Baxter

May 6, 2025

Submitted via *www.regulations.gov*

Bureau of Industry and Security
Office of Strategic Industries and Economic Security
U.S. Department of Commerce

Re: Notice of Request for Comments, XRIN 0694–XC120: Portal ID BIS-2025-0022 ("Notice")

Dear Sir or Madam:

Baxter International Inc. hereby submits its comments to this Notice.

Baxter is committed to ensuring the consistent availability of high-quality generic and differentiated hospital pharmaceutical products in the areas of pain, critical care, anti-infection, and oncology for critically ill patients in the United States and around the world. Baxter's products are critical to the health care infrastructure, and include anesthetics for surgical care, differentiated ready-to-use critical care and anti-infective products intended to enhance safety for patients and improve workflow efficiency at hospitals, and generic and legacy-brand critical care and oncology products. The United States already plays a key role in this supply chain. However, other countries also play a significant role. For example, over half of the active pharmaceutical ingredients (APIs) for prescription medicines in the U.S. come from India and the European Union.[1] With the U.S. government's backing, pharmaceutical industry infrastructure in the U.S. can expand and thereby may decrease dependence on any other one country or handful of countries for key pharmaceuticals or their ingredients. It will take time, but with proper regulatory relief and incentives for manufacturers, a larger share of domestic manufacturing is possible.

To achieve this goal, government and other incentives would help to make domestic capital investments viable. Building a new manufacturing facility, for example, can cost up to $2 billion and take five to ten years before it is operational, including the time and costs related to comply with complex regulatory requirements.[2] As discussed in more detail below, expanding existing facilities and transferring a single product to a new manufacturing site also takes time and expertise, requiring process transfer and scale-up, validation, stability protocols and regulatory filings, all of which can take years to complete. In addition, adequate payment or reimbursement for medicines, particularly for low cost, low margin generic drugs, would provide an additional incentive for manufacturers to consider for siting new or expanded facilities.

[1] USP. (2025). Supply Chain. Retrieved from Over half of the active pharmaceutical ingredients (API) for prescription medicines in the U.S. come from India and the European Union | Quality Matters | U.S. Pharmacopeia Blog.
[2] PhRMA. (2025). Biopharmaceutical Manufacturing. Retrieved from Manufacturing & Supply Chain | PhRMA.

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In the current supply chain environment, in certain cases, Baxter imports APIs, packaging components, and raw materials into the United States for manufacture of finished drug product, as well as manufactured finished drug products from centralized facilities located outside the United States. Sourcing and manufacturing facility selection is not based on convenience or cost alone, but rather on scientific, regulatory, and practical considerations essential to product quality, patient safety, and supply continuity.

For complex generic pharmaceutical products, the number of globally available sources of APIs and packaging materials that meet stringent quality and performance specifications is limited. In many cases, the only appropriate suppliers are located outside the United States. For example, at its manufacturing facility in Round Lake, Illinois, Baxter manufactures medications intended for intravenous administration to critically ill patients within hospital settings in which the therapeutic ingredient is provided pre-mixed in a solution and ready-to-use. These drugs utilize Baxter's proprietary GALAXY container technology. GALAXY is a non-PVC and non-DEHP sterile system that enables premixed medicines to have a longer shelf life when stored. Suppliers of packaging components and APIs that meet the stringent specifications required for this use are limited and Baxter must, in some cases, leverage the global supply chain to make these products available to patients.

Moreover, any change to the API or packaging components used in an approved drug product entails substantial redevelopment and regulatory obligations. Specifically, such changes typically require the following:

- Reformulation and analytical test method development.
- Advanced characterization studies to rule out formation of harmful impurities or interactions.
- Execution of both accelerated and long-term stability studies.
- In some cases, clinical trials in humans to demonstrate bioequivalence with the original Reference Listed Drug (RLD) product.

These activities are time-intensive, technically complex, and financially burdensome, often requiring several years to complete before regulatory approval can be obtained.

Pharmaceutical manufacturing, particularly for certain therapeutic classes, requires highly specialized and product dedicated infrastructure. Utilizing a centralized global manufacturing location for these products ensures that specialized products can be manufactured in a cost-effective and consistent manner.[3]

[3] For example: cytotoxic drugs (*e.g.*, chemotherapy agents) must be manufactured in dedicated, contained environments to ensure personnel and environmental safety and to prevent cross-contamination; hormones and certain antibiotics require exclusive dedicated production lines to prevent cross-contamination; and many products require custom-engineered equipment or advanced processing technologies.

Transferring manufacturing to an alternate site involves extensive investment, including construction, equipment procurement and validation, technology transfer of analytical and production methods, and, in some cases, new clinical trials. The new site must successfully undergo inspection and approval by relevant regulatory authorities. Timelines for alternative site construction to commercial readiness vary but at a minimum will require five or more years.

There is a risk of technical failure with any product change or manufacturing transfer activity, which can result in extended timelines and drug shortages once bridge supplies are depleted. In addition, the financial burden may lead to the exit of suppliers for lower cost, but medically essential, generic products, increasing the possibility of shortages of critical therapies such as antibiotics and cancer therapies.

Baxter welcomes invitations to engage in dialogue with the U.S. Government to discuss the potential opportunities to increase the role of the U.S. in the pharmaceutical supply chain, while at the same time not compromising patients' consistent access to high quality and affordable medicines.

Respectfully submitted,

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Vanessa M. Brill (May 6, 2025 15:47 EDT)

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