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International Trade Administration
U.S. Department of Commerce
1401 Constitution Avenue N.W.
Washington, D.C. 20240

Re: Comments of Amphastar Pharmaceuticals, Inc. on Docket No, 2504140-0065, XRIN 0694-XC 120, Section 232 National Security Investigation of Imports of Pharmaceuticals and Pharmaceutical Ingredients

On behalf of Amphastar Pharmaceuticals, Inc., we are pleased to submit these comments to the Department of Commerce's Notice on the Section 232 National Security Investigation of Imports of Pharmaceuticals and Pharmaceutical Ingredients.

Amphastar Pharmaceuticals, Inc. is a United States (US) based, publicly traded (AMPH) biopharmaceutical company focused on developing, manufacturing, and marketing injectable, intranasal, and inhalation products. This includes drugs, peptides, proteins, and interchangeable biosimilars prepared with DNA recombinant technology, as well as biologics that are derived from living cells or organisms; various innovative drug delivery systems for different routes of administration; and various proprietary products and technological platforms. Although Amphastar's historic focus has been on developing generic injectable critical care products, the company has evolved to have a diverse portfolio of branded products such as Primatene Mist®, BAQSIMI®, and Rextovy®. Overall, Amphastar manufactures and has Food and Drug Administration (FDA) approval for over 25 products for distribution primarily to the US market. Amphastar currently has five drug or biologic finished product applications under review with the FDA. Amphastar produces difficult to manufacture biopharmaceutical products. One hundred percent of the finished drug product that Amphastar produces is made in the US, and the company is proud to employ over 1,600 employees in the US. In 2025, Amphastar was granted the "Drug Shortage Assistant Award" by the FDA for its work to resolve the long-term shortage of a critical care sterile injectable finished product. For a more detailed background of Amphastar, see Appendix 1.

Amphastar is committed to manufacturing finished pharmaceutical products in the US. The company plans to invest $125 million to build a new state-of-the-art manufacturing facility on the campus in Rancho Cucamonga, CA. The facility will contain several sterile suites for manufacturing pharmaceutical and biological products. Additionally, it will house new chemistry labs and new packaging lines. This commitment to the US will help maintain a strong supply chain for critical products.

Amphastar's comments focus primarily on the impacts of tariffs on the production of pharmaceutical products in the US. Specifically, in developing its new tariff policy, Amphastar urges the Administration to ensure that tariff policies encourage the production of finished pharmaceutical products in the US, because finished products have the highest and most complicated quality requirements. In addition, frequently the ingredients or components needed to manufacture these finished products can only be obtained from foreign sources. If US manufactures are not able to continue manufacturing in the US (*i.e.*, because tariffs make purchasing the ingredients and components too expensive) then the US could face drug shortages. All these considerations suggest that the best industrial policy for drugs is one that imposes tariffs on finished products but not on ingredients and components.

The comments are presented in the context of the knowledge Amphastar has gained over 40 years developing pharmaceutical products, which Amphastar believes are relevant as the Administration considers the development of its pharmaceutical policies.

I. BACKGROUND

a. Specialized Components and Regulatory Barriers

Most of the products Amphastar produces are combination products, meaning they include both a drug and a device portion, such as a Metered Dose Inhaler (MDI), prefilled syringe or injection pen. The specialized device components are either imported into the US as a component (such as a finished pen ready to be filled) or as parts for further assembly or processing. At Amphastar, the corporate strategy is to perform as much of this assembly or processing in the US as possible. Experience has shown that this practice gives greater control of the quality attributes and greater control of the supply chain, both important security measures. In addition, some combination products Amphastar manufactures utilize pens and MDIs that require more precision and specialization and only a handful of companies in the world have the capability of supplying them. It has not been possible to find US manufacturers that can supply these devices, which separately require FDA approval, and therefore Amphastar must import them. For example, the MDI components (empty canister with assembled and attached valve and actuator) used for Amphastar products are being imported mostly from European countries. The proposed tariff rates for these products of 10 to 31%, depending on the country, will add several

million dollars to the annual cost of the finished products, increasing the cost of making the finished product by 5% to 10%.

Tariffs on these specialized components are significant to the total manufacturing cost of the finished products as these component costs are higher than traditional components such as vials. The additional tariffs on these components will create a significant burden on the profitability of these products and will either increase the cost of finished products sold in the US or lead to their discontinuation. Unfortunately, Amphastar will not be able to purchase these components from a US supplier, since in most cases there are none, and even if there were US suppliers, the change of supplier would require FDA approval, and this would take approximately 12-18 months. As a result of these regulatory barriers, suppliers are passing tariff costs on to Amphastar since they know that the company does not have any choice other than to absorb these tariff costs or discontinue the finished products that use these components.

b. Labor Costs in the US vs. Foreign Locations

The cost of labor represents a significant factor in pharmaceutical manufacturing, with notable disparities between the US and countries like China and India. In 2024, the average wage in the US manufacturing sector was approximately $73,133 annually.[1] Within the pharmaceutical and medicine manufacturing subsector, the median wage for all occupations is around $67,059 annually, with certain specialized roles earning higher rates.

On the other hand, labor costs in both China and India, where the majority of imported finished products originate, are significantly lower than those in the US. While specific data for pharmaceutical manufacturing in these countries can vary, the average annual manufacturing wage in China is estimated to be approximately $14,370 USD.[2] In India, the average annual salary across all sectors is reported to be around $4,658 USD.[3,4] While specific data for pharmaceutical manufacturing wages in India varies, it is clear that it is significantly lower than in the US. This substantial difference in labor costs creates a challenging landscape for American

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1 United States Bureau of Labor Statistics. “Employment and average hourly earnings by industry for all employees, March 2025, seasonally adjusted.” https://www.bls.gov/charts/employment-situation/employment-and-average-hourly-earnings-by-industry-bubble.htm and “Table B-3. Average hourly and weekly earnings of all employees on private nonfarm payrolls by industry sector, seasonally adjusted.” https://www.bls.gov/news.release/empsit.t19.htm.

2 Trading Economics. “China Average Yearly Wages in Manufacturing.” https://tradingeconomics.com/china/wages-in-manufacturing (Data referenced for 2023, with projection for 2024 not significantly different).

3 Mera Monitor. “Average Salary in India 2024.” https://meramonitor.com/average-salary-in-india/.

4 Time Doctor**.** “Average salary in India (2024 data).” https://www.timedoctor.com/blog/average-salary-in-india/.

finished product manufacturers competing globally on price for finished pharmaceutical products.

c. Cost of Environmental Compliance

In addition to the higher costs associated with labor, there are significant environmental costs associated with manufacturing biopharmaceutical products in the US. For example, the use of propellants such as hydrofluoroalkane (HFA), an ingredient that is required for many of the inhaled products produced by Amphastar's subsidiary in Massachusetts, USA, is heavily regulated by the Environmental Protection Agency. To use this propellant, Amphastar has to register and apply for an allotted quota on an annual basis. These quotas, which are not required for companies producing these finished products in countries such as India, are being reduced annually as lower greenhouse gas-emitting alternative propellants are being developed. As these US allotments become scarcer, the associated cost for the propellants is increasing.

II. RECOMMENDATIONS

In light of the additional challenges associated with producing in the US, Amphastar urges consideration of certain steps that should be taken to support US manufacturing of finished biopharmaceutical products, which will increase the national security of these products, by maintaining domestic infrastructure. First, Amphastar urges consideration of the use of import tariffs on all finished products. It is Amphastar's position that the tariffs on finished product should be proportionally focused on countries such as India that have disproportionate labor standards/costs as well as historic and sustained quality issues. Second, Amphastar urges consideration of imposing no import tariffs on active pharmaceutical ingredients (APIs). Amphastar has concluded that a policy of no tariffs on these would encourage the manufacturing of finished products in the US as there should be no "tariff penalty" for the importation of this critical ingredient. Third, the company believes that there should be no import tariffs on components. Should import tariffs be imposed, the company believes focus should be on reducing them from countries with historically high-quality standards such as those in European countries and North America, again to encourage manufacturing of finished products in the US, and because these components are not available in the US. The following sections will explain the rationale for these positions.

Our recommendations stem from the understanding that finished products represent the top of pharmaceutical innovation, requiring advanced technologies and stringent quality controls, resulting in the highest monetary value in the sector. In contrast, API and components are part of a foundational layer in this field. By aligning our tariff policies according to this hierarchy, we can create a more favorable environment for domestic manufacturers and ensure the sustainability of the biopharmaceutical sector in the US.

a. Import Tariffs on Finished Product

Finished pharmaceutical products have the highest quality requirements of any form in the supply chain. As compared to API's (which have relatively simple methods for their manufacture, testing and quality standards), and components (which have quality standards that are easy to quantify), finished products are difficult to manufacture and test. Many of the quality standards used to measure finished products are difficult to quantify. One example is sterility. There is no way to measure that every sterile vial or pen is sterile, since the test itself would be destructive of the unit being tested. Therefore, the release of a manufacturing batch relies on validation and oversight of the manufacturing process for that particular batch and the review of the batch documentation to help support the claim. Additionally, finished product manufacturing relies on the industry concept of current Good Manufacturing Practices (cGMP), where the manufacturing facility maintains its manufacturing practices in a compliant state and remains current with the industry as these standards evolve. One way FDA ensures manufacturing sites remain current with these standards is through routine, unannounced inspections. For example, Amphastar, as a corporation, has had nearly 20 US FDA inspections of its 3 finished product manufacturing sites since 2018. The frequency of these inspections seems appropriate given the ease with which FDA inspectors, with their local offices, can easily travel to these manufacturing sites to perform unannounced inspections. These inspections are critical for manufacturing sites to maintain cGMP.

As compared to finished products made in the US, it appears that there are quality differences in other countries, in particular those made in India. One reason for this is likely due to the frequency and pre-arranged inspection strategy for FDA inspections in foreign countries. In countries such as India, it is nearly impossible to perform inspections essential to ensuring quality as frequently as the US. As a result, studies have shown that there may be more risk in the use of finished products made in India as compared to the US. For example, when evaluating the number of reported adverse drug events reported on the FDA Adverse Reporting System (FAERS), a recent study found that generic products manufactured in India were "associated with significantly higher [54%] instances of serious adverse events than equivalent generic drugs made in the US."[5] Questions of quality standards for finished products manufactured in India can also be observed in a recent (April 2025) drug recall by Glenmark of over 40 types of generic drugs manufactured in India due to manufacturing issues.[6] During the FDA inspection of this

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[5] Noh, I. J., Gray, J., Ball, G., Wright, Z., & Park, H. (2025). Are All Generic Drugs Created Equal? An Empirical Analysis of Generic Drug Manufacturing Location and Serious Drug Adverse Events. Production and Operations Management, 0(0). https://doi.org/10.1177/10591478251319691.

[6] Callahan, P. (2025, April 16). An Indian Drugmaker, Investigated by ProPublica Last Year, Has Recalled Two Dozen Medications Sold to U.S. Patients. *Propublica* https://www.propublica.org/article/glenmark-recalls-two-dozen-drugs.

manufacturing site, it was found that the site was not maintaining its cGMP standards. This drug recall is just one of many issued by Glenmark in recent years for their finished products manufactured in India. Another example, relating specifically to inhalers is a 2015 study comparing albuterol inhalers purchased in Mexican border towns which found that "border town obtained inhalers varied significantly in pharmaceutical performance from one to another and from US products."[7] For these reasons, Amphastar believes that import tariffs should be imposed on finished products only, and proportionally focused on countries that have disproportionate labor standards/costs as well as historic and sustained quality issues such as India.

b. No Import Tariffs on API or Components

The way tariffs are currently implemented harms domestic manufacturers of finished pharmaceutical products. Amphastar manufactures in the US with components sourced from around the globe. Amphastar is currently paying tariffs on some of the components and raw materials it buys from outside of the US, which increases costs. Amphastar's competitors, who manufacture outside of the US don't have to pay these tariffs and can import pharmaceuticals with no tariff, putting the company at a significant cost disadvantage.

Having no import tariffs on API or components will encourage domestic manufacturing. First, it will allow pharmaceutical companies to focus their efforts on the critical portion of the manufacturing, the finished product. As stated above, it is relatively simple to measure quality on API and traditional components. The FDA rightly places the inspection burden of these facilities primarily on the finished pharmaceutical manufacturers and thus these companies have the appropriate resources to appropriately address any quality concerns. Having no import tariffs on these types of products will allow US pharmaceutical companies that manufacture finished products to prosper.

c. Proportional Tariffs Based on Technical Difficulty and Historic Quality

Finally, if tariffs continue to be imposed on APIs and specialized components, those imported from countries with historically high-quality standards such as those in European countries and North America should be excluded or provided with a lower rate. As noted above, some of these specialized components are only available from a handful of suppliers, which do not manufacture in the US. Tariffs on these specialized components will not encourage the

[7] Nocella, M., Kilber, E., Witmer, B., Karlage, K., & Myrdal, P. (2015). A Comparison of Pharmaceutical Product Performance of Albuterol Inhalers Available in the United States and Those Obtained in a Mexican Border Town. *The Journal of pharmacy technology: jPT : official publication of the Association of Pharmacy Technicians, 31*(6), 289–295. https://doi.org/10.1177/8755122515595052.

suppliers to move their finished product manufacturing to the US, since they pass the tariff costs to the firms with finished product manufacturing in the US. These components are critical to the finished product manufacturing of pens and MDIs and represent a significant cost to the product.

III. CONCLUSION

Lowering import tariffs on APIs and specialized components (especially those manufactured in countries with historically high-quality standards) would greatly benefit American patients. Reducing import costs would create a more competitive manufacturing environment in the US, allowing US companies such as Amphastar to allocate resources toward innovation, research and development, and create high-quality jobs.

While Amphastar advocates for lower tariffs on API's and components to encourage domestic manufacturing and innovation, the company also believes in the importance of leveling the playing field for finished pharmaceutical products. This means ensuring that foreign manufacturers selling their products in the US market comply with the same rigorous quality standards, environmental regulations, and intellectual property protections that American companies must meet.

Establishing fair and equitable trade practices for finished drugs can prevent foreign entities from undercutting American-made pharmaceuticals. This approach protects American jobs and investments and ensures that patients receive medications that adhere to the highest safety and efficacy standards. A balanced strategy that lowers input costs while ensuring fair competition for finished products is essential for maintaining a strong and reliable American pharmaceutical industry.

Sincerely,

William B. Schultz
Margaret M. Dotzel

APPENDIX I: AMPHASTAR FACILITIES

Amphastar and its two U.S. subsidiaries, International Medication Systems, Ltd. (IMS) and Armstrong Pharmaceuticals, Inc. (Armstrong), manufacture all of Amphastar's finished product in the US and currently support 1,642 US jobs. Amphastar also produces Active Pharmaceutical Ingredients (API), the raw material ingredient used to provide the therapeutic effect of the drug product at three facilities. These Food and Drug Administration (FDA) inspected and approved API manufacturing facilities are Amphastar's US based facility (IMS), the company's French facility, Amphastar France Pharmaceuticals, (AFP) and its Chinese facility, Amphastar Nanjing Pharmaceuticals (ANP). Amphastar also has a US based pre-clinical research laboratory which performs development work on our early-stage pharmaceutical products.

Amphastar Facility

Amphastar's facility located in Rancho Cucamonga, California, produces sterile, injectable drugs and biologic finished products in vials, pre-filled syringes and injection pens. Amphastar has multiple drug applications pending with the FDA, including an interchangeable (biosimilar) version of insulin in both a vial and pen presentation.

International Medication Systems, Limited (IMS) Facility

Amphastar's IMS facility, located in South El Monte, California, produces sterile, injectable finished drug products in vials and pre-filled syringes, including products for emergency use, critical-care products, instrumental in the treatment of hospital patients in critical medical conditions. Many of these products were listed on the FDA drug shortage list. By collaborating with the FDA Drug Shortage Team and expanding the IMS facility Amphastar was able to get many of these products off the drug shortage list. In fact, in March of 2025, IMS was presented with the FDA's Drug Shortage Assistance Award for their work to resolve the long-standing drug shortage of epinephrine injection, 0.1 mg/mL syringes.[8]

Armstrong Facility

The Armstrong facility, located near Boston, Massachusetts, produces inhaled metered dose inhalers (MDIs). These products are medications primarily used for the respiratory treatment of conditions such as asthma or COPD. To the company's knowledge, Armstrong is the only US supplier of two of these products, Albuterol and Primatene Mist® (the only FDA approved over-

[8] United States Food and Drug Administration. (2025, March 27). FDA Drug Shortage Assistance Award. https://www.fda.gov/media/185997/download?attachment.

the-counter (OTC) treatment for asthma). These inhaler products are critical to patients who have respiratory diseases.