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May 7, 2025

Secretary Howard Lutnick
U.S. Department of Commerce
1401 Constitution Avenue, NW
Washington, DC 20230

Re: Request for comments to assist in an investigation under section 232 of the Trade Expansion Act (19 U.S.C. 1862) to determine the effects on national security of imports of pharmaceuticals and pharmaceutical ingredients, and their derivative products.

Docket ID: XRIN 0694-XC120

Dear Secretary Lutnick:

Fresenius Kabi appreciates the efforts of the Administration to strengthen national security and reward manufacturers of essential medicines that put America first and invest significantly in U.S. manufacturing to support U.S. patients, despite the lower costs of operating in other countries such as China or India.

U.S. manufacturing, bolstered by a diverse supply chain from allied nations, is essential to maintaining a resilient and reliable drug supply in the U.S., and such a model can help strengthen national security by mitigating shortages resulting from natural disasters, surges in demand, manufacturing disruptions, or other issues. Recently, however, it has become clear that many drug shortages are caused by economic factors that the Administration can address with effective trade and other policies. Today, reliable U.S. manufacturers are exiting the U.S. because they cannot compete with artificially low-priced medicines made in India and China and subsidized by those nations.[1] A recent landmark study by U.S. Pharmacopeia found the root cause of drug shortages in America to be economic.[2]

Policy Changes Can Lower Drug Prices, Create Jobs, and End Shortages

In this response to the Commerce Department's request for comment, Fresenius Kabi will address these issues and propose solutions for applying tariffs strategically in a way that would support the economics of U.S. manufacturing and job creation, increase access to

[1] https://www.mckesson.com/siteassets/documents/about-mckesson/public-affairs/mckesson-drug-shortages-whitepaper/mckesson-drug-shortages-whitepaper/

[2] go.usp.org/l/323321/2024-05-31/92zsjg/323321/1717187146zgOpt4vW/GEA_GC_056R_MSM_Report_2024_05_FINAL.pdf

lower-cost medicines, and reduce the risk of future drug shortages. These priorities are not mutually exclusive, as we will demonstrate. Applied strategically, our policy proposals would drive local for local manufacturing paradigms, including preferencing U.S.-made medicines for sale in the U.S., drive down the price of high-priced specialty drugs that make up more than 80% of prescription drug spending in America, and make it possible for the first time for lower-cost biosimilar medicines to be made in the U.S.

Background on Fresenius Kabi

In the United States, Fresenius Kabi employs more than 4,000 people with key domestic manufacturing, research and development, and distribution centers in Illinois, Massachusetts, Nevada, North and South Carolina, New York, Pennsylvania, and Wisconsin, as well as Puerto Rico. Over the last several years, we've invested nearly $1 billion dollars in the U.S. to strengthen our pharmaceutical supply chain, including massive pharmaceutical expansions in urban and suburban centers in the East and Midwest. In addition to supplying the U.S. quality biosimilar products, Fresenius Kabi USA delivers more than 400 million doses of generic injectable medicines to U.S. hospitals and clinics every year. We have FDA approvals or pending approvals to produce most of the injectable medicines on FDA's list of Essential Medicines. We already source active pharmaceutical ingredient (API) in the U.S., including for two vitally important essential medicines used in hospital settings, heparin and propofol.

For context, below is a list of the top 10 drugs manufactured by Fresenius Kabi:

Top 10 Drugs	Use	API	Components	Finished Dose Manufacturing
Calcium Gluconate	To increase calcium	India	U.S.	U.S.
Dilaudid	To relieve surgery pain	U.S.	U.S./Mexico	U.S.
Propofol	To induce anesthesia	U.S./Switzerland	Italy/Croatia Belgium/Germany Slovakia	Austria / Sweden
Enoxaparin	To prevent blood clots	India	India	India
Glucagon	To regulate blood sugar	Switzerland	France/U.S. Singapore	U.S.
Heparin	To prevent blood clots	U.S./Spain/China	U.S./Mexico	U.S.
Potassium Phosphates	To replenish phosphorous	U.S.	U.S.	U.S.
Sodium Chloride	To replenish fluids	U.S.	U.S./France	U.S.
Sodium Phosphates	To replenish phosphorous	U.S.	U.S.	U.S.

Lidocaine	To prevent pain	U.S./Sweden	U.S./Italy	U.S.

Root Causes of Market Inequities

Fresenius Kabi focuses on root causes when looking at complex market and supply chain issues. These issues typically stem from systemic policy or economic failures occurring early in the supply chain for branded drugs, complex generics and biosimilars, and sterile injectable generic essential medicines. We will focus on the latter markets, detailing the root causes in the market that contribute to the need for a 232 investigation. We will also recommend how the Administration can achieve the desired results, while improving safety and viability of supply chains and encouraging innovation and healthy competition.

For generic sterile injectable essential medicines, foreign government incentives and funding for KSMs, APIs, and finished doses, along with the low labor cost to manufacture in China and India, have caused the prices for some drugs in the U.S. to dip under the cost to manufacture the same medicines in the U.S.

U.S. hospitals, which are under financial pressure themselves, seek the lowest price for pharmaceuticals, and this has resulted in forcing some U.S. manufacturers to exit the U.S. market. When foreign manufacturers then have supply issues, shortages result.

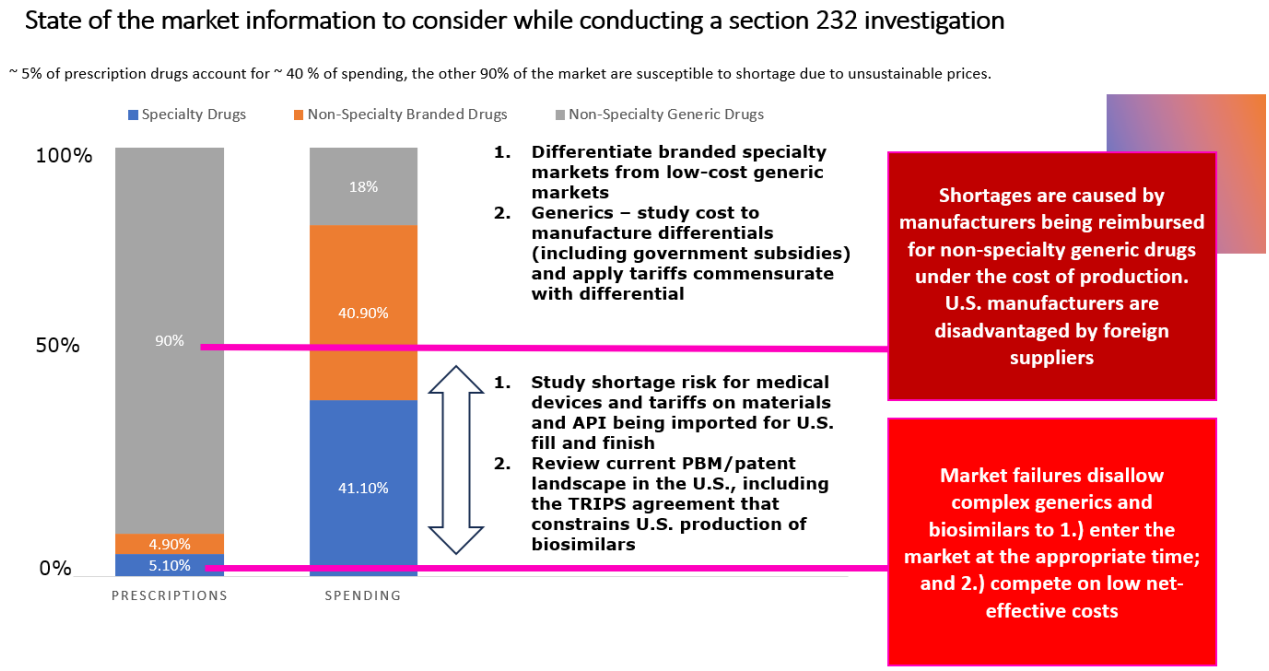
Fresenius Kabi will argue that the economic playing field could be leveled using strategic tariffs, but only in a manner that considers root causes and does not create unintended consequences that disadvantage U.S. fill and finish manufacturing by taking a narrow definition of country of origin.

For complex generics and biosimilars, and for branded drugs, Fresenius Kabi will present data showing that branded drug companies misuse the U.S. patent system to keep their specialty drug prices high in the U.S. compared to the EU and other developed countries. Patent misuse also prevents U.S. manufacturing of complex generics and biosimilars. In this sector, it is important to distinguish between brands and biosimilars/generics and avoid rewarding innovators who misuse the U.S. patent system to keep generics and biosimilars out of the market longer than any other country in the world.

In addition, pharmacy benefit managers also favor high-priced brands over low-cost biosimilars, forcing patients to pay more for drugs they depend on for chronic conditions. Without policy change, biosimilars, and their promise of lower prices, face extinction. If also required to pay tariffs, there would be little incentive left for biosimilar companies to develop new products.[1]

Fresenius Kabi believes the Administration could use tariffs, along with other pro-competitive policies, to balance markets by using the savings not currently realized in the specialty drug sector by enabling faster and deeper complex generic and biosimilar competition. The Administration could apply a small part of this savings to sustain U.S. made generic sterile injectable essential medicines by using tariffs to require China and India to fairly price their products, which today benefit from government financial support and low labor costs.

[1] Assessing the Biosimilar Void in the U.S. - IQVIA



Sterile Generic Injectable Essential Medicines

Goal

The U.S. Department of Commerce seeks to encourage more generic drug manufacturing in the U.S. to protect against shortages and decrease our reliance on China and India for essential medicine sourcing. The section 232 investigation is vital to realizing this objective.

The market for FDA-approved sterile generic injectable medicines is becoming increasingly unsustainable. Shortages highlight the fragile state of the supply chain and its critical impact on patient access to lifesaving medicines.[2] Hospitals, burdened by the high costs of branded drugs—which account for 85% of their pharmaceutical spending but only a small portion of their usage—are increasingly relying on savings from generic injectables, which make up the remaining 15%. According to USP, most medicines in shortage cost less than $5.00 with nearly a third of sterile injectables in shortage costing less than $2.00 a dose. That's less than bottled water. Injectable drugs in shortage are on average nearly 8.5 times lower in unit price than those not on shortage.

For some drugs, financial pressure has driven down prices to unsustainable levels, causing manufacturers, especially those in the U.S. with higher production costs, to stop producing essential medicines and close production lines. When this occurs, other generic manufacturers often do not have time to respond, and shortages can result. Many manufacturers have been forced to move operations offshore, usually to India and China, to remain competitive. As a result, supply chains

[2] Drug Shortages: HHS Should Implement a Mechanism to Coordinate Its Activities | U.S. GAO

become more complex and prone to failure, putting national security at risk. Further, the American Hospital Association (AHA) estimated that drug shortages increased drug spending by 20% in 2023, suggesting that leveling the playing field with manufacturing costs between China, India, and the U.S.[3] may create a net savings to providers. This move should promote redundancy, quality updates, and domestic supply viability. Additionally, as discussed later in this document, hospitals would have relief from their branded drug spend, which has increased more than 35% in 2023,[4] with targeted and reasonable reforms to the U.S. patent system.

The Administration is considering how tariffs can be part of a solution, and we agree that manufacturing cost differentials among the U.S., China, and India pose a problem in the generics market where price erosion often leaves no opportunity for U.S. manufacturing. Fresenius Kabi recommends that if tariffs are imposed, the Administration should consider those manufacturing cost differentials and apply them as a tariff commensurate with the cost differential, a differential that includes direct government funding to the industry in China[5] and India.[6]

This approach could naturally reform purchasing practices if all inputs are comparable. Without suitable reform, or if reform is not done carefully to avoid unintended consequences, this financial pressure for U.S. manufacturing could become more acute in a market that already offers little predictability for manufacturers and discourages investment in essential resiliency measures like surge capacity and utilizing and updating U.S. manufacturing sites.[7] Idle U.S. manufacturing plants and offshore manufacturing are symptoms of a failing market. Fresenius Kabi's comments will focus on ways tariffs and other actions could help reward supply reliability and resiliency, and level the competitive market which currently unfairly advantages firms sourcing low-cost production in India and China.

Proposed Solutions

In 2020, KPMG, a leading global accounting firm, ranked primary manufacturing costs around the globe, focusing on the following measures: labor costs, real estate costs, utility costs, corporate tax rates, and interest rates.[8] The study found that, among these basic cost measures, China and India were among the top 5 countries with the lowest manufacturing costs, whereby, the U.S. ranked 14th, with costs similar to Germany, the UK, and other EU countries. Further, China and India have significant government funding for vertically integrated systems that allow prices in the U.S. market to be unsustainable for U.S. made products. For example, India's Special Economic Zones, or SEZs, exempt Indian manufacturers from income tax for five years, offer capital investment subsidies up to three million dollars and offer significant discounts on land and real estate.[9] If the administration wants to curb these manufacturing cost deficits and level the playing field for U.S. manufacturing, it should:

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[3] Drug-Costs-Infographic-ver03

[4] Costs of Caring | AHA

[5] "Full-Chain Support for Innovation", Chinese Government Continues Its Supporting to the Biopharma Industries, and Implications to the Industry Companies

[6] Press Release:Press Information Bureau

[7] US Generic Pharmaceutical Manufacturer Available Capacity Research Study.pdf | Powered by Box

[8] https://www.themanufacturinginstitute.org/wp-content/uploads/2020/10/cost-manufacturing-operations- globe.pdf

[9] Special Economic Zones in India Driving Growth & Competitiveness | IBEF

1. Use the section 232 investigative methodology to study the primary cost differences for pharmaceutical manufacturing in both China and India. Apply a tariff equal to the manufacturing cost differential, when combined with Government funding, when compared to the same class of pharmaceutical manufacturing in the U.S. This should include all the primary costs listed above, and the cost of environmental and labor regulatory compliance in both regions for safely producing active pharmaceutical ingredient (API), components, and fill and finish (finished dose).

2. Exempt active Pharmaceutical Ingredients (APIs), components, and raw materials from tariffs as long as all fill and finish production is done in the U.S. Applying tariffs on raw materials, API, and components, imported into the U.S. would weaken U.S. finished product manufacturers who already bear a significant cost disadvantage compared to low-cost manufacturing countries like India and China. This could lead to discontinuation of many generic products, resulting in higher drug shortages for U.S. patients and possible job losses for skilled and hourly pharmaceutical production workers.

3. Incentivize generic manufacturers who have invested significantly in U.S. Instead of onshoring foreign manufacturers, bolster the already existing U.S. infrastructure by applying tariffs that level the cost to produce playing field. Once all inputs are equal, the decision to move back to the U.S. will be more attractive to manufacturers if they want to continue to compete for U.S. business.

4. Incentivize U.S. manufacturing by fast-tracking U.S. FDA approval timelines for approval of ANDAs & NDAs and approval of amendments.

If the goal is to bring API back to the U.S., why is Fresenius Kabi asking to exempt imports from tariffs for some foreign sourced API and raw materials?

Fresenius Kabi has made significant U.S. fill and finish manufacturing investments. Because of this, we will explore the feasibility of levying tariffs on non-U.S. API as the country of origin, and we will test how well this approach would promote U.S. API production, fill and finish, and the sourcing of components and other raw materials using the below hypothetical example.

Both drug X and Y are generic sterile injectables referencing the same product but are manufactured and marketed by two different firms. The product is a common sterile injectable essential medicine used in every hospital in the U.S.:

Assumptions and Methodology

1. We assume drug X is producing finished dose in the U.S. and sourcing API from China/India.
2. We assume drug Y is sourcing all materials and producing finished dose products in China/India for importing into the U.S.
3. Using IQVIA data, we estimate the average price being paid for the drug across manufacturers in the U.S. market for this example is $0.75 per unit and estimate the average cost to manufacture differentials through reverse engineering public financial data (this data is important for the administration to study as part of the section 232 investigation with more sophisticated tools that the U.S. government can access)
4. We assume that API is 30% of the value of the finished dose product.
5. We assume a 25% tariff.

Hypothetical comparison	Drug X	Drug Y	Notes
Average price in the U.S. market per unit	$0.75	$0.75	Average price per unit when averaging all manufacturers in the market.
Average cost of goods (CoGs)	$0.78	$0.42	CoGs includes cost to manufacture, API, ingredients, and components.
CoGs after tariff application at 25%	$0.85	$0.53	The drug X manufacturer would pay a 25% tariff on API and components, which is 30% of the total CoGs profile, while drug Y manufacturer would pay a tariff on finished dose, which includes all API, components, and foreign fill and finish costs.
Result	The U.S. manufactured drug is still not competitive with the foreign-made drug as $0.85 >$0.75	The foreign manufactured drug would continue to have a competitive advantage with customers as $0.53 <$0.75	For drug X to be competitive in the market, the manufacturer would have to move fill and finish out of the U.S. and into a lower-cost manufacturing domicile.

Key Messages:

1. The U.S. fill and finish manufacturer, in this hypothetical example, would still be significantly disadvantaged from tariffs, given that they are importing components like vials and stoppers, as well as API, and paying U.S. labor, tax, real estate, and environmental costs for U.S. fill and finish.
2. To retain U.S. investment in finished dose manufacturing, any tariff policy must protect the current fill and finish manufacturing in the U.S. while still encouraging U.S. API sourcing. Therefore, the Administration should exempt API and components entering the U.S. for fill and finish.
3. The Administration should not offer monetary incentives for onshoring foreign API manufacturers, but rather protect and bolster the already existing U.S. infrastructure from lower than cost to produce prices resulting from Indian and Chinese government subsidies and overall lower-cost labor, real estate, and environmental standards. Once all inputs are equal, the decision to move back to the U.S. will be more attractive to manufacturers if they want to continue to compete for U.S. business.

Avoid Unintended Consequences

1. Avoid applying tariffs to EU-produced products, as this could cause EU manufacturing to move to China and India to lower the cost of manufacturing to absorb a high tariff percentage. Patent quality issues in the US make it challenging to move EU manufacturing to the US, as explained below. The EU manufacturing costs are already similar manufacturing costs to the U.S., so EU tariffs are not necessary. In fact, EU manufacturing is vital to building redundancy outside of the U.S. to protect against shortages caused by natural disasters, or regional supply disruptions.

2. Avoid executing tariffs on drugs where either finished dose or API is produced or sourced in the U.S. as this may force U.S. fill and finish operations and/or API sourcing to China and India to absorb the tariff by relocating to a low-cost country.

Policy Proposal Result

In this scenario, the Administration would use tariffs strategically to equalize manufacturing costs across the U.S., China and India. By addressing the economic root cause of offshoring, the policy would incentivize companies to bring manufacturing back to the U.S. for those manufacturing in other countries with low production costs and government subsidies. In the short term, this policy would encourage the purchasing of U.S. manufactured essential medicines in long-term fixed price contracts, as unreliable foreign suppliers would be unable to undercut bids offered by domestic manufacturers who cannot lower prices below cost of production.

Finally, the policy could reduce shortages of generic sterile injectables that impact U.S. patients, as more reliable suppliers would no longer be forced to exit markets.[10] The United States Pharmacopeia (USP) has concluded that the impact of drug shortages on patients "has been significant: treatment delays, the use of less effective treatments, or missed doses of therapies, often with life-threatening results." The American Hospital Association has emphasized the severe cost implications of these sterile injectable shortages, with hospitals incurring over $359 million annually in additional drug spending.[11]

Biosimilars and Specialty Drugs

Goal

The Administration seeks to level the costs of specialty drugs between the U.S., Europe, and other countries to curb U.S. drug prices from subsidizing access to innovative medicines abroad.

Background

During President Trump's first term, the Administration proposed a "most favored nation" (MFN) policy for pharmaceuticals. This policy aimed to lower drug prices in the U.S. by using international reference pricing comparing the cost of the same drugs in the U.S., Canada, and the EU. The goal was to lower drug prices in the U.S. by aligning them with what is paid outside the U.S. Therefore, it follows that the Administration would be studying what could be done to curb the U.S. funding of R&D and patient access to innovation across the globe in the context of the section 232 investigation.

Currently, Fresenius Kabi has limited U.S. biosimilar manufacturing despite having a robust pipeline that has the potential to save Medicare and patients millions of dollars each year. Biosimilar companies cannot "make, use, import or sell" biosimilars in the U.S. until the relevant patents are cleared.[12] Because of the below-mentioned patent quality issues, that do not exist in the EU, the U.S. is typically the last country where a biosimilar can be manufactured. This means that

[10] Cheaper is not always better: Drug shortages in the United States and a value-based solution to alleviate them - PubMed
[11] Medical Product Shortages in the United States: Demographic and Geographic Factors and Impacts
[12] 35 U.S. Code § 271 - Infringement of patent | U.S. Code | US Law | LII / Legal Information Institute

biosimilar manufacturers cannot launch their drugs in other countries as net exporters from the U.S. Even if a manufacturer does not sell a single dose of a biosimilar in the U.S. and solely exports to the EU, they would infringe relevant U.S. patents by making the biosimilar in the U.S.[13] The delayed launches of complex generics and biosimilars compared to the EU is due to anti-competitive U.S. patent strategies that keep U.S. patients paying more longer than in the EU. Furthermore, tariffs on biosimilars coming from overseas would incentive use of the more expensive branded drug manufactured in the U.S. by the patent holder. This could essentially reward patent misuse by the innovator.

Therefore, the root cause of both offshoring biosimilar manufacturing and the EU paying lower costs for specialty drugs than the U.S. cannot be solved with tariffs, but rather, a few simple changes to the U.S. patent system.

Issue #1: Patent thickets

The U.S. patent office rejects subsequent patent filings that claim the same drug feature already claimed in earlier patents. This practice is called "double patenting" and is not allowed in Europe, where biosimilars have successfully lowered costs for governments and patients. Only in the U.S. does the patent holder have the option to overcome the double patenting rejection with something called a terminal disclaimer. A terminal disclaimer, voluntarily filed by the patent holder, causes the duplicative patent to expire at the same time as the original patent, but allows duplicative patents to issue and be asserted against competitors. This remains true even if the competitor invalidates the original patent in court. The American requirement to invalidate all the duplicative patents separately, causes serial litigations, increases litigation costs and renders significant uncertainty over generic and biosimilar launches.[14] Consequently, generics and biosimilars in the U.S. are delayed in coming to market compared to other developed countries.[15] Manufacturing in the U.S. is similarly curtailed by this misuse of patents in the pharmaceutical sector.

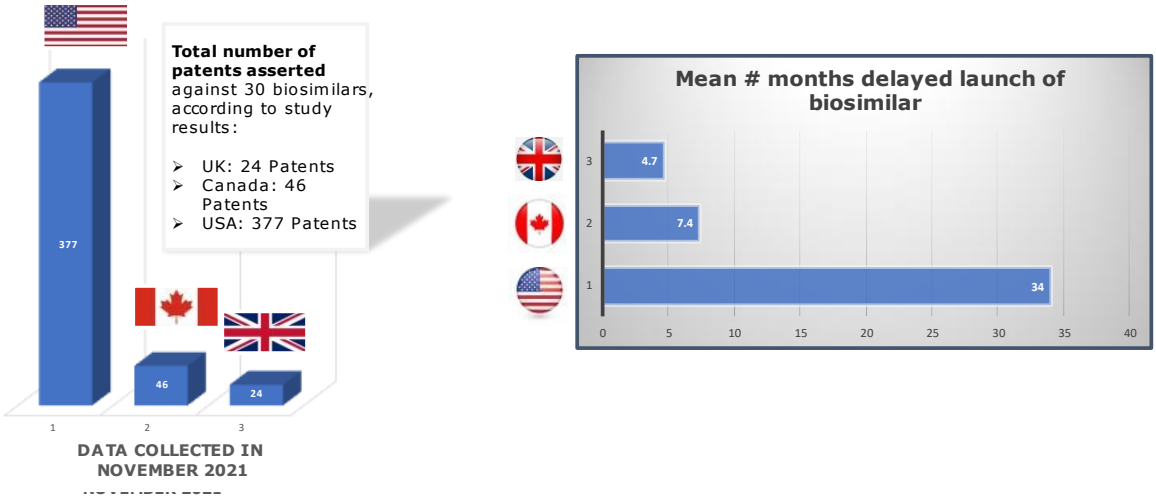
The graph below shows the number of patents litigated against the same 30 biosimilar drugs in the U.S., Canada, and the UK. It highlights the direct correlation between this patent misuse practice and delayed U.S. biosimilar launches. The high numbers of litigated patents in the U.S. are primarily driven by duplicative patents with terminal disclaimers, rather than novel innovations. Although this study compares with data outside of the EU (in Canada and the UK), the data can be extrapolated to the EU and the rest of the world, as no other country allows terminal disclaimer practice.

[13] PatentThickets_May2021_FINAL.pdf

[14] Tu SS, Goode R, Feldman WB. Biologic Patent Thickets and Terminal Disclaimers. JAMA. 2024 Jan 23;331(4):355-357. doi: 10.1001/jama.2023.25389. PMID: 38095894; PMCID: PMC10722383.

[15] Biological patent thickets and delayed access to biosimilars, an American problem | Journal of Law and the Biosciences | Oxford Academic

Study Results: Large patent estates correlate with delayed biosimilar market entry in the U.S. compared to abroad



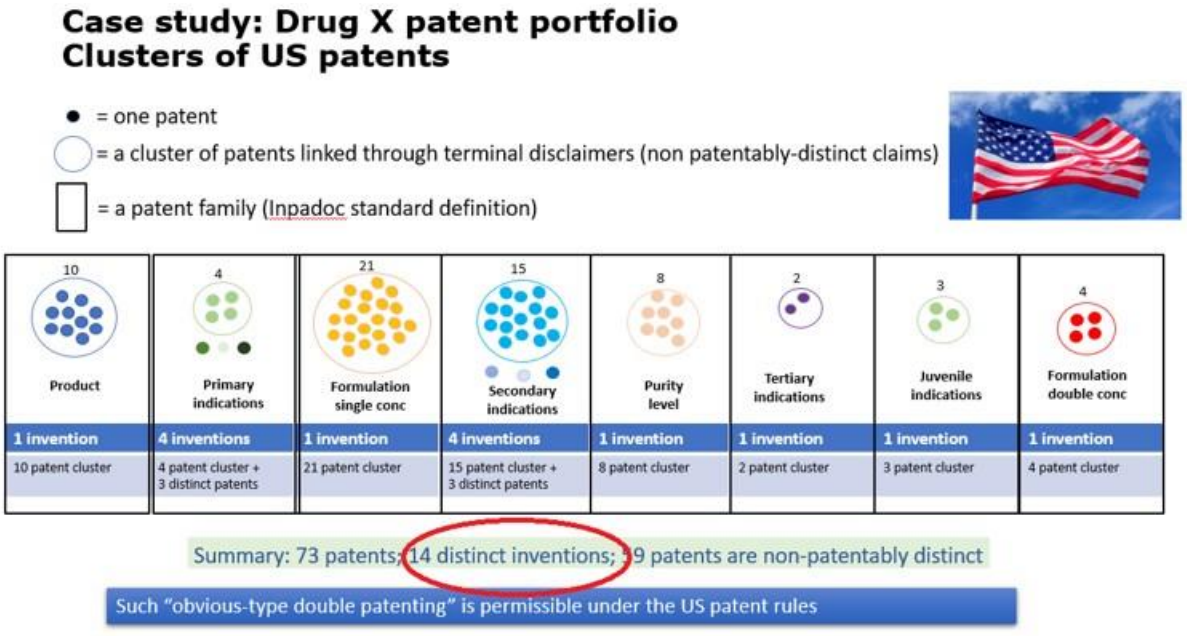
When we talk about "duplicative" patents, we refer to patents that are subject to a terminal disclaimer. These patents do not represent incremental improvements to an existing drug. Instead, they use synonyms to describe the same inventive feature. This practice is allowed under current U.S. patent system rules. Further, innovators would not voluntarily accept a terminal disclaimer if they believed they were filing for patent protection on a novel, distinct invention, as the terminal disclaimer would truncate the patent life for the new feature.

Example:

Patent	Summary of Claims
Patent 1	A method for treating rheumatoid arthritis in a human subject, administering subcutaneously a total body dose of 40 mg of [drug A] once every 13 - 15 days for a time period sufficient to treat the rheumatoid arthritis
Patent 2	A method of reducing signs and symptoms in a patient with moderately to severely active rheumatoid arthritis, administering subcutaneously a total body dose of 40 mg of [drug A], once every 13-15 days

Below is an example of a real drug that has an existing patent thicket, created by using terminal disclaimers. Each dot represents a patent. All the dots within the circles are terminally disclaimed patents, or duplicates of one another. All patents outside of the circles are incremental inventions, or

improvements, which the patent system should reward. You will see that, currently, a biosimilar/generic competitor would have to successfully challenge each dot, whether duplicative or not, to launch without risk. This approach is entirely permitted by current U.S. patent law rules.



In Europe, patents for the same pharmaceutical inventions may be filed as in the U.S., but in Europe terminal disclaimers do not exist. This means duplicative, terminally disclaimed patents are not present. By having more reasonable numbers of patents in the EU, patent litigation in European countries is more efficient compared to the U.S. European biosimilar manufacturers can identify weak patents that shouldn't have been granted, invalidate them by proving this in court. This enables earlier dates to initiate manufacturing biosimilars in Europe than is possible in the U.S. In the U.S., challenging each patent, whether it is original or duplicative costs ~ $1 million via third party proceedings called IPRs and PGRs, which makes it cost prohibitive to fight for access to the market and the freedom to manufacture.

Comparison case study:
Patent portfolio of the same drug in Europe

● = one patent

◯ = a cluster of patents linked through terminal disclaimers (non patentably-distinct claims)

▭ = a patent family (Inpadoc standard definition)

Filed in 1996	Filed in 2001	Filed in 2002	Filed in 2002	Filed in 2006	Filed in 2010	Filed in 2007	Filed in 2007
2	2	2	1	Patent not granted	1	Patent not granted	Patent not granted
Product	**Primary indications**	**Formulation single conc**	**Secondary indications**	**Purity level**	**Tertiary indications**	**Juvenile indications**	**Formulation double conc**
2 inventions	**2 inventions**	**2 inventions**	**1 invention**	**-**	**1 invention**	**-**	**-**
2 distinct patents	2 distinct patents	2 distinct patents	1 distinct patent	-	1 distinct patent	-	-

Summary: 8 patents; 8 inventions; 0 patents are non-distinct; 0% of the portfolio is duplicative

How does reforming terminal practice intersect with the goal of a "most favored nation" policy or international reference pricing?

The most favored nations policy aims to level the playing field between the U.S. and EU by tying prices paid by EU countries to prices paid by the U.S. It is widely believed that the profit made from high U.S. prices bankrolls innovator research and development, allowing the world to access new drugs at a fraction of the price that U.S. patients, Medicare, and private health plans pay. Fresenius Kabi does not disagree with this sentiment with respect to originator drugs and believes that complex generics and biosimilars are the solution to this problem, provided they can access the market at the appropriate time. On average, as detailed above, the U.S. waits approximately three years for access to biosimilars while the EU, UK and Canada has already realized savings on those drugs and made room to pay for true innovation. This difference, along with anti-competitive PBM practices, is the root cause of the price differential between the two regions. Enacting a most favored nations policy would replace competition, in favor of price setting, instead of rebalancing market forces in the U.S.

To supplement the data above about the U.S. vs. EU patent systems, we will explore a case study that considers Europe's low tolerance for anti-competitive patent behavior vs. that of the U.S., a nation that claims to be the protector of free market forces.

Case Study: Copaxone

On October 31, 2024, the European Commission ruled in the Teva Copaxone case (Case AT.40588 – Teva Copaxone) and fined Teva EUR 462 million for abusing its market position, which included gaming the EU patent system. The Commission found that Teva inappropriately extended

Copaxone's patent protection by misusing the European Patent Office (EPO) rules pertaining to so-called divisional patents. Divisional patents are based on an original invention, or inventive feature, but cover different or more narrow aspects of that invention. Although the EU does not allow terminal disclaimers, the divisional practice is similar in that the patents are assessed separately but get the same expiry date of the parent patent. In comparison, terminal disclaimer practice in the US is proactively initiated by the patentee to amass large numbers of patents on non-distinct inventions.

The Copaxone patents in question were filed over eight years in Europe, between 2010 and 2018, with an attempt to multiply duplicative patents with significantly overlapping claims. In other words, Teva tried to replicate their U.S. patent strategy in Europe. The European Commission found that the claims in the divisional patents were not new and were based on the science already contained in the parent patent. The Commission fined Teva for anti-competitive behavior. In contrast, duplicative terminally disclaimed patents are entirely permitted in the U.S. In the U.S., there are over 15 times more patents against 30 biosimilars than in the UK, and over seven times more patents against biosimilars than in Canada.[16]

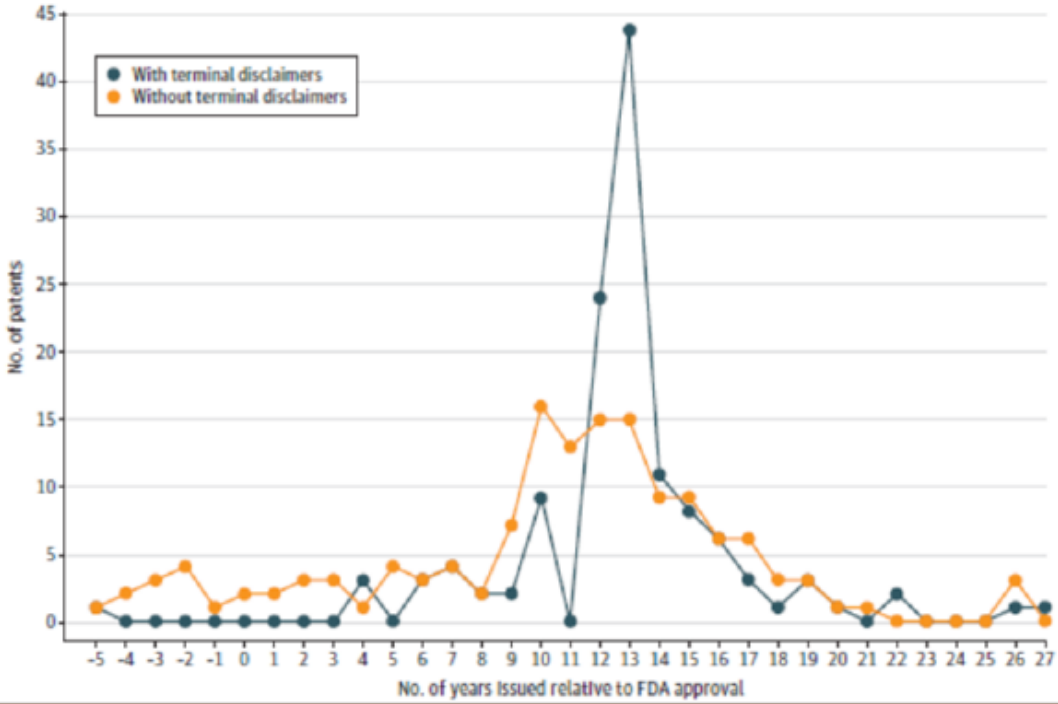
Furthermore, the EU Commission found that Teva systematically withdrew various divisional patents just before a negative decision on their validity, thereby denying generic drug competitors the possibility to clear the path to market entry and avoiding legal precedents that could have undermined other divisional patents having overlapping patent claims. While the European Commission condemns such behavior as anti-competitive, this is standard practice in the U.S. These claims brought by the Commission against Teva are common practice and completely legal in the U.S. and have become standard in delaying lower-cost generic and biosimilar competition on the most expensive drugs in the market.

For example, terminally disclaimed patents make up a majority of the patents asserted against biosimilars and they are filed and granted just before the end of the branded data exclusivity period.[17]

[16] Goode R, Chao B. Biological patent thickets and delayed access to biosimilars, an American problem. J Law Biosci. 2022 Sep 1;9(2):lsac022. doi: 10.1093/jlb/lsac022. PMID: 36072417; PMCID: PMC9439849.

[17] Biologic Patent Thickets and Terminal Disclaimers | Clinical Pharmacy and Pharmacology | JAMA | JAMA Network

Figure. Number of Patents With vs Without Terminal Disclaimers Involved in Litigation Relative to Drug Approval From the US Food and Drug Administration (FDA)



The pronounced peak for patents with terminal disclaimers in the study group occurred in years 12 and 13, coinciding with the end of FDA-granted statutory exclusivity and shortly before the typical expiration of product patent PTEs.

In conclusion, even with Teva's attempt to delay generic launch in the EU using a similar strategy as is commonplace and allowed in the U.S., generic versions of Copaxone were launched in the EU more than one year before the U.S., on September 5, 2016, while the U.S. did not have access until October 4, 2017. [18, 19] In 2017, Medicare paid $1.5 billion for branded Copaxone.[20]

How does reforming terminal disclaimer practice stack up to IRA's Medicare Negotiation?

[18] See Alvogen, Alvogen Launches First Generic Equivalent of CopaxoneTM in Europe, https://www.alvogen.com/newsroom/alvogen-launches-first-generic-equivalent-of-copaxonetm (last visted May 2, 2025).
[19] Mylan Confirms U.S. Launch of First Generic for Copaxone® 40 mg/mL 3-Time-a-Week and Generic for Copaxone® 20 mg/mL Once-Daily, PR Newswire (Oct. 4, 2017), https://www.prnewswire.com/news-releases/mylan-confirms-us-launch-of-first-generic-for-copaxone-40-mgml-3-times-a-week-and-generic-for-copaxone-20-mgml-once-daily-300531448.html (last visited May 2, 2025).
[20] Pricing of Drugs for Multiple Sclerosis

	Tecfidera	Imbruvica
FDA Approval year	2013	2013
Medicare Spend per Year (2020) – total claims	$1.1B 233k	$2.9B 109k
Medicare Spend per year (2022) – total claims	$343M 196k	$2.9B 38k
Date Generics Enter market/Medicare negotiation	Q4 2020 – launch @ risk	2026 – Medicare negotiation
Total Discount when competition/negotiation occurred	>90% in Q4 2020	38% in 2026
# of Terminal Disclaimers and # number of OB patents listed after product patent expiry	1 patent not subject to a terminal disclaimer	31 of 41 OB listed patents terminally disclaimed (75%)

In 2022, the Inflation Reduction Act was passed, including Medicare direct negotiation. The time when negotiation is triggered correlates to when biosimilars come on to the market in Europe, which is not surprising, as the EU patent system does not allow the use of terminal disclaimers. The chart to the left shows evidence that market forces and competition can outperform government negotiation of drug prices in Medicare

- Although the two drugs have the same FDA approval date, Tecfidera went generic in 2020 and Imbruvica is still patent protected. The difference: terminal disclaimers.
- The price erosion from generic competition is 90% without terminal disclaimers vs. 38% with Medicare negotiation as the remedy for allowing terminal disclaimers.
- IRA ONLY applies to Medicare where patents impact all drug markets.

Proposed Solutions:

1. The U.S. patent office could require patentees to file an "admission of Obviousness type double patenting" should they file a terminal disclaimer. In litigation, patents joined together by terminal disclaimers should rise and fall together. The U.S. patent office suggested this policy in its proposed rule released in 2024.[21]

2. Branded drug companies should only be allowed to assert one patent per duplicative group against biosimilar and generic drug companies. This policy is set out in the Arrington/Welch Patent Thicket Act.[22]

Issue # 2: Ancillary Product Patents:

Challenges to extended biologic patent protections have revealed a scheme that involves providing inconsistent information to the FDA and the patent office. More specifically, ancillary product patents are being filed on features of a drug that were inherently present during the original FDA approval process. Rather than filing ancillary product patents as part of their initial primary patent filing, branded drug companies often keep ancillary product features confidential as trade secrets and wait years before seeking ancillary product patents, prolonging their patent life. This strategy

[21] Federal Register :: Terminal Disclaimer Practice To Obviate Nonstatutory Double Patenting

[22] Arrington Leads Bipartisan Effort to Address Patent Thickets and Increase Competition in the Prescription Drug Market | U.S. Representative Jodey Arrington

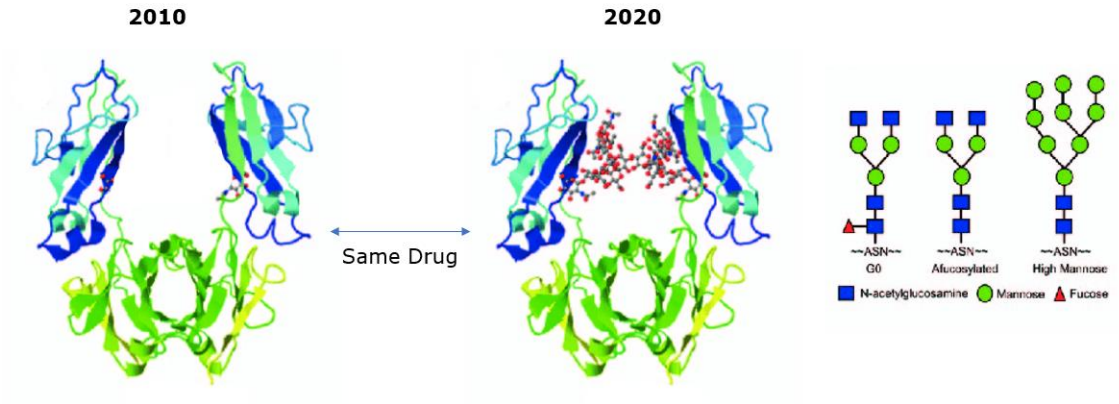
may allow branded drug companies to extend periods of market exclusivity because later-filed ancillary patents typically expire after the primary patents. These ancillary product patents cover aspects of the biologic's active ingredient such as glycan profiles, oxidation levels, and other physiochemical properties.

Rather than filing all the existing features of the primary invention as part of the primary patent family, some branded drug companies are filing on just the skeleton of the drug's structure. Subsequently, these companies file "ancillary product patents" sometimes a decade later to cover technical features of the drug's structure that were, inherently, present all along. This practice extends the period of market exclusivity beyond the initial 20-year patent term.

Primary and Secondary Product Patents

Brands are extending product patent protection for biologics by claiming specific technical features of the product in later filed applications. Glycosylation, purity

For Example:

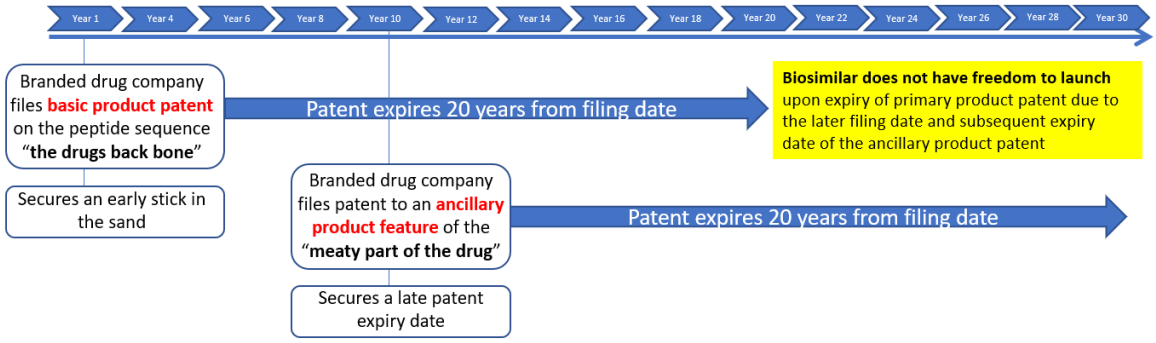


Primary Product Patent
Amino Acid Sequence

Secondary Product Patent
Technical features on the Amino Acid

Ancillary product patents

- The evergreening strategies in question enable branded drug companies to inappropriately extend the patent protection on the biological drug product by staggering claims on specific technical features of <u>one and the same drug</u>.
- Example timeline:



Maintaining these features as trade secrets and purposefully staggering their patent filings, prevents biosimilar and generic drug competitors from accessing the essential information needed to develop biosimilars and results in patents having inappropriately late expiry dates. The financial implications of this practice are significant. In 2021, biologics accounted for 46% ($260 billion) of all gross prescription drug spending in the US. Delaying entry of biosimilar competition allows branded drug companies to preserve market exclusivity and, without alternatives, maintain demand for high prices. Currently, the European patent system has not resulted in any ancillary product patent being litigated against a biosimilar manufacturer. Again, this patent quality issue appears to be uniquely American.[23]

<u>How does reforming ancillary product patent practice intersect with the goal of a "most favored nation" policy or international reference pricing?</u>

<u>Case Study: Enbrel</u>

To illustrate the financial impact of patent misuse on the Medicare program compared to the prices paid in Europe, consider the drug Enbrel, which is marketed by Amgen in the U.S. and Pfizer in Europe. In the U.S., Enbrel will continue to enjoy patent protection until 2029, due to a patent strategy colloquially called a "submarine patent." The submarine patent strategy in the U.S. is a tactic where the issuance and publication of a patent application are delayed. This is done to catch potential infringers off guard once the patent is granted and prolong the patent term. For patent applications filed before June 1995, the patent term was 17 years from the grant date. This allowed

[23] Goode R, Feldman WB, Tu SS. Ancillary Product Patents to Extend Biologic Patent Life. *JAMA.* 2023;330(21):2117–2119. doi:10.1001/jama.2023.19547

patent holders to prolong patent life by slowing down the grant process for many years[24][25].

This strategy was used by Amgen in the U.S. to enjoin two biosimilar manufacturers when a submarine patent "surfaced" concerning Enbrel. These patents were closely tied to the composition of matter, also referred to as the "product patent," making them nearly impossible to design around for biosimilars. As a result, the biosimilar manufacturers lost the case on a patent they did not know existed until it was too late. The last of the Enbrel "submarine patents" will expire in 2029. Given that this strategy is only available for patents filed before June 1995—after which time a patent's term is tied to patent filing instead of patent grant—this particular problem should be solved going forward. As discussed above, however, the ancillary product patent strategy creates a similar effect to delay competition.[26]

The old law which permitted submarine patents was open to abuse because some patent applicants would intentionally delay the patent grant process, resulting in a concomitant delay to patent expiry. Although submarine patents are not permitted under current law, there are clear parallels in the overall effect of the submarine patent strategy and the ancillary patent strategy, as both result in delayed patent expiry. In fact, the ancillary patent strategy can be seen as a modern replacement for the submarine strategy.

To illustrate the effect of submarine patent strategy of drug costs, we will compare prices in Europe versus the U.S. for the drug Enbrel. In 2014, Pfizer (Amgen's commercialization partner) reported its Enbrel sales outside of the U.S. and Canada peaking at $3.8 billion. Biosimilar competitors achieved regulatory approval in the EU in 2017,[27] and Enbrel revenues had shrunk to $690 million in 2024. Indeed, within a year of biosimilar launch in Europe, the price of Enbrel declined by 50% and biosimilars held 40% of the market.[28]

For purposes of comparison, in the U.S., where Enbrel's patents are still in force, Amgen reported sales of $5.2 billion dollars in 2019 and $3.3 billion in 2024, the downward trend primarily due to competing branded products being launched in the U.S. and gaining market share. The effect of the submarine patent strategy in the case of Enbrel was to deny the U.S. market biosimilar competition, which achieved billions of dollars in savings in the EU over the past 8 years.

The ancillary product patent strategy, similar to the submarine patent strategy, is now a common occurrence in the U.S., with the following drugs currently impacted:

[24] https://www.hrfmlaw.com/ip-101-submarine-patents-ready-to-torpedo-you/
[25] https://en.wikipedia.org/wiki/Submarine_patent
[26] Microsoft Word - Sandoz v. Amgen - DRAFT Complaint - 4.11.2025_SJP Signature(45910640.1)
[27] Sandoz receives approval in Europe for Erelzi® (biosimilar etanercept) to treat multiple inflammatory diseases | Novartis
[28] Sandoz files antitrust litigation against Amgen regarding patient access to etanercept biosimilar in the US | Sandoz

Table. Biosimilars With Litigated Ancillary Product Patents[a]

Branded drug name (generic name)	Primary patent (expiration date)[b]	FDA approval date	Litigated ancillary product patent (expiration date)[c]	Extension of time, d[d]	Ancillary product claim subject matter
Epogen/Procrit (epoetin alfa)	US 5 547 933 (Aug 20, 2013)	Jun 1, 1989	US 5 856 298 (Jan 5, 2016)	868	Silylation profile
Eylea (aflibercept)	US 7 070 959 (Jun 16, 2023)	Nov 18, 2011	US 11 186 625 (Aug 18, 2040) US 11 306 135 (Aug 18, 2040) US 11 066 458 (Jun 14, 2027) US 10 464 992 (Jun 14, 2027)	6273	Oxidation profile Oxidation profile Glycosylation profile Aggregation profile
Herceptin (trastuzumab)	US 5 821 337 (Oct 13, 2015)	Sep 25, 1998	US 6 339 142 (May 3, 2019) US 9 249 218 (May 3, 2019)	1298	Acidic profile Acidic profile
Humira (adalimumab)	US 6 090 382 (Dec 31, 2016)	Dec 31, 2002	US 8 916 153 (Nov 14, 2034) US 9 550 826 (Nov 14, 2034) US 9 181 337 (Nov 12, 2033) US 9 200 070 (Nov 12, 2033) US 9 505 833 (Nov 12, 2033) US 9 085 618 (Nov 12, 2033) US 9 522 953 (Nov 12, 2033) US 9 334 319 (Mar 14, 2033) US 9 683 033 (Mar 14, 2033) US 9 708 400 (Mar 14, 2033) US 9 365 645 (Apr 26, 2032) US 9 255 143 (Apr 26, 2032) US 8 231 876 (Apr 4, 2027) US 8 895 009 (Apr 4, 2027) US 9 096 666 (Apr 4, 2027)	6527	Purity level Glycosylation profile Lysine species Acidic profile Methylglyoxal species Acidic profile Acidic profile Acidic profile Acidic profile Lysine species Fucosylation profile Fucosylation profile Purity level Purity level Purity level
Avastin (bevacizumab)	US 6 407 213 (Jun 20, 2020) US 6 054 297 (Feb 26, 2018)[e]	Feb 26, 2004			
Enbrel (etanercept)	US 8 163 522 (Apr 24, 2029) RE 36 755 (Oct 23, 2012)[e]	Nov 2, 1998			
Neulasta (pegfilgrastim)	US 5 824 784 (Oct 20, 2015)	Jan 31, 2002			
Neupogen (filgrastim)	US 5 580 755 (Dec 3, 2013)	Feb 20, 1991			
Remicade (infliximab)	US 6 284 471 (Sep 4, 2018)	Aug 24, 1998			
Rituxan (rituximab)	US 5 736 137 (Apr 7, 2015) US 5 677 180 (Oct 14, 2014)	Nov 26, 1997			
Stelara (ustekinumab)	US 6 902 734 (Sep 25, 2023)[e]	Sep 25, 2009			
Tysabri (natalizumab)	US 5 840 299 (Apr 27, 2017)[e] US 6 602 503 (Aug 5, 2020)	Nov 23, 2004			

Table taken from peer-review paper: Goode R, Feldman WB, Tu SS. Ancillary Product Patents to Extend Biologic Patent Life. JAMA. 2023;330(21):2117–2119. doi:10.1001/jama.2023.19547

In conclusion, the MFN policy would not be needed if a few reasonable patent reforms were executed that would unleash the power of competition that currently exists in Europe and around the world and would allow these biosimilars to be manufactured in the U.S.

Proposed Solution:

1. To address ancillary product patents by improving the flow of information between the patent office and the FDA, branded drug companies should be required to disclose to the patent office any corresponding submissions they have made to the FDA on the subject matter for which they plan to seek patent protection.

2. Additionally, a new defense to infringement should be enacted for generic and biosimilar manufacturers against patents where the branded drug company does not comply with this disclosure process. Hassan/Braun *Medication, Affordability, and Patent Integrity Act.*[29]

Issue # 3: Patent Manufacturing Waiver

U.S. law prohibits the commercial manufacturing of drugs while relevant patents are in force. This means that manufacturing biosimilars in the U.S. for export to other countries with more balanced patent rules is not advantageous for biosimilar and generic drug manufacturers. American manufacturing is further disadvantaged since in 2019 when the EU enacted a manufacturing waiver

[29] Senators Hassan, Braun and Representatives Kuster, Harshbarger Introduce Bipartisan Bill to Lower Prescription Drug Costs by Cracking Down on Abuses of Medication Patent Process

permitting the manufacture of biosimilar and generic drugs even prior to key patent expiry. The European SPC waiver allows manufacturers of generic and biosimilar medicines to produce and stockpile these medicines during the SPC period, balancing intellectual property rights with public health needs.

In Europe, a Supplementary Protection Certificate (SPC) extends the protection of patented medicines beyond the standard patent term, similar to a patent term extension (PTE) in the U.S. Both SPCs and PTEs can add up to five years of market exclusivity for pharmaceuticals, compensating for the time taken to obtain regulatory approval. The U.S. does not currently have an equivalent PTE waiver. For such a waiver to be effective in the U.S., it would need to permit manufacturing under secondary patents that expire later than the PTE.

The addition of the SPC waiver has made the EU more attractive to manufacturers who want to export drugs to countries with even less rigorous patent systems, like China or India, even before patent litigation is concluded in Europe and the U.S.[9]

The European SPC waiver is compatible with TRIPS because it waives infringement of such acts only under the SPC, i.e. following expiry of the basic patent. If the Administration were to consider a manufacturing waiver under secondary patents as well as the PTE, it would have to consider carefully how to make it compatible with TRIPS.

Proposed Solution:

The U.S. could enact a similar manufacturing waiver, that could sidestep trade agreements and apply to terminally disclaimed patents to bring manufacturing of complex generics and biosimilars back to the U.S.

Avoid Unintended Consequences

The cost differential and lack of manufacturing in the U.S. are primarily due to the U.S. patent office's failure to regulate branded patent misuse, not trade or manufacturing costs. To bring manufacturing to the U.S. and lower costs to be more in line with Europe, the above policies would achieve that goal through competition. Any use of tariffs that on biosimilars, would have the opposite effect of moving manufacturing to China and/or India or inflating prices in the U.S. by encouraging use of the branded product.

Policy Proposal Result:

Through increased competition from generic drugs and biosimilars, U.S. drug prices would align with the EU drug prices. This can be achieved by making small changes to the U.S. patent system rules, avoiding the unintended consequences of product-specific tariffs. This policy would allow these drugs to be manufactured in the U.S. and essentially eliminate the trade deficits between the prices paid by EU patients and payers and those in the U.S.

"Trade Deficits" in Practice

Patents	Allowed in U.S.?	Allowed in EU?	Allowed in China/India?	Approximate Impact
Terminal Disclaimers	Yes	No	No	~2.5 year market delay[10]
Ancillary product patents	Yes	No	No	~10 year market delay[11]
SPC manufacturing waiver	No	Yes	Not needed	Disallows specialty generics and biosimilars to onshore without delaying U.S. launces and net exporting to other markets with more balanced patent systems.[12]

Additional Solutions outside of Tariffs that Would Speed Competition to market and Further Erase Cost and Accessibility deficits:

- Rebalance incentives in the specialty drug pharmacy benefit market (PBM reform)
- Waive phase III clinical trials for biosimilars
- Discontinue the interchangeable designation for biosimilars

Medical Devices

Fresenius Kabi remains concerned about tariffs on medical devices for use in hospitals or blood collection facilities that are in or in danger of being in shortage. If possible, limit tariffs to medical devices that are sourced from countries where national security threats are proven, like China, and apply those tariffs commensurate with state funding and government financial support. As an example, there are critical products that are required for administration of fluids and medicine that are only made in the Dominican Republic. Any shortage of these products could potentially result in a catastrophic disruption in the ability of US hospitals to provide patient care.

Thank you for the opportunity to provide comments to the Commerce department in response to the section 232 investigation. We remain ready to assist the Trump Administration with policies that strengthen national security and balance the value that U.S. manufacturing of generic drugs and biosimilars bring to U.S. patients and health systems. For more information, please contact Sarah D'Orsie (sarah.dorsie@fresenius-kabi.com), SVP, Government Affairs and Policy, Fresenius Kabi, LLC.

Sincerely,

Arunesh Verma
President, Region U.S.
Fresenius Kabi USA, LLC