International Pharmaceutical Excipients Council of the Americas

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Chair

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Department of Commerce
Bureau of Industry and Security (BIS),
Office of Strategic Industries and Economic Security

Re: Bureau of Industry and Security, U.S. Department of Commerce Docket No. 25041-0065 (XRIN 0694-XC120): Notice of Request for Public Comments on Section 232 National Security Investigation of Imports of Pharmaceuticals and Pharmaceutical Ingredients. Regulations.gov ID BIS-2025-0022.

Dear Sir or Madam,

Members of the International Pharmaceutical Excipients Council of the Americas (IPEC-Americas) have reviewed the above-named Docket. IPEC-Americas members appreciate the Department of Commerce soliciting comments and would like to thank you for the opportunity to share our thoughts related to the Bureau of Industry and Security, U.S. Department of Commerce Docket No. 25041-0065 (XRIN 0694-XC120).

IPEC-Americas Background

IPEC-Americas represents more than 50 pharmaceutical excipient manufacturers, distributors, and pharmaceutical/biopharmaceutical companies. IPEC-Americas is dedicated to working closely with regulatory authorities, industry organizations, and scientific bodies (globally) to advance public health on matters relating to the quality, safety, manufacture, distribution, use and functionality of excipients. IPEC is the sole association with expertise and focus on pharmaceutical excipients. A complete list of IPEC-Americas member companies can be found at: https://ipecamericas.org/what-ipec-americas/member-companies.

IPEC-Americas Comments

Background:

IPEC-Americas comments primarily address pharmaceutical excipients, which are critical components of almost all drug products. Pharmaceutical excipients are inactive ingredients that are intentionally added to a drug product; excipients are not the therapeutic agent but contribute to drug product performance and stability leading to effective patient treatment. Pharmaceutical excipients can, and often do, comprise significant composition of a drug product formulation. For example, it is common for as much as 90% or more of the components in an oral drug product to be excipients.

Some pharmaceutical excipients are mainly, and in some cases solely, manufactured and sourced outside of the United States. Even when pharmaceutical excipients are manufactured domestically, the raw materials needed for manufacture of many of these (e.g. cellulose, lactose, etc.) are sourced from outside the United States.

Many pharmaceutical excipients are special grade commodity chemicals manufactured specifically for the pharmaceutical industry in accordance with Good Manufacturing Practices

(GMPs) to ensure their quality and suitability for use in pharmaceutical drug products. Pharmaceutical excipient manufacturing is often a small volume within the much larger manufacturing capacity of industrial grade material, making excipient production more economically viable.

Please find our comments to the selected docket questions below:

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

The US imports a significant amount of the excipients used in pharmaceuticals manufactured domestically. At this time, domestic pharmaceutical excipient manufacturers would be unable to fully meet the current domestic excipient demand, in part because pharmaceutical excipients are not always interchangeable among suppliers. While multiple companies globally may produce pharmaceutical excipients that meet similar overall standards, each company's products may have quality attributes that can impact performance in specific drug products. New excipient sources or grades require qualification prior to use and require time to facilitate the approval for routine use in manufacturing of finished drug products.

Certain types or grades of pharmaceutical excipients are manufactured in only one location worldwide, often due to the need to be located near raw material sources. Many pharmaceutical excipients are manufactured from naturally derived sources, e.g. agriculture, plants, animals, minerals, oceans that only exist in certain locations globally and have no alternatives in the US. Consequently, it would be unlikely that all types and grades of excipients could be manufactured within the US, regardless of tariff status.

For example, lactose is a common pharmaceutical excipient used in a large number of drug products; however, the two largest lactose manufacturing companies are located in Europe. The small domestic lactose supply would be insufficient for domestic pharmaceutical excipient needs. Furthermore, the use of lactose as a starting material for pharmaceutical excipients alone would likely not be sufficient justification to expand US lactose production.

As another example, sodium stearyl fumarate is present in numerous finished drug formulations but has no domestic sources. Sodium stearyl fumarate has unique functionality and often cannot be substituted with an alternative due to formulation requirements, quality standards, performance and a complex regulatory approval process.

Similarly, lipid-based excipients derived from palm oil, which are used in many pharmaceutical products, cannot be sourced domestically. These lipid-based excipients were critical in the development of Covid mRNA vaccines.

(iii) the role of foreign supply chains, particularly of major exporters, in meeting United States demand for pharmaceuticals and pharmaceutical ingredients;

It is estimated that around 40% of worldwide pharmaceutical excipients are manufactured in the US, with around 30% manufactured in Europe, and 24% in Asia Pacific (Global pharma excipients market share 2023| Statista). However, as mentioned in our response to (ii), excipients are often not interchangeable. Some drug products manufactured in the US rely upon pharmaceutical excipients solely available by importation.

Certain high-volume pharmaceutical excipients, used in critical and high-volume drug products, are predominantly manufactured outside the US; these excipients are essential for meeting the pharmaceutical demand in the United States. Any disruption or uncertainty in the pharmaceutical excipient supply chain could negatively impact the supply of essential medicines in the United States. Applying tariffs to pharmaceutical excipients or their starting materials would not improve their availability for the drug products that rely on each component approved for the manufacture of the various finished product(s).

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

It is difficult to determine the amount of imported pharmaceutical excipients available from a small number of suppliers. A survey of pharmaceutical manufacturers could help determine the reliance on foreign single sourced suppliers.

When feasible, pharmaceutical excipient manufacturers produce excipients in multiple locations worldwide, which supports business continuity of both the excipient manufacturer and the pharmaceutical manufacturer. However, as mentioned earlier, pharmaceutical excipient manufacturing is often geographically limited with a small number of suppliers, often located in the regions where the raw materials are readily available, regardless of if they are naturally or synthetically derived.

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

Since some single-sourced pharmaceutical excipients are only available from certain foreign countries, trade restrictions could severely impact the ability of pharmaceutical companies to manufacture specific drugs, which could lead to drug shortages and jeopardizing patient health. While it may be possible to circumvent the unavailability of pharmaceutical excipients through drug product reformulation, such development efforts would be costly and lengthy (estimated 5+ years) and add significantly to healthcare related cost.

Severe pharmaceutical excipient shortages could also open the opportunity for falsified materials and economically motivated adulteration, potentially leading to patient harm or death. Such circumstances have been seen in the recent cases of methanol in pharmaceutical alcohols and diethylene and ethylene glycol in glycerin.

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

It is possible to expand the manufacture of some pharmaceutical excipients currently made in the US for increased domestic capacity. However, relocating manufacture to the US is a multiyear process that comes with significant economic cost. It takes years to build new pharmaceutical excipient manufacturing sites and additional years to validate the equivalency, safety, and quality of the product made in a new facility. Additionally, as mentioned earlier, because of the specific requirements of some pharmaceuticals, it is not feasible to support all domestic pharmaceutical manufacturing through domestically manufactured excipients.

Government support might be needed to increase pharmaceutical excipient manufacture in the US for critical medicines. Pharmaceutical manufactures may also need incentives to use domestically manufactured excipients. Pharmaceutical manufacturers switching to domestic sources of excipients would likely face long timelines associated with reformulation, testing, and regulatory approval of the change.

(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;

Tariffs on general commodity chemicals are expected to affect pharmaceutical excipients and their raw materials. Harmonized tariff codes are based on chemical composition and structure and are usually independent of intended use. Most chemicals used as pharmaceutical excipients have other larger scale usage in the industrial chemicals sector. For example, isopropyl alcohol can be a pharmaceutical drug product for hand sanitizer, an excipient for a topical drug, or an industrial chemical. Lactose and cellulose derivatives are common pharmaceutical excipients with an even greater use in food products. Under the current tariff structure, tariffs on these items would impact multiple industries, including pharmaceuticals.

Tariffs on excipients would equally penalize both high value drug products as well as low-cost generic alternatives. High tariffs on pharmaceutical excipients could significantly raise the cost of the lowest margin pharmaceuticals, which are also the ones most susceptible to shortages. The consequences of the increased cost due to tariffs potentially include higher cost of medicines, increased drug shortages, or total unavailability of essential medicines routinely prescribed to US patients.

It should be recognized that excipient manufacture is typically a minor part of a chemical manufacturing operation and is unlikely to justify new facilities. Consequently, ensuring a robust pharmaceutical excipient supply chain based on a robust risk analysis should be a priority.

In some cases, incentives might be needed to encourage domestic manufacture and ensure supply of essential medicines. Alternatively, pharmaceutical excipients could be designated as exempt from tariffs as a way to minimize the potential for shortages.

Without a strategic approach for onshoring pharmaceutical excipients and other pharmaceutical ingredients, tariffs could threaten national security rather than protect it due to shortages in critical drug products, putting the nation's health at risk.

(x) any other relevant factors.

While high margin branded drug manufacturers may have flexibility to increase manufacturing in the US or switch to domestically sourced pharmaceutical excipients (if available) in the next few years, their generic alternatives may have limited to no capability to do the same under their current cost structure.

IPEC-Americas believes that broad tariffs on pharmaceutical excipients are counterproductive to security of the US pharmaceutical supply chain. Each pharmaceutical drug product has unique requirements for the excipients used in its manufacture. For many drug products, substitution of

foreign sourced pharmaceutical excipients with domestic sources would require extensive development efforts and regulatory approval. Reformulation is particularly challenging for lower cost generics, many of which are supplying critical medicines for public health. Rather than a broad financial penalty for importation of pharmaceutical excipients, IPEC Americas recommends strategic government investment into critical medicines, including their constituent pharmaceutical excipients.

Respectfully yours,

Joseph Zeleznik
Chair, IPEC-Americas