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XRIN 0694-XC120 Pharmaceuticals 232 Notice Posted by the Bureau of Industry and Security on Apr 15, 2025

Docket **BIS-2025-0022**

Docket Summary:
The Secretary of Commerce initiated an investigation to determine the effects on the national security of imports of pharmaceuticals and pharmaceutical ingredients, including finished drug products, medical countermeasures, critical inputs such as active pharmaceutical ingredients, and key starting materials, and derivative products of those items. This investigation has been initiated under section 232 of the Trade Expansion Act of 1962, as amended. Interested parties are invited to submit written comments, data, analyses, or other information pertinent to the investigation to the Department of Commerce's (Department) Bureau of Industry and Security (BIS), Office of Strategic Industries and Economic Security. This notice identifies issues on which the Department is especially interested in obtaining the public's views.

Sentio BioSciences Comments: National Security Position Paper for the Department of Commerce, Bureau of Industry and Security Submitted in Response to BIS-2025-0022

Introduction
This comments is submitted by Sentio BioSciences LLC “Sentio”, a U.S.-based pharmaceutical manufacturer of key starting materials (KSMs), active pharmaceutical ingredients (APIs), and finished pharmaceutical products. Sentio operates a vertically integrated (KSM, API and Drug Product) development and manufacturing site in St. Louis, Missouri, and has supported U.S. healthcare (Human and Animal) needs since 2009 with 2 approved drug products on the US market and multiple others in the pipeline at different stages of the development and regulatory approval cycle.
Sentio has managed to have a great track record, despite being a small business with only 35 employees and all internal investment and customer milestones. Sentio’s cGMP facility (22k sq ft) has over 10 years of successful FDA inspections with no quality issues. Sentio has in-house capabilities in development of small molecules, including KSMs and APIs, scale up, cGMP commercial manufacturing and a strong regulatory foundation to be able to prepare high quality drug master files and CMC dossiers for FDA approvals.
Sentio’s strong and robust cGMP systems and business strategy ensures commercial manufacturing is reliable, sustainable, profitable and ensures highest quality and safety culture.

This documents provides Sentio’s views/comments on how to address the Department of Commerce’s investigation into the national security risks posed by the import dependence on pharmaceuticals and pharmaceutical ingredients with specific attention to medical readiness, supply chain resilience, and strategic autonomy for critical drug supplies.

Request for Public Comments
This investigation is being undertaken in accordance with part 705 of the National Security Industrial Base Regulations (15 CFR parts 700 through 709) (“NSIBR”). Interested parties are invited to submit written comments, data, analyses, or information pertinent to this investigation to BIS's Office of Strategic Industries and Economic Security no later than May 7, 2025. The Department is particularly interested in comments and information directed at the criteria listed in § 705.4 of the regulations as they affect national security, including the following:

(i). The Current and Projected Demand for Pharmaceuticals and Pharmaceutical Ingredients in the U.S.

Pharmaceutical ingredients, particularly those on the **Essential Medicines List** and used in **life-saving therapies**, are overwhelmingly manufactured overseas. This includes not only the active pharmaceutical ingredients (APIs), but also the **key starting materials (KSMs)** that form the foundation of drug production. A significant portion of these

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KSMs are manufactured in **China**, posing serious national security risks due to the concentration of global supply in a geopolitically sensitive region.
China also dominates the global supply of several categories of **antibiotics**, further exacerbating the vulnerability of the U.S. pharmaceutical supply chain. Additionally, **India supplies a large share of finished dosage forms and APIs**, but itself depends heavily on China for KSMs. These interconnected dependencies represent a fragile global structure that is prone to disruption from **geopolitical conflict, trade restrictions, natural disasters, or global health crises.**
In this context, the **national security risk is substantial**. A breakdown in access to these essential components—even temporarily—could threaten the health and safety of millions of Americans and impede military and emergency preparedness.

How Sentio Can Help

Sentio, an established U.S.-based manufacturer located in **St. Louis, Missouri**, is well-positioned to support national efforts to reduce reliance on foreign pharmaceutical imports. Since its inception in **2009**, Sentio has implemented a **vertically integrated manufacturing model**, producing both key starting materials and APIs on-site. This approach enhances quality control, traceability, and supply chain independence.
Sentio has a **strong regulatory track record**, including over **10 years of FDA inspections without major findings**, two **FDA-approved drug products**, and a **third currently under review**. The company also maintains **in-house R&D capabilities** for the development of small molecules, with expertise spanning KSMs. APIs and Drug Products.
Further, Sentio's regulatory infrastructure includes the preparation of **high-quality Drug Master Files (DMFs)** and **CMC dossiers**, demonstrating its readiness to meet rigorous FDA standards. Its **robust CGMP systems** ensure sustainable, high-quality, and reliable commercial manufacturing, making it a strategic partner for building **domestic resilience** in pharmaceutical production.
By supporting U.S.-based manufacturers like Sentio through strategic incentives and procurement policies, the Department of Commerce can **significantly strengthen the pharmaceutical industrial base**, mitigate geopolitical risks, and enhance national security.

(ii). Extent to Which Domestic Production of pharmaceuticals and pharmaceutical ingredients can Meet Domestic Demand

While domestic capacity for pharmaceutical production exists, it is currently insufficient to fully meet U.S. demand, particularly for **essential medicines and their upstream ingredients**. The process of **onshoring** production of a single molecule—including development, scale-up, and regulatory approval—typically takes between **2.5 to 3 years**. This includes 12–18 months for formulation and process development and scale-up, followed by up to 12 months for **FDA review and site approval**.
This extended timeline underscores the need for **pre-positioned infrastructure, technical expertise, and regulatory readiness**—all of which are required to successfully shift production from offshore suppliers to domestic sites.

How Sentio Can Support Domestic Production

Sentio is uniquely positioned to support rapid onshoring efforts due to its **end-to-end in-house capabilities** in developing, scaling, and filing regulatory dossiers for pharmaceutical molecules. Sentio has both the **physical infrastructure and specialized personnel** to compress development timelines and accelerate **FDA submission readiness**. Its proven track record includes **single-cycle FDA reviews** and rapid progression from development to market authorization.
To further support domestic resilience, **expanding into sterile injectable drug product manufacturing**, a critical capability for hospital-based and emergency medicines. This would advance Sentio's model of **vertically integrated manufacturing**—from key starting materials to finished drug products—enhancing supply chain stability and lowering costs to compete with foreign producers.
However, **government support is essential** to accelerate this transformation. Strategic investment in infrastructure, equipment, and long-term procurement commitments would enable companies like Sentio to **scale faster and more**

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broadly, bridging the gap between current capacity and national security needs.

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iii. The Role of foreign supply chains, particularly of major exporters, in meeting United States demand for pharmaceuticals and pharmaceutical ingredients;

The U.S. currently relies heavily on foreign supply chains—particularly in China and India—for both finished pharmaceutical products and active pharmaceutical ingredients (APIs). While these countries serve as major exporters, their manufacturing facilities often experience **recurring quality issues**, including FDA import alerts, non-compliance with current Good Manufacturing Practices (CGMP), and lapses in data integrity.

When such quality issues arise overseas, **foreign suppliers are often unable to fulfill U.S. demand**, leading to **significant drug shortages**. The U.S. healthcare system is left vulnerable, with limited recourse for quickly replacing these supplies.

This underscores the urgent need for **reliable, domestic manufacturing capacity** that adheres to stringent quality standards and regulatory oversight.

How can Sentio help?

Sentio is prepared to play a key role in **mitigating the risk of foreign supply chain failures**. With its U.S.-based facility and over a decade of **FDA-compliant operations**, Sentio offers a **stable, high-quality alternative** to foreign suppliers. Sentio's vertically integrated manufacturing model—covering everything from key starting materials to APIs to drug products —ensures control over quality, consistency, and availability.

By expanding domestic capabilities through partners like Sentio, the U.S. can reduce its dependence on vulnerable foreign supply chains and strengthen its national pharmaceutical resilience.

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iv. The concentration of United States imports of pharmaceuticals and pharmaceutical ingredients from a small number of suppliers and the associated risks;

The current structure of the global pharmaceutical supply chain is **highly concentrated** in a few overseas geographies—primarily **China and India**—and among a small number of large manufacturers. This concentration has been largely driven by **cost-reduction strategies**, including the pursuit of **economies of scale**, low labor costs, and government subsidies that favor offshore production.

While this model has succeeded in lowering prices, it has also created **significant national security and public health vulnerabilities**. A disruption caused by **geopolitical tensions, war, natural disasters, or logistical breakdowns** could immediately jeopardize the availability of critical medicines in the United States. This is not only a health crisis waiting to happen—it is also a **national security issue** with implications for military readiness, emergency preparedness, and the stability of the healthcare system.

How This Can Be Addressed

To reduce dependency and promote diversification and onshoring of pharmaceutical production, a comprehensive policy shift is required. Specifically:

- **Targeted incentives** must be provided to domestic manufacturers willing to take on the upfront **development, scale-up, and regulatory risks** of producing APIs and key starting materials in the U.S.
- **Capital investment and startup support** are essential to build or repurpose facilities and acquire advanced equipment.
- **Tariffs on overseas manufacturers where domestic sources are available.**
- **Ongoing procurement incentives** are needed to offset the competitive pricing advantage held by foreign suppliers. These may include:
    - **User fee differentials** for foreign vs. domestic manufacturers
    - **More stringent inspections** and compliance standards for overseas facilities
    - **Priority reviews** for U.S.-based manufacturers' filings
    - **Removal of rebate requirements like 340B** or other commercial disadvantages for domestic producers especially of essential generic medicines that are already at very low prices.
    - **Preferential treatment** in U.S. healthcare distribution system, Group Purchase organizations, government purchasing and national stockpiles

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These changes will make it feasible for domestic manufacturers to sustain operations, compete on price and reliability, and ensure long-term supply stability.

Sentio's Role

Sentio is well-positioned to support this transformation. As a **U.S.-based vertically integrated manufacturer** with a proven track record, Sentio is ready to **expand capacity**, take on **high-priority onshoring projects**, and deliver quality-controlled APIs and KSMs from its **St. Louis, Missouri facility**. With the right support framework, Sentio can help diversify the supplier base and reduce the risks associated with overconcentration in foreign markets.

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v. the impact of foreign government subsidies and predatory trade practices on United States pharmaceuticals industry competitiveness;

Foreign governments—most notably **China**—actively subsidize their pharmaceutical sectors, enabling companies to operate at extremely low costs and dominate global markets. These subsidies are often coupled with **predatory trade practices**, including the **theft of intellectual property**, and large-scale, state-backed investments aimed at building export-ready industries regardless of profitability.
In **India**, while the government is less directly involved, a strong **entrepreneurial ecosystem** and robust investment culture have fueled the growth of a vibrant pharmaceutical manufacturing base—even in the face of **low margins and tight pricing pressures**. Private investors in India are generally more willing to commit capital to generic and API production despite modest returns.
In contrast, the **U.S. investment climate** is driven by expectations of **high returns and quick exits**. Most venture capital and institutional investors focus on high-growth biotech startups, rather than **long-term investments** in low-margin, essential manufacturing such as generic pharmaceuticals or active pharmaceutical ingredients. As a result, **U.S. manufacturers struggle to secure funding** to build and scale domestic capabilities, despite national security imperatives.

What Needs to Be Done

To level the playing field and enable the U.S. to compete against heavily subsidized foreign producers, the federal government should implement **targeted, time-bound incentives** that make domestic pharmaceutical manufacturing economically viable. These may include:

- **Low-interest loans** for capital expansion and equipment
- **Grants** to support jump starting development and facility build-outs
- **Public-private partnerships** and advanced purchase contracts for key products
- **R&D investment** to support innovation in efficient, cost-effective manufacturing
- **Tariffs or user fee adjustments** that disincentivize predatory pricing by foreign suppliers
- **Regulatory incentives**, such as priority review or reduced barriers for domestic manufacturers

These interventions should be structured to support **industry sustainability**, not perpetual dependency. The goal is to **enable domestic manufacturers to compete effectively**, expand capacity, and reduce vulnerability to foreign trade practices that are misaligned with U.S. national interests.

Sentio's Perspective

As a **privately held U.S. pharmaceutical manufacturer** that has operated successfully in a difficult investment environment since 2009, **Sentio** exemplifies what is possible when companies are committed to long-term manufacturing. With the right support—especially in infrastructure, technology, and regulatory facilitation—Sentio and similar firms can **anchor a revitalized, resilient domestic pharmaceutical supply chain**.

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vi. the economic impact of artificially suppressed prices of pharmaceuticals and pharmaceutical ingredients due to foreign unfair trade practices and state-sponsored overproduction;

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The United States pharmaceutical manufacturing sector faces a profound economic disadvantage due to **artificially low pricing of pharmaceutical ingredients and drug products from countries like China**. These suppressed prices are primarily driven by:

- **Massive government subsidies** that shield Chinese manufacturers from true market costs
- **Economies of scale** enabled by state-supported mega-facilities
- **Minimal environmental and labor compliance costs**, which lower operating expenses significantly
- **Abundant labor or state-supported automation**, further reducing production costs
- **Lack of enforcement around intellectual property**, often allowing copied or unlicensed products to enter global markets
- **Highly educated workforce with strong technical knowledge and work ethics.**

These conditions make it exceedingly difficult for U.S.-based manufacturers to compete, especially when contract manufacturing operations domestically are inherently **more expensive due to regulatory compliance, labor costs, and capital investment needs**.

Why Vertically Integrated Manufacturing Matters

In this context, **vertically integrated operations**—where a company controls the entire production chain from **key starting materials (KSMs)** to **active pharmaceutical ingredients (APIs)** and **finished drug product**—become essential to controlling cost and maintaining competitiveness.
Sentio, based in St. Louis, Missouri, has embraced this model from its inception, building in-house capabilities that allow it to streamline production, reduce third-party markups, and manage quality end-to-end. This structure enables Sentio to **offer pricing that is more competitive**, while maintaining high standards of regulatory compliance and quality control.

What Is Needed from the U.S. Government and Investors

To level the economic playing field, targeted support is crucial. This includes:

- **Access to low-interest financing** for facility and equipment expansion
- **Grants or contract incentives** to support the cost of scaling essential medicine production
- **Support for research and process optimization**, especially in cost-efficient manufacturing technologies
- **Market protections** through tariffs or trade restrictions on heavily subsidized imports that distort fair competition
- **Relax domestic regulatory requirements for EPA, 340B, and FDA support for generics including providing longer exclusivity and preferred review for domestic manufacturers.**

These interventions will enable U.S. manufacturers not only to survive—but to **thrive in producing essential medicines** reliably, domestically, and at competitive pricing. The role of **impact investors** in this space will also be pivotal, especially those willing to invest in sustainable, mission-driven pharmaceutical infrastructure with long-term returns.

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vii. the potential for export restrictions by foreign nations, including the ability of foreign nations to weaponize their control over pharmaceuticals supplies;

The risk of foreign nations imposing **export restrictions on critical pharmaceutical products and ingredients** poses a serious **national security threat** to the United States. This is particularly true with respect to **China**, which holds a dominant position in the global supply of **key starting materials (KSMs)**, **active pharmaceutical ingredients (APIs)**, and **certain classes of finished drugs**, including life-saving antibiotics and other essential medicines.
In times of geopolitical tension or conflict, there is a **very real possibility** that China could strategically **withhold exports of these materials**. Such an action could result in:

- **Acute drug shortages**, particularly for vulnerable populations and critical care
- **Widespread health crises**, due to lack of access to essential medications
- **Massive disruption to the U.S. healthcare system and emergency preparedness**
- **National security implications**, if key medical countermeasures become inaccessible

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This scenario is **not theoretical**—it represents a **known vulnerability** that could be exploited with severe consequences for both public health and national defense.

The Urgent Need to Expand U.S. Domestic Manufacturing
To mitigate this threat, the U.S. must act with urgency to **expand its domestic pharmaceutical manufacturing capacity**, particularly for:

- Essential medicines listed on the FDA and WHO essential drug lists
- Medical countermeasures for emergency preparedness
- High-risk APIs and intermediates currently sourced from single foreign suppliers

Sentio, with its **established vertically integrated manufacturing platform** in St. Louis, Missouri, is well-positioned to play a leading role in this national effort. Sentio has demonstrated capabilities in **scaling critical molecules**, **producing KSMs and APIs in-house**, and **meeting rigorous FDA standards**. With appropriate support, Sentio can rapidly **ramp up production** of high-priority pharmaceuticals to ensure **uninterrupted domestic supply**—even in the face of export bans or geopolitical disruption.

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viii. the feasibility of increasing domestic capacity for pharmaceuticals and pharmaceutical ingredients to reduce import reliance;

The expansion of domestic manufacturing capacity for key starting materials (KSMs), active pharmaceutical ingredients (APIs), and drug products is both **feasible and urgent** in reducing the United States' reliance on imports—especially for **essential and life-saving medicines** that currently lack a domestic source.

Sentio is positioned to play a pivotal role in this effort. As an established manufacturer based in **St. Louis, Missouri**, Sentio has the **infrastructure, technical expertise, and regulatory track record** to expand operations and meet national needs.
Key strengths that support the feasibility of scaling domestic capacity include:

- **Vertically integrated manufacturing model**: Sentio develops and manufactures KSMs, APIs, and finished drug products all in-house, reducing dependency on fragmented or overseas supply chains.
- **Track record of success**: Sentio has successfully taken **two drug products from development through to FDA-approved commercial manufacturing**, including all associated components—KSMs, APIs, and finished dosage forms.
- **Existing capacity and room for expansion**: Sentio is already working on a pipeline of **essential medicines** and has identified additional opportunities that align with national priorities.
- **Regulatory competence**: Sentio has consistently passed FDA inspections without major findings, demonstrating robust CGMP systems and regulatory expertise to bring new molecules to market efficiently.
- **Public-private partnership potential**: Sentio seeks to collaborate with the Department of Commerce and the industrial base expansion team to **align manufacturing priorities**, overcome regulatory hurdles, and **accelerate capacity-building efforts**.

To move forward quickly, **investment in infrastructure and equipment** is critical. Public-private partnerships and targeted government support—especially for **site expansion, technology upgrades, and equipment acquisition**—will enable Sentio and other qualified domestic manufacturers to rapidly scale up production and enhance national resilience.

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ix. the impact of current trade policies on domestic production of pharmaceuticals and pharmaceutical ingredients, and whether additional measures, including tariffs or quotas, are necessary to protect national security; and
Current U.S. trade policies have not sufficiently addressed the structural disadvantages faced by domestic pharmaceutical manufacturers. While global competition has driven down costs, it has also left the U.S. vulnerable to foreign control over critical drug supply chains, particularly for **essential medicines** and their **key starting materials (KSMs)** and **active pharmaceutical ingredients (APIs)**. To strengthen national security and ensure supply chain resilience, additional strategic policy interventions are required.

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Several measures are essential:

1. **Regulatory Support and Flexibility**: Domestic manufacturers need more efficient regulatory pathways to bring essential drug products—both traditional and advanced technologies—to market. A supportive regulatory environment that accommodates innovative approaches will accelerate development and approval, ensuring timely availability of critical medicines.
2. **Public-Private Partnerships**: Collaboration between government and industry is crucial to navigate regulatory, infrastructure, and market access hurdles. These partnerships can support development timelines and expand domestic production capacity.
3. **Fair Market Access and Distribution Channel Reform**: Domestic manufacturers face severe **price competitiveness challenges**. These are worsened by complex rebate structures and unfavorable distribution channel economics. Reform is needed to ensure that domestic producers are not penalized by pricing mechanisms that favor low-cost foreign suppliers.
4. **Tariffs and Trade Protections**: To protect and encourage domestic production, **higher user fees and tariffs** on foreign-manufactured pharmaceuticals and ingredients may be necessary. These tools can help level the playing field and disincentivize predatory pricing and unfair trade practices from foreign governments.
5. **Strategic Waste Management Infrastructure**: One of the major barriers for U.S. manufacturers, especially those dealing with hazardous chemical processes, is the **high cost and complexity of waste management**. The federal government should establish **national hazardous waste management support systems** that provide cost-effective and reliable disposal solutions. Exemptions or streamlined requirements under EPA and local regulations could also be considered—provided safety and environmental standards are maintained—to reduce operational burdens.
6. **Cost Offsets and Environmental Compliance Support**: Incentives in the form of **subsidies, grants, or low-interest loans** for waste disposal, environmental compliance, and infrastructure upgrades will further improve the feasibility of domestic manufacturing.

In summary, trade protections like tariffs and quotas are only part of the solution. A broader strategy is needed—one that includes regulatory modernization, fair market practices, investment in manufacturing infrastructure, and support systems for waste and environmental management. These combined efforts are necessary to make domestic pharmaceutical manufacturing **economically viable**, **environmentally sustainable**, and **nationally secure**.

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(x) any other relevant factors.

Government contracts and grants should be provided directly to domestic manufacturers and not through intermediaries, to ensure sustainable and reliable long-term domestic manufacturing and supply. Contract development and manufacturing for other organizations will only increase the cost and reduce price competitiveness. The generic drug IP developed with government funding should be owned by the manufacturer or the government. Vertically integrated manufacturing is critical for keeping the pricing of the product competitive.

Government has supported new domestic manufacturers with investment to setup very large infrastructures. However, these organizations have had a very difficult time being sustainable and will continue relying on the government or investor funding to remain viable. Vertically integrated development and manufacturing of products will keep prices lower. However, ensuring commercial customers are available is very important, for the manufacturer and the products to be sustainable and reliable.

It is critical for government to support domestic pharmaceutical manufacturers that are small business. Small domestic manufacturers will continue to support with manufacturing KSM, APIs and drug products that are niche, critical, and products that are below the revenue threshold requirements for large domestic manufacturers.

Large domestic manufacturers have strategic requirements on revenue generation. Especially publicly traded large companies may exit critical essential medicine markets due to low margins, low revenues or not novel or not in their strategic interest. This can cause a huge issue with the essential medicines supply in the US too.

US distribution system and the impact on prices pressures, including 340B regulations should be reviewed with respect to its impact on domestic manufacturers.

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