appear independent may rely on the same API producer,

intermediate manufacturer, packaging component, or specialized input. Domestic production of a finished medicine therefore does not necessarily eliminate external exposure. The resilience of the finished product depends on the resilience of the critical tiers that support it.^[12,13]

3.2 Globalization and geographic dependency

Globalization has increased access to specialized manufacturing and reduced production costs, but it has also created dependencies that can be difficult to observe and substitute. A substantial share of manufacturers serving the U.S. market operate overseas, and important portions of API and intermediate production are concentrated outside the United States.^[13,14] The policy implication is not that foreign production is intrinsically unsafe or undesirable. Geographic risk should be evaluated at the product and production-stage level. Multiple finished-dose suppliers may still share a single upstream source or depend on facilities concentrated in the same region. Diversification that exists only at the final manufacturing tier can therefore create an appearance of redundancy without reducing common-mode risk.^[12,15]

3.3 Economic incentives and market fragility

The economics of pharmaceutical production provide a central explanation for why resilience may be underprovided. Redundancy, unused capacity, multiple qualified suppliers, modern equipment, larger inventories, and diversified sourcing all impose costs during normal operations. The benefit of those investments becomes most visible only when disruption occurs. In low-margin markets, individual firms may have weak incentives to finance system-wide resilience when purchasers primarily reward lower acquisition prices.^[8,16]

This creates a classic alignment problem. From a health-system perspective, maintaining additional capacity may have substantial option value because it reduces the expected cost of disruption. From the perspective of an individual supplier, however, underutilized capacity can be commercially unattractive. Resilience should therefore not be assumed to emerge automatically from conventional price competition. Policy must determine when continuity has sufficient social value to justify paying for reliability explicitly.

3.4 Information and visibility gaps

Resilience also depends on the quality and timeliness of information. Regulators and downstream purchasers may have incomplete visibility into upstream suppliers, inventories, facility constraints, quality events, and the extent to which apparently independent products rely on common inputs. Delayed information narrows the window for preventive action and limits the ability to distinguish temporary variation from an emerging systemic shortage.^[17,18]

Predictive tools can improve this situation only if the underlying data are sufficiently complete and interoperable. A sophisticated forecast built on fragmented or selectively reported information can provide false reassurance as easily as useful warning. For this reason, supply-chain intelligence should be evaluated not only by predictive accuracy but also by coverage, lead time, false-alarm burden, and whether warnings trigger effective action.^[19–21]

3.5 Regulatory and operational constraints

Regulation is indispensable to pharmaceutical resilience because manufacturing quality failures are themselves a major source of supply disruption. The challenge is not

to trade safety for speed but to create regulatory processes that preserve rigorous quality standards while allowing qualified manufacturers to modify, expand, or diversify production with greater predictability when risk warrants it.^[4]

This distinction is important. A system in which changes are rapid but poorly controlled may increase patient risk, whereas a system in which every adjustment is slow may be unable to respond to an emerging shortage. Resilience therefore requires regulatory adaptability: the capacity to distinguish scientifically necessary controls from avoidable administrative delay and to scale review intensity to product, process, and supply risk.^[22]

Table 1: Structural drivers of U.S. pharmaceutical supply-chain vulnerability.

Structural driver	Mechanism of vulnerability	System-level consequence
Manufacturing concentration	A small number of producers may hold most effective capacity.	Failure or exit of one producer can materially reduce national availability. ^[4,10]
Upstream concentration	Multiple manufacturers may share APIs, intermediates, components, or specialized suppliers.	Common-mode failures can affect several downstream products simultaneously. ^[12,13]
Geographic dependency	Critical production stages may be concentrated in a limited number of regions.	Regional disruption can propagate across the U.S. market. ^[5,13,14]
Weak resilience incentives	Low margins and price-focused purchasing can discourage redundancy and capacity investment.	Normal-time efficiency can coexist with inadequate surge capacity. ^[8,11,16]
Limited supply-chain visibility	Fragmented information obscures upstream constraints, inventories, and emerging quality or capacity problems.	Risk detection and preventive intervention occur too late. ^[17,18]
Forecasting limitations	Demand and supply conditions can change faster than capacity can adjust.	Shortages may become visible before substitute supply is available. ^[1,19,20]
Regulatory/operational constraints	Quality controls and production changes require time, evidence, and coordination.	Necessary adjustments may lag the pace of disruption. ^[4,22]
Limited substitutability	Some medicines have few clinically or commercially viable alternatives.	Localized production failure can become a system-wide access problem. ^[1,3]

3.6 Product-specific patterns of supply-chain vulnerability

Pharmaceutical supply-chain vulnerability is not uniform across product categories. Generic sterile injectables provide an important model because production is technically demanding, manufacturing capacity may be concentrated, and rapid substitution can be difficult; however, these mechanisms should not be generalized across the pharmaceutical market.^[4,10] Solid oral medicines can face different constraints. The 2022–2023 amoxicillin shortage, for example, was associated with a sharp increase in demand, while recent shortages of

amphetamine-based stimulants have also reflected active-ingredient and international sourcing constraints; controlled-substance production is additionally governed by DEA quota mechanisms.^[32,33] Complex injectable therapies, including GLP-1 receptor agonists, present another pattern: rapid demand growth and manufacturing-capacity constraints can limit availability, while scaling injectable production requires specialized manufacturing and downstream capacity.^[34] Resilience policy should therefore be product-specific, with risk assessment accounting for manufacturing complexity, upstream dependencies, regulatory constraints,

substitutability, capacity-expansion timelines, and the clinical consequences of interruption.

4. From Drug Shortages to Systemic Healthcare and Economic Risk

Drug shortages are the visible endpoint of a wider system of costs. Once supply becomes constrained, the effects are transmitted through clinical decisions, procurement systems, hospital operations, manufacturers, patients, and public agencies. The relevant policy outcome is therefore not only whether a shortage exists, but how severe it is, how long it lasts, how substitutable the affected product is, and how much effort the health system must devote to managing the disruption.^[3,23]

At the clinical level, shortages can delay treatment, force therapeutic substitution, alter established regimens, and increase medication-safety risks when unfamiliar products or formulations are introduced. These effects are particularly important for time-sensitive therapies and products with imperfect substitutes. Substitution may preserve nominal access while still imposing clinical and operational costs.^[3,24]

The economic burden extends beyond the price of replacement medicines. Health systems must allocate

personnel time to locating alternatives, monitoring inventories, revising formularies, communicating with clinicians, modifying protocols, and managing emergency procurement. Evidence from U.S. health systems demonstrates that drug-shortage management imposes substantial personnel and operational costs.^[23]

The national-security dimension follows from the role of medicines in routine care, cancer treatment, surgery, emergency medicine, and chronic disease management. A system with fewer shortage events may still be vulnerable if recovery is slow, supply is highly concentrated, or critical products lack substitutes. Recent federal reporting has highlighted the persistence or duration of shortages even as the number of newly reported events has changed over time.^[1,3]

These observations expose a limitation of conventional shortage metrics. Counting products in shortage does not capture duration, therapeutic criticality, availability of substitutes, upstream concentration, geographic exposure, patient populations affected, or recovery capability. A stronger resilience metric should therefore combine the probability of disruption with the expected clinical, operational, and economic consequences and the time required to restore supply.^[1,15]

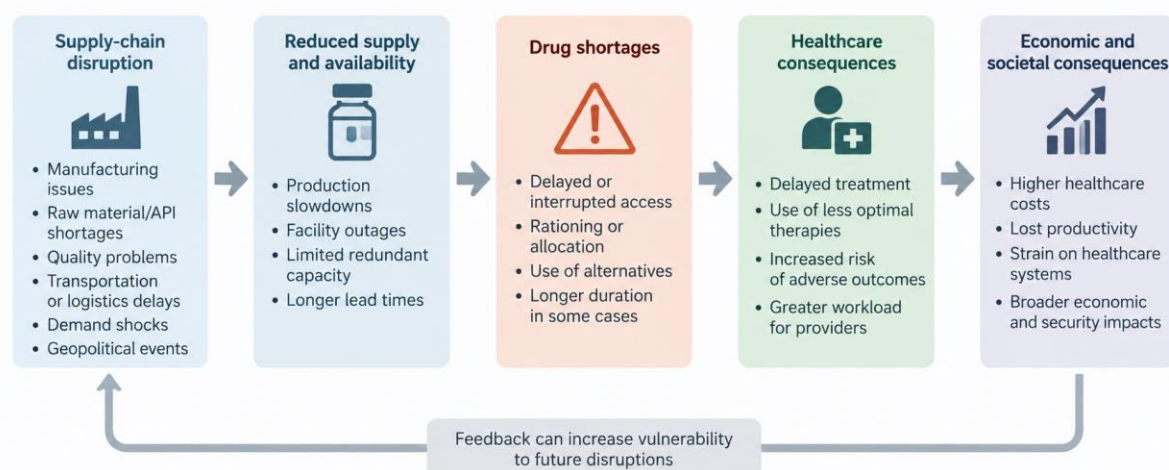


Figure 1: Pathway from pharmaceutical supply-chain disruption to healthcare and economic consequences. Supply-chain disruptions can constrain production and medicine availability, contribute to drug shortages, and generate downstream healthcare, economic, and societal consequences. Feedback from these consequences may further increase vulnerability to future disruptions. Source: Authors' conceptual synthesis based on the literature.^[1,3,15,23,24]

5. What Current U.S. Policies Achieve—and Where They Fall Short

The United States has developed a substantial set of policy tools for shortage detection, regulatory response, emergency preparedness, manufacturing support, procurement, and supply-chain intelligence. These instruments matter, but they address different stages of the problem. Their principal limitation is not that they

are ineffective in isolation; it is that they do not yet function as a sufficiently integrated architecture for preventing vulnerability from becoming disruption. Table 2 summarizes the principal strengths and structural limitations of the current policy toolkit.^[25]

5.1 Federal shortage surveillance and early warning

Federal shortage surveillance has improved through manufacturer notifications, public reporting, and increasingly data-driven monitoring. These tools can identify emerging constraints earlier and allow regulators to coordinate with manufacturers before a disruption becomes acute. FDA reported preventing hundreds of potential shortages through such interventions in a recent year.^[17]

Surveillance, however, remains dependent on the completeness and timeliness of data supplied by manufacturers and other actors. More importantly, detection does not eliminate the conditions that generated risk. An early warning may create time to respond, but it cannot by itself change fragile market economics, concentrated capacity, or inadequate redundancy.^[17,18]

5.2 FDA regulatory mechanisms

FDA regulation protects patients from unsafe or substandard products, but supply resilience requires that oversight also respond effectively when qualified capacity must change. During shortages, expedited reviews, prioritized regulatory engagement, or scientifically justified manufacturing changes can shorten the time required for some responses.^[17,18]

These tools remain primarily responsive. Regulatory flexibility cannot create economically sustainable capacity, correct procurement incentives, or eliminate upstream dependencies. The broader policy challenge is therefore to connect regulatory responsiveness to earlier risk assessment and to the economic conditions that determine whether alternative capacity exists before a shortage occurs.

5.3 Strategic stockpiling and emergency preparedness

Strategic inventories can preserve access during disasters, acute production failures, or other temporary disruptions by buying time for alternative supply arrangements. They are especially relevant for clinically critical products with limited immediate substitutes or long replenishment times.^[26]

Stockpiles do not remove the underlying vulnerability. Medicines expire, storage and rotation impose costs, and finite inventories cannot indefinitely compensate for concentrated manufacturing or weak production incentives. Stockpiling is therefore best treated as a buffer within a broader resilience system rather than a substitute for diversified production, visibility, and economically sustainable capacity.

5.4 Domestic manufacturing initiatives

Recent U.S. policy has placed greater emphasis on domestic pharmaceutical manufacturing and advanced

manufacturing. Targeted domestic capacity can reduce selected external dependencies and improve visibility into strategically important production.^[27]

Reshoring should not, however, be equated with resilience. A domestic facility can remain dependent on a single foreign API source, operate at high utilization, or lack commercially sustainable demand. Temporary subsidies can establish capacity without ensuring that the capacity remains viable after support ends. The relevant test is therefore not location alone but whether production is diversified, economically durable, and capable of expanding when disruption occurs.

5.5 Procurement and reimbursement

Procurement and reimbursement can reinforce resilience or intensify fragility. Short-term contracting and aggressive price competition reduce immediate purchasing costs but can also weaken incentives to maintain spare capacity, modernize facilities, qualify additional suppliers, or remain in low-margin markets.^[8,11]

A resilience-oriented procurement model would evaluate reliability and continuity alongside price. Longer-term contracts, supplier diversification, and performance criteria related to quality maturity or continuity planning could create stronger incentives for durable capacity. The objective is not to pay more indiscriminately; it is to recognize the expected cost of supply failure where clinical criticality, concentration, and recovery difficulty justify an explicit resilience premium.^[1,7,8]

5.6 Policy fragmentation

A central weakness of the current response is fragmentation across agencies, authorities, and objectives. Shortage surveillance, quality oversight, preparedness, manufacturing support, purchasing policy, and industrial policy operate through different institutions. Recent federal review has identified the absence of a formal mechanism for coordinating drug-shortage strategies across HHS and emphasized that FDA cannot independently address many of the underlying economic and supply-chain factors contributing to shortages.^[8,25]

Fragmentation can produce policies that are individually rational but collectively incomplete. Surveillance may identify vulnerability without altering procurement incentives; manufacturing support may expand capacity without creating durable demand; and stockpiles may absorb a disruption without changing the probability of recurrence. Resilience governance therefore requires a mechanism for connecting information to the policy lever capable of addressing the identified risk.

Table 2: Major U.S. pharmaceutical supply-chain policy instruments: strengths and structural limitations.

Policy instrument	Primary objective	Mechanism	Principal strength	Structural limitation
Shortage surveillance	Detect emerging supply problems	Notifications, public reporting, analytics	Improves visibility and warning time	Detection does not itself correct structural vulnerability. ^[17,18]
Regulatory response	Protect quality while facilitating continuity	Review prioritization, inspection, manufacturing oversight	Can accelerate selected qualified responses	Cannot independently create sustainable capacity. ^[4,22]
Strategic stockpiling	Buffer temporary disruption	Reserves, rotation, emergency distribution	Provides time during acute disruption	Finite inventory does not remove upstream fragility. ^[26]
Domestic manufacturing support	Strengthen selected U.S. capacity	Investment support, incentives, advanced manufacturing	Can reduce selected external dependencies	Location alone does not ensure diversification or commercial durability. ^[25,27]
Procurement/reimbursement	Control cost and structure demand	Contracting, purchasing, payment incentives	Can influence supplier behavior and investment	Price pressure can discourage redundancy and resilience investment. ^[8,11]
Interagency coordination	Align federal responses	Cross-agency governance and shared planning	Can connect regulatory, economic, and preparedness functions	Authority and accountability may remain fragmented. ^[8,25]
Supply-chain intelligence	Anticipate disruption	Data integration, forecasting, predictive tools	Supports preventive governance	Incomplete upstream data can limit predictive coverage. ^[18–20]

Source: Authors' synthesis based on the cited literature.

6. Toward an Integrated Resilience-Oriented Policy and Regulatory Architecture

The preceding analysis suggests that pharmaceutical resilience cannot be achieved by layering isolated interventions onto a system whose incentives and information architecture remain unchanged. Surveillance, stockpiles, domestic production, and regulatory flexibility each address part of the problem, but none is sufficient when fragility is generated jointly by economics, concentration, limited visibility, and slow recovery. A more durable strategy is to treat resilience as a designed property of the pharmaceutical market: one created through coordinated information, incentives, diversification, buffering, adaptability, recovery, and learning.

6.1 Reframing resilience as a system capability

For policy purposes, resilience can be defined as the capacity of the pharmaceutical supply system to anticipate disruption, absorb shocks, maintain access to essential medicines, recover within an acceptable period, and learn from failure. Inventory is only one element of this capacity. The broader system also requires viable

production, meaningful redundancy, visibility across critical tiers, substitutability, regulatory adaptability, and mechanisms for institutional learning.^[6,7,21]

This definition shifts the policy objective from minimizing shortage counts to managing the probability, severity, and duration of access failure. It also makes explicit that resilience is product-specific. The socially appropriate level of redundancy for a life-sustaining injectable with few substitutes may differ from that for a widely substitutable medicine with flexible production.

6.2 Aligning economic incentives with resilience

The central economic problem is that suppliers may bear the cost of resilience while the broader health system receives much of the benefit when disruption is avoided. Procurement should therefore incorporate reliability attributes alongside price where supply failure would impose substantial clinical or system costs. Longer-term contracts can provide demand certainty, supplier diversification can reduce single-source dependence, and targeted financial support can preserve strategically

important capacity where market returns are persistently inadequate.^[7,8,11]

Such interventions should be selective, measurable, and conditional. A resilience payment should purchase an observable capability—such as qualified backup supply, verifiable spare capacity, diversified sourcing, or continuity performance—rather than simply increasing revenue without changing risk. This principle is essential for avoiding subsidies that protect firms without protecting patients.

6.3 Building supply-chain visibility and predictive intelligence

Preventive governance requires visibility before a shortage becomes clinically apparent. Integrated risk intelligence should connect data on manufacturers, facilities, APIs, critical inputs, inventories, quality events, demand, and production capacity. Predictive disruption monitoring has increasingly been proposed and developed for pharmaceutical supply chains, but its broader effectiveness depends on data completeness, interoperability, and the ability to identify common dependencies across supply-chain tiers.^[18–21]

Artificial intelligence and advanced analytics may be useful for anomaly detection, demand forecasting, dependency mapping, and risk prioritization, but these tools should remain decision support rather than substitutes for regulatory or clinical judgment. Their performance should be evaluated prospectively for false alarms, generalizability, drift, interpretability, and whether earlier warnings actually improve supply outcomes.^[19–21]

6.4 Regulatory reform for adaptive capacity

Regulatory reform should focus on adaptability rather than deregulation. Quality and safety standards remain non-negotiable, but oversight can be structured to recognize demonstrated manufacturing maturity, robust quality systems, and reliable production performance. Emerging federal initiatives involving earlier engagement, risk-based inspection, quality-management maturity, or advanced manufacturing point toward this approach.^[22,27]

A resilience-oriented model would pre-identify scientifically credible response pathways before an emergency. When supply risk rises, qualified changes could then be prioritized without creating a lower standard of evidence. The policy objective is to reduce avoidable response time while preserving the controls that prevent supply continuity from being achieved at the expense of product quality.

6.5 Strategic domestic and distributed manufacturing

Domestic manufacturing should be targeted to products and inputs whose disruption has high clinical consequences and for which alternative capacity is difficult to mobilize. This may include selected APIs,

critical starting materials, and finished medicines with limited substitutability. Advanced or distributed manufacturing could add flexibility where technologies permit smaller, more modular, or more rapidly scalable production.^[27,28] More broadly, optimization research in additive manufacturing demonstrates how production planning can be integrated with alternative material-sourcing decisions to maintain production under material constraints, illustrating the potential importance of operational flexibility in distributed manufacturing systems.^[31]

The key criterion is strategic value, not geography alone. Public-private investment should be linked to durable demand, measurable capacity, diversified inputs, and continuity commitments. Otherwise, policy may relocate rather than reduce vulnerability.

6.6 Strategic buffers and recovery capacity

Strategic reserves should evolve from indiscriminate accumulation toward targeted risk management. Products can be prioritized according to clinical criticality, supplier concentration, replenishment time, shelf life, substitutability, and recovery difficulty. Rotational inventories can reduce expiration losses, while reserves of selected APIs or inputs may protect multiple downstream products.^[7,26]

Buffering should also include surge capability. From a resilience perspective, the ability to increase production within weeks may be more valuable than a large static inventory if disruptions are prolonged. This broadens the concept of a reserve from “what is stored” to “what can be mobilized.”

6.7 The eight-function resilience architecture

The proposed framework integrates these policy mechanisms into eight linked functions: Detect, Assess, Incentivize, Diversify, Buffer, Adapt, Recover, and Learn. Detect identifies emerging supply risk; Assess evaluates criticality, concentration, substitutability, and expected consequences; Incentivize aligns purchasing and investment with continuity; Diversify reduces common-mode dependencies; Buffer creates inventory or capacity options; Adapt enables qualified regulatory and operational change; Recover restores supply within an acceptable period; and Learn uses outcomes to update risk assessment, procurement, manufacturing, and regulatory policy. The framework is not intended as a rigid linear sequence. Several functions should operate concurrently, and learning should continuously update every preceding function.

Its contribution is to connect three policy domains that are often considered separately: supply-chain intelligence, the economics of production and procurement, and regulatory/operational adaptability. The framework therefore treats resilience as a governance cycle rather than a collection of emergency tools.



Figure 2: Integrated pharmaceutical supply-chain resilience framework. The framework conceptualizes resilience as a continuous cycle of eight interconnected functions—Detect, Assess, Incentivize, Diversify, Buffer, Adapt, Recover, and Learn—that collectively support safe and continuous access to essential medicines. Learning from disruptions feeds back into risk detection and assessment, enabling continuous adaptation and improvement. Source: Authors’ conceptual synthesis based on the literature.^[6,7,18,21,22,25]

7. An Evidence-Based Reform Agenda for U.S. Pharmaceutical Resilience

An integrated architecture becomes policy-relevant only when it can be translated into actions with different time horizons. Sequencing matters because information deficits, economic incentives, and productive capacity are interdependent. Near-term reforms should improve visibility and coordination; medium-term reforms should alter purchasing and investment incentives; and long-term reforms should institutionalize adaptive capacity, strategic redundancy, and continuous evaluation.

7.1 Near-term priorities: visibility, risk stratification, and coordination

The immediate priority is to improve the information infrastructure on which preventive action depends. Federal agencies and supply-chain participants should improve the timeliness and completeness of information on manufacturing interruptions, critical inputs, production capacity, inventories, and upstream dependencies. Risk-based monitoring should distinguish products by clinical criticality, concentration, substitutability, replenishment time, and recovery difficulty rather than treating all shortage signals as equivalent.^[17,18,20]

Clearer coordination is equally important. A warning generated by surveillance should trigger the appropriate regulatory, procurement, preparedness, or industrial-policy response. This requires agreed escalation pathways and accountability for deciding when a vulnerability justifies intervention.

7.2 Medium-term priorities: resilience-linked purchasing and targeted capacity

Once vulnerability is measured more systematically, procurement can begin to reward reliability alongside price. Resilience-linked contracting could give greater value to diversified sourcing, adequate capacity, quality maturity, and credible continuity plans. Longer-term purchasing arrangements may give manufacturers the demand certainty needed to justify investments that short-term price competition discourages.^[8,11]

Targeted incentives may also be appropriate for products whose clinical importance is high but whose market economics are persistently weak. Such support should be conditional on measurable resilience outcomes, periodically reviewed, and withdrawn when it no longer purchases additional public value.

Resilience-linked purchasing also creates distributional and governance risks. Hospitals and health systems operating under constrained margins may be unable to absorb higher acquisition costs, creating the possibility that resilience premiums are transmitted to payers and, depending on benefit design and contracting arrangements, ultimately to patients. Conversely, additional payments intended to strengthen manufacturing resilience may be retained within downstream contracting arrangements rather than generating corresponding investment in upstream API production, redundant capacity, or supplier diversification. These risks are especially relevant in markets where group purchasing organizations and other intermediaries influence contracting and purchasing incentives.^[35,36] Resilience payments should therefore be tied to verifiable capabilities and accompanied by

sufficient contractual transparency to establish where additional revenue flows and what resilience capacity it purchases. Where public or purchaser funds support higher prices for continuity, evaluation should determine whether those payments actually reach the supply-chain tiers responsible for the targeted vulnerability.

7.3 Long-term priorities: institutionalized resilience governance

Long-term policy should institutionalize the capacity to anticipate and absorb disruption rather than repeatedly

constructing ad hoc responses. This implies a standing national capability that links supply-chain intelligence, procurement, manufacturing policy, regulatory oversight, and emergency preparedness. Regulatory systems should incorporate evidence of manufacturing maturity and reliability into risk-based oversight while preserving quality standards, and national risk assessment should be continuously updated as suppliers, technologies, markets, demand, and geopolitical conditions change.^[22,25]

Table 3: Proposed policy and regulatory reforms for U.S. pharmaceutical supply-chain resilience.

Vulnerability	Current policy gap	Proposed reform	Lead stakeholders	Expected resilience mechanism	Implementation challenge
Incomplete visibility	Risk is detected after constraints become acute	Integrated critical-product mapping and early-warning data	Regulators, manufacturers, purchasers	Earlier detection and more targeted intervention	Data completeness, confidentiality, interoperability. ^[17–20]
Fragile generic economics	Price signals underreward continuity	Resilience-linked contracts and selective continuity incentives	Purchasers, payers, manufacturers, policymakers	Improved commercial case for reliable capacity	Cost pass-through, gaming, defining measurable resilience. ^[8,11,16]
Supplier/API concentration	Nominal competition masks common dependencies	Qualified backup suppliers and tier-level diversification	Manufacturers, regulators, purchasers	Lower common-mode failure risk	Qualification cost and limited alternative capacity. ^[12,13,15]
Strategic capacity gaps	Critical products may lack economically viable backup production	Targeted long-term capacity support for high-criticality products	Federal programs, manufacturers, purchasers	Sustained strategic redundancy	Fiscal cost and long-term demand sustainability. ^[7,11,27]
Slow adaptation during disruption	Qualified changes may require time when supply is already constrained	Preplanned adaptive regulatory pathways and prioritized review	Regulators and manufacturers	Faster safe capacity adjustment	Preserving evidence and quality standards. ^[4,22,27]
Limited buffering/recovery	Static inventories may be insufficient for prolonged shortages	Rotating reserves plus surge-capacity planning	Preparedness agencies, purchasers, manufacturers	Longer response window and faster recovery	Expiry, storage cost, maintaining deployable capacity. ^[7,26]
Fragmented governance	Risk information and policy levers sit in separate institutions	Formal cross-agency resilience coordination and escalation	Relevant federal agencies and health-system partners	Policy coherence and accountability	Authority, data-sharing, and institutional incentives. ^[25]
Weak evaluation	Success is measured mainly by shortage counts	Resilience scorecard tracking continuity, duration, recovery, diversification, cost	Policymakers, evaluators, health systems	Accountable learning and policy adaptation	Metric burden and risk of proxy optimization. ^[6,29]

Source: Authors' synthesis based on the cited literature.

8. Implementation Challenges, Trade-Offs, and Unintended Consequences

Resilience is not costless. Maintaining multiple suppliers, geographically distributed production, inventories, and unused capacity can increase procurement and operating costs during normal

conditions. A policy that maximizes redundancy without regard to cost could undermine affordability or preserve inefficient capacity. The appropriate question is therefore not how to maximize resilience, but where additional resilience produces enough expected social value to justify its cost.^[7,11]

Domestic manufacturing presents a similar trade-off. Reducing reliance on foreign production may strengthen control over selected critical inputs, but relocating production for geographic reasons alone can sacrifice some benefits of specialization without eliminating supplier concentration or upstream dependence. A U.S.-based facility that relies on a single critical input can remain highly exposed. Reshoring can therefore change the geography of vulnerability without changing its structure.

Regulatory adaptability also requires clear boundaries. Faster review and manufacturing changes can improve responsiveness, but excessive flexibility can create quality risk. Data integration raises parallel concerns because supply-chain information may be commercially sensitive or security-relevant. Governance must define what information is required, who can access it, how it can be used, and how confidential information is protected.^[22,25]

Government intervention creates risks of its own. Subsidies, guaranteed contracts, or reserve purchases can preserve strategically important capacity, but poorly designed support can protect firms without reducing system risk. Support should therefore be conditional on measurable outputs and reviewed against explicit counterfactuals: whether dependence, recovery time, continuity, or substitutability improved relative to what would otherwise have occurred.

Finally, metrics can distort behavior. If suppliers are rewarded for a narrow indicator, they may optimize that indicator without improving actual resilience. A credible evaluation system should therefore use a balanced set of measures and periodically test whether those measures still correspond to continuity of patient access.^[29]

9. Research Gaps and Future Directions

The field still lacks a sufficiently consistent framework for determining whether pharmaceutical resilience has actually improved. Shortage occurrence, inventory levels, and supplier counts are useful but incomplete. Future research should develop multidimensional measures combining continuity of supply, recovery time, upstream concentration, substitutability, production flexibility, clinical criticality, and economic cost.

A second priority is estimating the economic value of redundancy. Additional suppliers and productive capacity impose costs during normal conditions, but avoided losses during disruption may be substantial. Research should estimate this trade-off across medicine categories and identify transparent criteria for when strategic intervention generates sufficient societal value to justify additional expenditure.

Procurement reform also requires rigorous empirical evaluation. Long-term contracts, resilience-linked purchasing, supplier diversification, and manufacturing

incentives should be tested for their effects on market entry and exit, quality, prices, continuity, and recovery. The relevant outcome is not whether a policy changes purchasing behavior, but whether it reduces clinically meaningful supply risk over time.

Predictive analytics warrants similar caution. Models should be evaluated prospectively for calibration, false alarms, external validity, data drift, interpretability, and decision impact. An early-warning system has policy value only if its warnings arrive early enough to change action and if those actions improve supply outcomes.^[30]

Finally, resilience research needs longitudinal and cross-sectoral evaluation. A system should not be judged more resilient because it experiences fewer shortages in a single period. Studies should examine whether interventions reduce disruption duration, diversify critical dependencies, improve recovery, and remain economically sustainable. This research agenda will require collaboration across health economics, pharmaceutical sciences, operations and supply-chain research, regulatory science, and data science.

10. CONCLUSION

U.S. pharmaceutical supply-chain vulnerability is not fundamentally a problem of insufficient emergency response. It is a consequence of structural conditions that can make economically efficient markets fragile under disruption. Concentrated manufacturing, common upstream dependencies, weak incentives for redundancy, incomplete visibility, and fragmented policy responsibilities can allow localized failures to become prolonged shortages with clinical and economic consequences. Surveillance and emergency response are therefore necessary, but they cannot by themselves correct the conditions that repeatedly generate vulnerability.

A more durable approach requires resilience to become an explicit objective of pharmaceutical market governance. Procurement systems should recognize continuity and diversification alongside price; regulatory systems should preserve rigorous quality requirements while enabling qualified capacity to adapt; and public investment should be directed selectively toward capabilities whose social value is not adequately rewarded by conventional market incentives. Supply-chain intelligence should move from retrospective shortage reporting toward continuous assessment of critical dependencies, capacity, and recovery risk.

The eight-function framework proposed in this review—Detect, Assess, Incentivize, Diversify, Buffer, Adapt, Recover, and Learn—provides a structure for connecting those policy levers. Its central premise is that resilience emerges from coordinated capabilities rather than from any single intervention. The framework therefore shifts the policy question from “How should the United States respond to the next shortage?” to “What market and

regulatory architecture makes prolonged shortage less likely, less severe, and faster to recover from?”

The answer will necessarily involve trade-offs. Resilience has a cost, domestic production is not automatically diversified production, faster regulatory action cannot compromise quality, and better data do not guarantee better decisions. The policy objective should therefore be measurable resilience: targeted, evidence-based investments that reduce common-mode risk, improve recovery, preserve access, and remain economically sustainable.

Declarations

Data availability

No original patient-level, clinical, or experimental dataset was generated or analyzed for this narrative policy review. All evidence used in the review was obtained from the published literature and publicly available sources cited in the manuscript.

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Conflict of interest

The authors declare that they have no conflicts of interest relevant to this work.

Author contributions

All authors contributed to the conception and design of the review, literature evaluation, interpretation and synthesis of evidence, development of the conceptual framework, drafting of the manuscript, and critical revision of the manuscript. All authors reviewed and approved the final version of the manuscript.

Ethics approval

Not applicable. This article is a narrative policy review and conceptual synthesis and did not involve human participants, animals, or identifiable patient data.

Consent to participate

Not applicable.

Consent for publication

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