BioPrincipia

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May 6, 2025

The Honorable Howard Lutnick
Secretary of Commerce
1401 Constitution Ave NW
Washington, D.C. 20230

Comment to Docket BIS-2025-0022: XRIN 0694-XC120 Pharmaceuticals 232 Notice

Dear Secretary Lutnick:

Thank you for leading this important investigation to determine the effects on national security of imports of pharmaceuticals and active pharmaceutical ingredients (APIs), and their derivative products. BioPrincipia is a provider of biological fermentation process technologies for next-generation chemicals and pharmaceutical manufacturing. We are headquartered in Columbus, Georgia and through our subsidiaries Crysalis Biosciences and Fermworx, we have R&D and operating facilities in Colorado, Illinois, and Georgia.

We support a strong, broad tariff on imported pharmaceuticals and pharmaceutical ingredients to promote domestic production and believe that America has the capacity to rapidly respond and stand up new domestic manufacturing leveraging our enormous agricultural resources and low energy costs for advanced bio-feedstock processing of tailor-made APIs and biochemicals.

BioPrincipia has a unique and timely capacity to help meet projected national defense and security requirements related to onshoring pharmaceutical manufacturing because we can leverage idle equipment and a shovel ready fully designed biomanufacturing plant. The equipment was previously in use for pharmaceutical manufacturing by Merck at their Danville, PA facility but was decommissioned and sold in 2019. Products that have been made using this equipment include:

- Penicillin G
- Azithromycin
- Mectizan® (antiparasitic for river blindness)
- Asparaginase (treatment for childhood leukemia)
- Animal health and ag products
- Riboflavin (Vitamin B2)
- Dextran
- Biopesticides and biofungicides

BioPrinicipia is repurposing this equipment into a new facility with twenty (20), 75,000 liter fermenters (1.5 million liters total capacity). The facility is planned to be an FDA, GMP Compliant Facility for the manufacture of bio materials as well as antibiotics. All cGMP and FDA Guidance

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on the manufacture of APIs to prevent cross-contamination will be planned into these facilities.

With this project in mind we are pleased to provide our response to the questions posed in the request for comment, with particular focus on the essential issue embodied in 15 CFR § 705.4, namely the capacity of domestic industries to meet projected national defense requirements.

Response to Questions:

(ii) the extent to which domestic production of pharmaceuticals and pharmaceutical ingredients can meet domestic demand;

Domestic capacity remains limited, with many APIs and precursor ingredients being sourced from abroad, particularly China and India. New fermentation capacity can be rapidly mobilized to close this gap. The idle equipment owned by BioPrincipia's subsidiary Fermworx is positioned to contribute meaningfully to domestic production of biobased pharmaceutical ingredients, such as penicillin.

APIs like penicillin and azithromycin represent the greatest opportunity to demonstrate rapid scale-up for reshoring essential medicines. In 2023, the global penicillin G sodium market attained a size of 67 kilotons. IMARC Group forecasts the market to expand to 89.5 kilotons by 2032.

US trade in penicillin is imbalanced and as of 2019, more than 1.5 kilotons of penicillin are imported. With a strong and consistent market signal and federal support, we could stand up 3 kilotons at this single site within 18 - 24 months, fully displacing imports and providing a supply chain that goes from the American farmer to the American factory and into American doctors' offices without ever leaving the country.

A practical approach would leverage the 20 trains of fermenters to provide a multitude of products and enable the Fermworx site to displace 10–35% of U.S. imports for several critical APIs at a single location. Even lower-volume, high-value APIs offer strategic national security and cost advantages.

In addition to penicillin, the following APIs are a potential fit for this manufacturing approach with the approximately 3 kiloton capacity distributed by 150 metric ton/year/fermenter-train with some allowance for batch fermentation and changeovers:

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API / Intermediate	Therapeutic Use	U.S. Production (% est.)	Estimated U.S. Imports (MT/year)	Fermworx Import Displacement Potential	
				Sample Mix (MT)	*As a % of Imports*
Penicillin G / V	Antibiotic	<10%	1500	450	30%
See discussion above.					

API / Intermediate	Therapeutic Use	U.S. Production (% est.)	Estimated U.S. Imports (MT/year)	Fermworx Import Displacement Potential	
				Sample Mix (MT)	*As a % of Imports*
Azithromycin	Antibiotic	<10%	800	300	38%
Over 90% of U.S. supply is imported, primarily from India and China. High and stable demand as a front-line treatment for respiratory and sexually transmitted infections.See discussion above					

API / Intermediate	Therapeutic Use	U.S. Production (% est.)	Estimated U.S. Imports (MT/year)	Fermworx Import Displacement Potential	
				Sample Mix (MT)	*As a % of Imports*
Mectizan® (Ivermectin)	Antiparasitic (river blindness)	<10%	400	150	38%
Most API production occurs overseas, with India as the primary exporter. Demand spikes periodically due to tropical disease programs and off-label uses.					

API / Intermediate	Therapeutic Use	U.S. Production (% est.)	Estimated U.S. Imports (MT/year)	Fermworx Import Displacement Potential	
				Sample Mix (MT)	*As a % of Imports*
Asparaginase	Leukemia chemotherapy	<20%	50	50	100%

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Imported almost entirely, primarily from India and China; no large-scale U.S. production. Critical for pediatric leukemia treatment; narrow but high-value demand.

API / Intermediate	Therapeutic Use	U.S. Production (% est.)	Estimated U.S. Imports (MT/year)	Fermworx Import Displacement Potential	
				Sample Mix (MT)	*As a % of Imports*
Riboflavin (Vitamin B2)	Vitamin supplement	<15%	600	300	50%
Over 85% of global and U.S. supply comes from China. Widely used in food, supplements, and fortified products; demand is consistent and growing.					

API / Intermediate	Therapeutic Use	U.S. Production (% est.)	Estimated U.S. Imports (MT/year)	Fermworx Import Displacement Potential	
				Sample Mix (MT)	*As a % of Imports*
Dextran	Plasma expander / industrial	<10%	1200	150	13%
Pharma-grade dextran is largely imported from Europe and Asia. Specialized demand for plasma volume expanders, chromatography, and wound dressings.					

API / Intermediate	Therapeutic Use	U.S. Production (% est.)	Estimated U.S. Imports (MT/year)	Fermworx Import Displacement Potential	
				Sample Mix (MT)	*As a % of Imports*
7-ACA	Cephalosporin intermediate	<10%	950	250	26%
Highly centralized supply chain; critical precursor.					

API / Intermediate	Therapeutic Use	U.S. Production (% est.)	Estimated U.S. Imports (MT/year)	Fermworx Import Displacement Potential

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				Sample Mix (MT)	*As a % of Imports*
Lovastatin / Simvastatin	Statin (cholesterol control)	<15%	750	300	40%
Often imported as intermediates or formulated drugs.					

API / Intermediate	**Therapeutic Use**	**U.S. Production (% est.)**	**Estimated U.S. Imports (MT/year)**	**Fermworx Import Displacement Potential**	
				Sample Mix (MT)	***As a % of Imports***
Vitamin B12	Supplement / anemia treatment	<5%	175	150	86%
Complex process requirements, but Fermworx could demonstrate domestic resilience.					

API / Intermediate	**Therapeutic Use**	**U.S. Production (% est.)**	**Estimated U.S. Imports (MT/year)**	**Fermworx Import Displacement Potential**	
				Sample Mix (MT)	***As a % of Imports***
L-DOPA (Levodopa)	Parkinson's treatment	<10%	350	350	100%
High-value niche drug; scalable with enzymatic routes.					

API / Intermediate	**Therapeutic Use**	**U.S. Production (% est.)**	**Estimated U.S. Imports (MT/year)**	**Fermworx Import Displacement Potential**	
				Sample Mix (MT)	***As a % of Imports***
Hyaluronic Acid	Biopolymer (medical, cosmetic)	<10%	550	550	100%
Growing demand, currently almost entirely imported.					

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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 United States manufactures only 12% of its APIs, leaving the bulk of production to foreign sources. India and China are the primary providers of APIs for U.S. prescription medications, according to data gathered by the U.S. International Trade Commission and concerns raised by U.S, legislators during President Trump's first term.1 From 2020 through 2022, U.S. imports of Chinese pharmaceuticals jumped 485 percent; much of this import surge was comprised of Chinese drugs dosed and ready for use by American consumers and hospitals.2

Given that 90% of prescriptions filled in the U.S. are for generics, India's dominant role in global generic drug production is particularly significant. Europe supplies 43% of the APIs used in branded (non-generic) drugs, while China, though responsible for only 8% of finished APIs, remains a critical global source of pharmaceutical starting materials and intermediates.

In the case of penicillin, India currently holds 27% of the global penicillin export market, followed by China at 20%, while the United States contributes just 10%. Despite participation from over 100 countries in the global penicillin trade, the U.S. relies heavily on imports to meet domestic demand.

This heavy dependence exposes the U.S. pharmaceutical supply chain to risks stemming from geopolitical instability, export controls, supply shocks, and pricing volatility. The COVID-19 pandemic and ongoing global tensions have highlighted these vulnerabilities, underscoring the need for domestic, resilient manufacturing capacity. If Fermworx were to operate at full capacity, it would represent a critical domestic counterweight to these vulnerabilities.

Since Fermworx's infrastructure was acquired from a previous pharmaceutical fermentation operation, it offers validated equipment, experienced process lines, and proven scale-up capacity, providing a faster pathway to full-scale commercial production compared to greenfield builds. Fermworx has the existing footprint, process flexibility, and scalability to serve as a strategic domestic production site for critical fermentation-derived APIs, supporting resilience and reshoring goals across multiple essential drug classes.

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

The decline in U.S. pharmaceutical manufacturing competitiveness is primarily driven by the state-directed subsidization of strategic manufacturing sectors by foreign governments, notably the People's Republic of China. China employs a proactive, strategic, and well-financed industrial policy, exemplified by programs such as Made in China 2025, which provide substantial subsidies for infrastructure, energy, land, and credit access to its pharmaceutical and

1 https://www.finance.senate.gov/imo/media/doc/2019-08-06%20CEG%20to%20HHS%20FDA%20(Importation%20Plan).pdf
2 https://www.atlanticcouncil.org/blogs/econographics/the-us-is-relying-more-on-china-for-pharmaceuticals-and-vice-versa/

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chemical manufacturing sectors. In addition, the PRC's 14th Five-Year Plan for the Development of the Pharmaceuticals Industry specifically calls for resources to be devoted to the creation of a competitive pharmaceutical industry.3

These subsidies disrupt global markets by enabling Chinese firms to operate below cost, saturate international supply chains, and displace foreign competitors, including U.S. firms. This elimination of competition allows Chinese suppliers to subsequently increase prices or restrict supply, creating significant vulnerabilities for American health and national security. In fact, Chinese officials suggested during President Trump's first term that the PRC should use its position as the dominant supplier of APIs to the United States as a retaliatory tool in a trade war.4

For many critical APIs, including fermentation-derived antibiotics and intermediates, Chinese subsidies facilitate the construction and operation of advanced manufacturing facilities through low or zero-interest loans from state financial institutions. Additional acquisition of free land, subsidized utilities, and governmental guarantees is undercutting U.S. and European-produced equivalents by 30–70%, irrespective of actual efficiency or quality. Consequently, the U.S. is now heavily reliant on imports for nearly all its essential fermentation-derived APIs.

To address this competitive imbalance, the United States must recognize pharmaceutical manufacturing as critical infrastructure deserving of public support and long-term investment. In addition to tariffs, the Defense Production Act (DPA) represents a potent mechanism for reducing the investment risk in large-scale U.S. fermentation and biomanufacturing capacity. It can also offer low-interest loans, loan guarantees, and direct purchase commitments to U.S. firms developing essential API production infrastructure to ensure resilient domestic supply chains capable of product manufacturing without distortion from unfair foreign competition.

BioPrincipia, our subsidiary Fermworx, and others in the growing biomanufacturing sector demonstrate the potential of modest public investment and clear market signals to displace significant percentages of U.S. pharmaceutical imports. However, substantial capital costs and the ongoing presence of subsidized imports deter private investment without governmental intervention.

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

Our acquisition of the former Merck assets is a telling case study in the impact of unfair foreign trade practices. The Merck Riverside, formerly known as the Cherokee Pharmaceuticals plant, has a significant history in pharmaceutical manufacturing, specifically in the production of APIs

3 http://english.nmpa.gov.cn/2021-12/30/c_736377.htm#:~:text=The%20Plan%20calls%20for%20strengthening,fulfill%20their%20duties%20and%20responsibilities.
4 https://www.thetimes.com/world/asia/article/china-threat-to-halt-us-antibiotics-supply-36tm2v2xp?region=global

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for antibiotics. Since its establishment in 1950, the plant has been engaged in the production of APIs for antibiotics such as imipenem/cilastatin (Primaxin/Tienam), ertapenem (Invanz), and cilastatin (Recarbrio). As bulk production in the US became uncompetitive with low-cost imports, Merck pivoted their strategy toward high revenue drugs like Keytruda, while relocating and reducing focus on products like antibiotics. Merck has not publicly disclosed specific details about the relocation of antibiotic production previously handled at the Cherokee plant.

This divestment provided an opportunity for Fermworx in 2019 to purchase large-scale fermentation tanks, bioreactors, centrifuges, filtration systems, and other specialized equipment essential for API fermentation. This infrastructure has been relocated to the Fermworx site in Columbus, GA, providing 20 tanks of 75,000 liters each of additional capacity ready to be outfitted for large scale fermentation production of critical APIs.

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

It is entirely feasible to reduce our nation's reliance on pharmaceutical imports by increasing domestic capacity for pharmaceuticals and pharmaceutical ingredients. BioPrincipia and Fermworx are poised to do precisely that, in alignment with President Trump's priorities and with federal market support.

We would also like to acknowledge the broadly transformative power of biomanufacturing and the increase in US start-ups, biomanufacturing entrepreneurs, laboratories, and commercial companies and the growing pipeline of talent and R&D being fostered by the BioMADE initiative.

In addition to the eleven items listed above (7-ACA, Asparaginase, Azithromycin, Dextran, Hyaluronic Acid, L-DOPA (Levodopa), Lovastatin / Simvastatin, Mectizan® (Ivermectin), Penicillin G / V, Riboflavin (Vitamin B2), and Vitamin B12), BioPrincipia would like to flag seventeen other APIs where the US produces less than 50% of the market and we can use our biomanufacturing technology:

API	**Therapeutic Use**	**Estimated U.S. Production**
Amphotericin B (Liposomal)	Antifungal for serious infections and leishmaniasis	10%
Ceftazidime–Avibactam (Avycaz)	Antibiotic for complicated infections	10%
Clindamycin	Lincosamide antibiotic for bacterial infections	30%
Colistin (Polymyxin E)	Antibiotic for multidrug-resistant Gram-negative bacteria	5%

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Cyclosporine	Immunosuppressant for organ transplantation	20%
Daptomycin (Cubicin)	Antibiotic for Gram-positive bacterial infections	20%
Doxycycline	Tetracycline antibiotic for various infections	30%
Fidaxomicin (Dificid)	Antibiotic for Clostridioides difficile infection	10%
Filgrastim/Pegfilgrastim (G-CSF biologics)	G-CSF biologics for neutropenia	40%
Insulin (Human & Analogs)	Hormone for diabetes management	50%
Micafungin (Mycamine)	Antifungal for candidemia and other infections	10%
Tacrolimus (Prograf)	Immunosuppressant for organ transplantation	20%
Tigecycline (Tygacil)	Antibiotic for complicated infections	10%
Tobramycin (Inhalation) (TOBI)	Antibiotic for Pseudomonas aeruginosa in cystic fibrosis	30%
Vancomycin (IV & oral)	Antibiotic for Gram-positive bacterial infections	30%
Sirolimus (Rapamycin)	Immunosuppressant and mTOR inhibitor	10%
Rifapentine (Priftin)	Antibiotic for tuberculosis	10%

While we believe Fermworx is well positioned to help lead the on-shoring of manufacturing for the materials described above, other market participants will be able to follow and address other APIs.

Finally, incorporating biomanufacturing into our nation's pharmaceutical production strategy will provide America's farmers with additional revenue streams, benefiting them and farming communities around the country. Agricultural products like corn stover, glucose, and high fructose corn syrup – including waste and off-spec streams from food and beverage manufacturing that would otherwise be discarded are excellent and abundant feedstocks for biomanufacturing of pharmaceuticals, providing a stable, domestic source of inputs to enable our country to meet its demand for pharmaceuticals.

(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;

Supporting domestic manufacturing of pharmaceuticals and pharmaceutical ingredients is a

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national security *imperative*. While we believe there are benefits from global trade across goods and services, an America First policy demands that we are able to satisfy our critical health needs – on a daily basis and in times of crisis – before supplying the rest of the world. We must transition into makers and exporters of these products to protect our fundamental health and increase our strategic leverage over nation-state trading partners who recognize pharmaceuticals and pharmaceutical ingredients are not normal trade goods but instead are essential underpinnings of a safe and healthy society.

The policies of the prior Administration have left us more vulnerable to disruption and adulteration of critical medicines. We urge you to help reverse this trend and deploy all the tools available to protect our national security. Specifically we recommend strong, broad tariffs for pharmaceuticals and pharmaceutical ingredients and use of Defense Production Act and other authorities to provide low-interest loans, purchase orders, and offtake agreements to stand up new biomanufacturing immediately.

Conclusion

Thank you for the opportunity to provide these comments. We look forward to working with the Trump Administration to create the right regulatory framework to bring pharmaceutical manufacturing back to America and start using all the tools in the federal toolbox to support building advanced new plants to meet critical national security, public health, wellness, and economic goals. Please do not hesitate to reach out to me at sgandhi@bioprincipia.com with any questions.

Sincerely,

Sanket Gandhi
CEO
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