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May 7, 2025

Eric Longnecker
Deputy Assistant Secretary for Technology Security
Bureau of Industry and Security
Department of Commerce
1401 Constitution Ave. NW
Washington, DC 20230

Subject: Notice of Request for Public Comments on Section 232 National Security Investigation of Imports of Pharmaceuticals and Pharmaceutical Ingredients – Docket No. BIS-2025-0022 / XRIN 0694-XC120

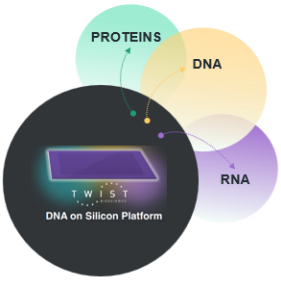
Comments submitted electronically via regulations.gov

Dear Deputy Assistant Longnecker:

Thank you for the opportunity to submit information in response to the request for public comments on the Department of Commerce's Section 232 National Security Investigation of Imports of Pharmaceuticals and Pharmaceutical Ingredients (Docket No. BIS-2025-0022 / XRIN 0694-XC120). Twist Bioscience (Twist) is a leading and rapidly growing synthetic biology and genomics company that has developed a disruptive DNA synthesis platform to industrialize the engineering of biology. The core of the platform is a proprietary technology that pioneers a new method of manufacturing synthetic DNA by "writing" DNA on a silicon chip. Twist is leveraging its unique technology to manufacture a broad range of synthetic DNA-based products, including synthetic genes, target enrichment panels for next-generation sequencing and antibody libraries for pharmaceutical discovery and development to address cancer, infectious diseases, and more. Twist manufactures all of its products in the United States.

To address the national security concerns described below and deter non-domestic manufacturing of synthetic DNA given its role as a strategic good, Twist is supportive of increased tariffs on nucleic acids (HTS 2934.99.90) imported into the United States.

Next Generation Gene Synthesis = Increased Scale



Traditional Method	Twist's Method
1 gene per plate	9,600 genes per silicon chip
Limited scale	**Significantly increased scale, many opportunities for cost efficient expansion**

Synthetically manufactured DNA is built using chemical or enzymatic processes that link nucleotides (i.e., adenine, thymine, cytosine, and guanine) into a specific genetic sequence, which are then used in research or commercial applications, including to develop pharmaceuticals. Historically, synthetically manufactured DNA is produced using hundreds of workers, all individually pipetting solutions into a 96-well plate by hand. In fact, most companies still use this outdated, labor-intensive approach, with one company based in China (Genewiz, a subsidiary of Azenta) requiring the use of several hundred PhD scientists[1] (average annual salary in the U.S. = $120,000 (USD) for doctoral scientists in industry[2] versus average annual salary in China = ¥296,020 (CNY) or $40,771.31 (USD)[3]), greatly limiting the scale and cost-effectiveness of gene synthesis. To make the outdated manual approach more cost-effective, other companies (e.g., Genewiz, GenScript) manufacture synthetic DNA in other countries like China. By manufacturing their products in China, they are creating an imbalance of employed researchers in that country to sustain the U.S.'s synthetic DNA needs.

Conversely, Twist has revolutionized and automated this process by miniaturizing the chemistry and using silicon wafers and ultra-throughput machinery to dramatically scale production in the United States.[4] Twist's high-throughput gene synthesis platform enables us to produce high-quality gene fragments starting at $.07 (USD) per base pair and next generation sequencing-verified sequence perfect clonal genes starting at $.09 (USD) per base pair. These prices are more

[1] https://seekingalpha.com/article/4755226-azenta-inc-azta-q1-2025-earnings-call-transcript
[2] https://ncses.nsf.gov/surveys/earned-doctorates/2023
[3] https://www.salaryexpert.com/salary/job/researcher-scientific/china#:~:text=%C2%A5295%2C985%20(CNY)%2Fyr&text=The%20average%20researcher%20scientific%20gross,and%20anonymous%20employees%20in%20China
[4] Twist Bioscience: Writing the Future with Synthetic DNA video: https://www.youtube.com/watch?v=KUm173PZJBQ

competitive than those offered by other companies. Importantly, expanding from our headquarters in South San Francisco, CA, three years ago, we spent $100M to build a second manufacturing facility in Wilsonville, OR, to expand our entirely US-based manufacturing.

Synthetic DNA is a critical input for many sectors, especially pharmaceuticals. Many of our customers are pharmaceutical and biotech companies that are discovering the next innovative therapeutic for devastating diseases. These researchers design and then test the DNA sequences we make for them, in order to determine the sequences that have the properties desired for treating specific diseases or conditions. This is a cyclical process of design, build, test, learn that repeats multiple times until the 'right' sequence is identified for advancement, ultimately to be tested in humans for safety and efficacy.
In addition, Twist offers a biopharma solution using synthetically manufactured DNA to support in vitro drug discovery, optimization, and screening; in silico lead optimization, humanization, and lead picking; and more, specializing in hard-to-drug targets. To highlight the financial importance of maintaining, bolstering, and growing the U.S.'s research and manufacturing edge with regard to pharmaceuticals, the global biologics market size was valued at USD 461.74 billion in 2022 and is expected to grow at a compound annual growth rate (CAGR) of 10.3% from 2023 to 2030.[5]
Moreover, synthetic DNA also supports biomanufacturing, which is a process that utilizes living cells, microorganisms, or enzymes to produce commercial products. In its final report released in April 2025, the National Security Commission on Emerging Biotechnology recognized that biomanufacturing could reduce U.S. dependence on foreign supply chains for pharmaceuticals.[6]

The National Security Commission on Emerging Biotechnology has highlighted synthetically produced nucleic acids as a key supply chain vulnerability, warning that the first country to scale this technology will secure a significant strategic edge.[7] The Government of the People's Republic of China is heavily investing in synthetic nucleic acid synthesis technologies. Still, the United States is fortunate to have innovative companies significantly advancing the scalability of our domestic production capacity. In fact, Twist has the current capacity to produce 3 million genes a year but is only using a fraction of that capacity, and in 2024, we only shipped 772,000 genes. Other U.S. companies likely have untapped gene synthesis capacity as well.

This is a national security concern for the United States for several reasons. First, synthetic DNA sequences are the blueprint for pharmaceutical R&D plans. When placing orders for synthetic

[5] https://www.grandviewresearch.com/industry-analysis/biologics-market#:~:text=Biologics%20Market%20Size%20%26%20Trends,10.3%25%20from%202023%20to%202030.
[6] https://www.biotech.senate.gov/final-report/chapters/introduction/
[7] https://www.biotech.senate.gov/wp-content/uploads/2024/01/Biotech-Commission-Dec2023-Report.pdf

nucleic acids, a sequence is digitally exported detailing the instructions for what nucleic acid strand to manufacture. The provider then writes the DNA and ships it back to the customer in a tube for the customer's commercial or research applications. That sequence that is digitally exported often represents highly valuable intellectual property. For pharmaceuticals, the sequence encodes the potentially therapeutic product (e.g., a biologic) and is the map that allows the DNA synthesis provider to reverse engineer the product. As a pharmaceutical company orders additional sequences, the DNA synthesis provider understands the pharmaceutical company's long-term R&D intention, research progress, failures, and capabilities. For this reason, it is imperative that there is trust and accountability, preventing the unlawful and unethical sharing or use of this sensitive information.

There are also national [and international] biosecurity concerns. As a leading synthetic DNA provider, Twist is deeply committed to promoting the beneficial and responsible application of gene synthesis technology while safeguarding biosecurity. Twist has, since the company's inception, been committed to meeting all legal requirements and advancing biosecurity standards and good practices to prevent the possibility of this technology being used for nefarious purposes. For example, Twist exceeds the standards published by the Administration for Strategic Preparedness and Response[8] which recommends that providers understand whether the product they are manufacturing for a customer contains any known genetic sequences of concern and that the synthetic DNA provider verify and document that the customer is ordering the sequence for a legitimate, bona fide, and peaceful purpose.
However, Twist is hearing with increasing frequency from Twist customers who are aware of instances of disparate application of biosecurity standards across manufacturers. The United States federal government has made tremendous progress in establishing biosecurity standards for DNA synthesis and encouraging the adoption of these standards by working with agencies to require that federal funding is only used to procure synthetic DNA from providers that meet certain criteria. Still, compliance with U.S and international standards is voluntary, and it is not always the case that non-domestic companies employ rigorous screening processes. Some biosecurity practices are enforced via export control mechanisms. As an example, many pathogenic biological agents are subject to export licensing requirements and prohibitions. Many countries are committed to harmonizing export controls to deter the development of chemical or biological weapons and participate in an informal multilateral arrangement known as the Australia Group. Countries like China, Russia, and Iran do not participate. While this may not represent a violation of law, it demonstrates that other countries like China are not promoting strong biosecurity practices,

[8] https://www.federalregister.gov/documents/2023/10/13/2023-22540/screening-framework-guidance-for-providers-and-users-of-synthetic-nucleic-acids

which could allow synthetic DNA providers in their country to engage in proliferative behavior with dual-use materials.

The use of non-domestic synthetic DNA providers also means that the United States is not fully investing in domestic supply chains and growing America's competitive capabilities and its bioeconomy. This is despite the fact that the U.S. already has the capacity to support the need for synthetic DNA in this country and that switching providers is as simple as making the change in an entity's procurement system (which takes days). This is drastically different from the resource-intensive effort and the time needed to switch advanced pharmaceutical ingredients. There are also downstream consequences if we lose domestic manufacturing of synthetic DNA and the future U.S. workforce essential to maintaining the United States' technological edge in innovation and next-generation manufacturing.

The combination of these significant national security issues warrants action to increase tariffs to deter the use of foreign providers of synthetic DNA to prevent sensitive information from being shared with foreign adversaries and bolster U.S. supply chains. Currently, HTS 2934.99.90 is listed in Annex II to Executive Order 14257, and as such, the recent increased levies on imported goods were not applicable to synthetic DNA. Therefore, we urge the Department of Commerce to address this national security risk by increasing the tariff on synthetic DNA as a strategic good. Further, it is important that synthetic DNA imports from China are not eligible for the de minimis exception because, for a typical U.S.-based order stream for gene-length DNA, more than 70% of shipments have a value of less than $800 and thus, would not be subject to payment of import duties.

Twist is encouraged by the Administration's America First Trade Policy and greatly appreciates the opportunity to describe how non-domestic manufacturing of synthetic DNA is impacting our country. We are proud to serve our customers who are developing next-generation therapeutics, biothreat countermeasures, and more, and we seek to ensure that companies such as ours can continue to enable this important work while maintaining a strong commitment to regulatory compliance and biosecurity. I hope you will consider Twist as a resource as the Department conducts its investigation.

Sincerely,

Angela Bitting
SVP, Corporate Affairs
Twist Bioscience Corporation